# A STUDY OF ORAL GLUCOSE TOLERANCE IN PULMONARY TUBERCULOSIS

**By**

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Under the guidance of

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would also like to thank my sister **Mrs Vijayalaxmi** and my brother-in law **Mrs Chanaveer also my best friends Mr.Sanjeev, Dr.Nitin , Dr Jayanth , Dr.Ambresh and Dr Vipin** for their assistance.

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**DR SANDEEP S KAVALIKAI**

# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| ‘p’ value | - | Probability value |
| A.D. | - | Anno Domini |
| AFB | - | Acid-fast bacilli |
| AIDS | - | Acquired immuno deficiency |
| ALT | - | Alanine aminotransferase |
| AST | - | Aspartate aminotransferase |
| ATP | - | Adenosine triphosphate |
| BACTEC | - | Bactenicin |
| BC | - | Before Christ |
| BCG | - | Bacille Calmette-Guérin |
| BMI | - | Body mass index |
| CBC | - | Complete blood count |
| CDC | - | Centers for Disease Control |
| CI | - | Confidence interval |
| CMI | - | Cell mediated immunity |
| CO2 | - | Carbon di-oxide |
| CT | - | Computed tomography |
| DBP | - | Diastolic blood pressure |
| DCCT | - | Diabetes Control and Complications Trial |
| DF | - | Degree of freedom |
| dL | - | Deciliter |
| DM | - | Diabetes mellitus |
| DNA | - | Deoxyribonucleic acid |
| DOTS | - | Directly observed treatment short course |

| | | |
|---|---|---|
| DTH | - | Delayed type hypersensitivity |
| ELISA | - | Enzyme linked immunoassay |
| ESRF | - | End-stage renal disease |
| FPG | - | Fasting plasma glucose |
| g | - | Gram |
| GDM | - | Gestational diabetes mellitus |
| GTT | - | Glucose tolerance test |
| h | - | Hour |
| HIV | - | Human immunodeficiency virus |
| ICMR | - | Indian Council of Medical Research |
| IDDM | - | Insulin-dependent diabetes mellitus |
| IDF | - | International Diabetes Federation |
| IDF | - | International Diabetes Federation |
| IFG | - | Impaired fasting glucose |
| IGRA | - | Interferon-gamma release assay |
| IGT | - | Impaired glucose tolerance |
| IGT | - | Impaired glucose tolerance |
| INH | - | Isoniazid |
| IP | - | In patient |
| L | - | Litre |
| LAM | - | Lipoarobinomannan |
| MAC | - | Mycobacterium avium complex |
| MDR | - | Multi drug resistant |
| mg | - | Milligram |
| mmol | - | Milli mole |

| | | |
|---|---|---|
| MODS | - | Microscopic-observation drug susceptibility |
| MODY | - | Maturity onset diabetes of young |
| MRI | - | Magnetic resonance imaging |
| n | - | Total number |
| NIDDM | - | Non insulin-dependent diabetes mellitus |
| OGT | - | Oral Glucose Tolerance |
| OGTT | - | Oral glucose tolerance test |
| PCR | - | Polymerase chain reaction |
| PODIS | - | Prevalence of Diabetes in India Study |
| PPD | - | Purified protein derivative |
| PTB | - | Pulmonary tuberculosis |
| QFT-G | - | QuantiFERON-TB Gold |
| QFT-GIT | - | QuantiFERON-TB Gold In-Tube |
| RIF | - | Rifampicin |
| RNA | - | Ribonucleic acid |
| RNTCP | - | Revised National Tuberculosis Control Program |
| SBP | - | Systolic blood pressure |
| SD | - | Standard deviation |
| TB | - | Tuberculosis |
| TLA | - | Thin-layer agar |
| WHO | - | World Health Organization |
| *x2* | - | Chi-square |
| XDR | - | Xtensively drug resistant |

# ABSTRACT

**Background and objectives**

The relation of pulmonary tuberculosis and development of altered OGT are not well documented and very few studies have reported that the incidence of diabetes mellitus in patients with pulmonary tuberculosis. The present study was aimed to find the incidence of glucose intolerance in patients with pulmonary tuberculosis.

**Methodology**

This one year cross sectional study was conducted in the Department of Medicine , Shri B M Patil Medical College , Vijayapur on patients with pulmonary tuberculosis. A total of 75 patients with patients with positive sputum smear for acid fast bacilli or chest x-ray features suggestive of pulmonary tuberculosis aged more than 30 years and less than 65 years were selected for the study.

**Results**

The results showed majority of the patients were males (84%) with maleto female ratio of 5.25:1. . The most commonest age group was 41-50 years (25.33%) followed by age >60 years (21.33%). The commonest presentation of pulmonary tuberculosis was cough and expectoration of sputum (100% each)followed by loss of appetite (96.67% ) followed by fever(76%). AFB findings showed +++ in 29.33% patients. On chest x-ray almost 60% of the patients had cavitatory lesions with infiltration . In 18.67% and 16% of patients fibrotic changes and cavitatory lesions without infiltration were noted.

**Conclusion and interpretation**

This study of 75 cases showed overall incidence of impaired glucose tolerance as 17.33% in patients with pulmonary tuberculosis. Among 82.67% patients GTT was normal (Fasting < 110 mg/dL and 2 hours < 140 mg/dL). In 13.33% of patients

impaired glucose tolerance (Fasting < 126 mg/dL and 2 hours> 140 mg/dL) was recorded and among 4% patients diabetes mellitus (Fasting >126 mg/dL and 2 hours > 200 mg/dL) was diagnosed. No statistically significant association of sex, age and chest X-ray findings was seen in patients with pulmonary tuberculosis and diabetes mellitus.

**Key words**

Diabetes mellitus; Glucose tolerance test; Impaired glucose tolerance; Pulmonary tuberculosis

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# INTRODUCTION

**DEFINITION :**

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis.

It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The disease spreads by droplet infection when people suffering from pulmonary TB expel bacteria, for example by coughing. In general, a relatively small proportion of people infected with Mycobacterium tuberculosis will go on to develop TB disease; however, the probability of developing TB is much higher among people infected with Human immunodeficiency virus (HIV). TB is also more common among men than women, and affects mostly adults in the economically productive age groups; around two-thirds of cases are estimated to occur among people aged 15–59 years.[1]

Despite dramatic improvements in public health and medical care, Mycobacterium tuberculosis remains as much of a threat in the 21st century as it was when first identified as a pathogen by Koch in 1882. Tuberculosis is a major cause of morbidity and mortality throughout the world. One-third of the world's population is infected with the TB bacillus. The World Health Organization (WHO) cites TB as the single most important fatal infection, with around 8.8 million new cases and 1.4 million deaths per year, 95% in developing countries.[2]

Tuberculosis is a major public health problem in India. In 2010, there were 2 to 2.5 million new cases accounting for one quarter of the total cases worldwide.1 The impact of TB can be devastating, especially in developing countries suffering from high burdens of both TB and HIV infections. Tuberculosis, is a major barrier to economic development of the country costing India about Rs. 12,000 crore a year.[3]

The issue of increasing drug resistant strains has lead to increase in TB incidence over the last decade, in both developing and developed countries. Drug resistance in TB is a matter of great concern for TB control programs since there is no cure for some multidrug-resistant strains of M. tuberculosis. There is concern that these strains could spread around the world, stressing the need for additional control measures, such as new diagnostic methods, better drugs for treatment, and a more effective vaccine. Multi-drug resistant MDR-TB, defined as resistance to at least rifampicin (RIF) and isoniazid (INH), is a compounding factor for the control of the disease, since patients harboring MDR strains of M. tuberculosis need to be entered into alternative treatment regimens involving second-line drugs that are more costly, more toxic, and less effective. Moreover, the problem of extensively drug resistant (XDR) strains has recently been introduced.[4]

It has been estimated that India and China account for nearly 50% of the global burden of MDR-TB cases. Approximately 5% of all pulmonary TB cases in India may be MDR. MDR rates are low in new, untreated cases. The incidence in such cases ranges from 1 to 5% (mostly <3%) in different parts of India.[5-7] However, during the last decade, there has been an increase in reported incidences of drug resistance in Category II cases, particularly among those treated irregularly, or with incorrect regimens and doses. In such cases, the incidence of MDR-TB varies from 12-17%.[7]

In recent years, strong evidence has been gathered to confirm a link between TB and yet another disease diabetes mellitus. That link had been suspected for centuries.[8]

Diabetes Mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[9]

Diabetes mellitus (DM) is a chronic and potentially disabling disease which is reaching an epidemic proportion in many parts of the world. It is a major and growing threat to global public health. The biggest impact of the disease is on adults of working age; particularly in developing countries. The vast majority of cases of the diabetes fall into two broad categories: those having little or no endogenous insulin secretory capacity (IDDM or type 1 DM) and those who retain endogenous insulin secretory capacity but have a combination of resistance to insulin action and an inadequate compensatory insulin secretory response (NIDDM, or Type 2 DM).[9,10]

Centers for Disease Control and Prevention (CDC) report in 2011 estimated that nearly 26 million Americans have diabetes.[11] Type 2 diabetes mellitus (DM) accounts for more than 90% of the diabetic population worldwide. Additionally, an estimated 79 million Americans have pre-diabetes. Rates of diabetes are increasing worldwide. The International Diabetes Federation predicts that the number of people living with diabetes will to rise from 366 million in 2011 to 552 million by 2030.[12] The top 10 countries in number of people with diabetes are currently India, China, the United States, Indonesia, Japan, Pakistan, Russia, Brazil, Italy, and Bangladesh. The prevalence of diabetes and its adverse health effects have risen more rapidly in South Asia than in any other region of the world.[13]

Thirty years ago, the prevalence of diabetes in India based on the Indian Council of Medical Research (ICMR) multicentric survey[14] was around two percent in urban India and one percent in rural India. In just three decades, these prevalence rates have shot up to 12 to 16% in urban India and three to eight percent in rural India,

in adults over 20 years of age. These represents a 600 to 800% increase in prevalence rates of diabetes something which is unparallel in any Western nation. Indeed, India is now referred to as the "Diabetic Capital" of the world.

Further, DM is associated with several complications. The complications of diabetes mellitus include retinopathy, nephropathy, and neuropathy (both peripheral and autonomic). The risk for atherosclerotic vascular disease is also increased in persons with DM. The risk for microvascular and neuropathic complications is related to both duration of diabetes and the severity of hyperglycemia; the increased risk for vascular disease actually antedates the onset of hyperglycemia to the degree associated with diabetes mellitus.[9]

Several recent publications have described the association between diabetes and TB, specifically the increased prevalence of active TB among patients with diabetes and the poorer treatment outcomes in these patients when compared to those without diabetes.[15,16] The link between these two diseases may become even more meaningful in coming years, as the prevalence of obesity and diabetes are expected to rise dramatically in the resource-poor areas where TB thrives.[17]

The evidence that diabetic patient have an increased risk of developing pulmonary tuberculosis is a well-known. Unlike patients of diabetes developing tuberculosis where the disease tends to be extensive and bilateral. What makes the diagnosis of the combination difficult is the fact that the symptoms of the complicating disease are masked by the co-existing disease.[18]

However, the converse relationship that the patients with tuberculosis have higher incidence of impaired Oral Glucose Tolerance (OGT) was less widely accepted till 1950. Despite, it is now accepted that altered OGT is observed in pulmonary tuberculosis patients, the relation of pulmonary tuberculosis and development of

altered OGT are not well documented and very few studies have reported that the incidence of diabetes mellitus is predated in pulmonary tuberculosis. With this hypothesis the present study was undertaken to assess the OGT and its clinical profile in patients with pulmonary tuberculosis.

# NEED FOR STUDY

People with diabetes are at higher risk of developing tuberculosis (TB) than those without diabetes. The growing prevalence of diabetes poses a challenge for TB control as uncontrolled diabetes leads to a greater risk of developing TB. This suggests that increasing diabetes prevalence could make attainment of the Millennium Development Goals on tuberculosis more difficult to achieve[1].

People with a weak immune system, as a result of chronic diseases such as diabetes are at a higher risk of progressing from latent to active TB. People with diabetes have a 2-3 times higher risk of TB compared to people without diabetes. About 10% of TB cases globally are linked to diabetes all people with TB should be screened for diabetes screening for TB in people with diabetes should be considered, particularly in settings with high TB prevalence. People with diabetes who are diagnosed with TB have a high risk of death during TB treatment and of TB relapse after treatment. WHO-recommended treatments should be rigorously implemented for people with TB/diabetes[1].

Several theories have been put forwarded to explain why tuberculosis patients develop glucose intolerance. Bloom (1969) suggested that occult glucose tolerance predisposes to diabetes. Zack et al (1973) suggested that glucose intolerance was not merely a reaction to acute tuberculosis infection but rather a pre-diabetic state. Hadden (1967) suggested malnutrition in TB as a possible cause. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon and cortisol which raise the blood sugar level (Guptan et al, 2000). Roychoudhary and Sen(1980) suggested tuberculosis of pancreas as the possible cause. Similarly higher incidence of chronic calcific pancreatitis occur in patients of diabetes and pulmonary tuberculosis leading to absolute and relative insulin deficiency state (Mollentz et al,

1990). Clinical and subclinical hypoadrenalism has been described in these patients (Guptan and Shah, 2000). Plasma levels of IL-1 and TNF-alpa are also raised in severe illness, which can stimulate anti-insulin responses. Age co-existing illness and alcoholism also influence the host response (Fernandez et al, 1997) [19].

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The disease spreads by droplet infection when people suffering from pulmonary TB expel bacteria, for example by coughing[20].

Diabetes Mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[21]

The relation of pulmonary tuberculosis and development of altered OGT are not well documented and very few studies have reported that the incidence of diabetes mellitus in patients with pulmonary tuberculosis. Hence this study is aimed to find the incidence of OGT and its clinical profile in patients with pulmonary tuberculosis.

Tuberculosis is most commonly transmitted by inhalation of infected droplet nuclei which are discharged in the air when a patient with untreated TB coughs or sneezes. TB disease usually affects the lungs but can involve any part of the body. pulmonary TB which affects the lungs is an infectious form disease extra-pulmonary TB can affect the lymph nodes. pleura, bones and joints the genito-urinary tract, the nervous system (meningitis, tuberculoma), abdominal TB (intestines, mesentry, solid organs), skin, etc. all those who get infected do not necessarily develop TB disease. the life time risk of breaking down to disease among those infected with TB is 10 - 15 %, which gets increased to 10 % per year amongst those co-infected with HIV. other

determinants such as diabetes mellitus, smoking, tobacco products, alcohol abuse and malnutrition also increase the risk of progression from infection to TB disease.[22]

# OBJECTIVE OF THE STUDY

The objective of the present study was to assess oral glucose tolerance in pulmonary tuberculosis.

# TUBERCULOSIS

## HISTORY[23]

Consumption, Phthisis, Scrofula, Pott's disease, and the White Plague are all terms used to refer to tuberculosis throughout history. Over time, the various cultures of the world gave the illness different names: Yaksma (India), Phthisis (Greek), Consumption (Latin) and Chaky Oncay (Incan), each of which make reference to the "drying" or "consuming" affect of the illness, cachexia. Its high mortality rate among middle-aged adults and the surge of romanticism, which stressed feeling over reason, caused many to refer to the disease as the "romantic disease."

### Tuberculosis in ancient times[23]

The first evidence of the infection in humans was found in the neolithic bone remains that show evidence of spinal tuberculosis. Signs of the disease have also been found in Egyptian mummies dated between 3000 and 2400 BC. The term phthisis first appeared in Greek literature around 460 BC. Hippocrates identified the illness as the most common cause of illness in his time, stated that it typically affected individuals between 18 and 35 and was nearly always fatal, Galen, the most eminent Greek physician after Hippocrates, defined phthisis as the "ulceration of the lungs, thorax or throat, accompanied by a cough, fever, and consumption of the body by pus."

The first references to tuberculosis in Asian civilization is found in the Vedas. The oldest of them (Rigveda, 1500 BC) calls the disease yaksma. The Sushruta Samhita, written around 600 BC, recommends that the disease be treated with breast milk, various meats, alcohol and rest. The first mention of tuberculosis in Chinese literature appears in a medical text written by Emperor Shennong of China (2700 BC) in which he describes xulao bing (weak consumptive disease).

**Renaissance and after (1400-1800)**[23]

With the spread of Christianity, the touch of the sovereign of England or France, could cure diseases due to the divine right of sovereigns. King Henry IV of France usually performed the rite once a week, after taking communion.

**Seventeenth and eighteenth centuries**[23]

In the book ‘Systematik de speziellen Pathologie und Therapie’, J. L. Schönlein, Professor of Medicine in Zurich, proposed that the word "tuberculosis" be used to describe the affliction of tubercles.

**Nineteenth century**[23]

It was during this century that tuberculosis was dubbed the White Plague, mal de vivir, and mal du siècle. It was seen as a "romantic disease." Suffering from tuberculosis was thought to bestow upon the sufferer heightened sensitivity.

**Scientific advances**[23]

One of the most important physicians dedicated to the study of pthisisology was René Laennec, who died from the disease at the age of 45, after contracting tuberculosis while studying contagious patients and infected bodies. Laennec invented the stethoscope which he used to corroborate his auscultatory findings. In 1869, Jean Antoine Villemin demonstrated that the disease was indeed contagious, conducting an experiment in which tuberculous matter from human cadavers was injected into laboratory rabbits, who then became infected.

On 24 March 1882, Robert Koch revealed the disease was caused by an infectious agent. In 1895, Wilhelm Roentgen discovered the X-ray, which allowed physicians to diagnose and track the progression of the disease, in 1890 Koch developed tuberculin, a purified protein derivative (PPD) of the bacteria. It proved to

be an ineffective means of immunization but in 1908, Charles Mantoux found it was an effective intradermic test for diagnosing tuberculosis.

**Twentieth century**[23]

In 1902, the International Conference on Tuberculosis convened in Berlin. National campaigns spread across Europe and the United States to tamp down on the continued prevalence of tuberculosis.

After the establishment in the 1880s that the disease was contagious, tuberculosis was made a notifiable disease in Britain; there were campaigns to stop spitting in public places, and the infected poor were pressured to enter sanatoria that resembled prisons; the sanatoria for the middle and upper classes offered excellent care and constant medical attention.

**Vaccines**[23]

The first genuine success in immunizing against tuberculosis was developed from attenuated bovine-strain tuberculosis by Albert Calmette and Camille Guérin in 1906. It was called Bacille Calmette-Guérin (BCG). The BCG vaccine was first used on humans in 1921 in France, but it was not until after World War II that BCG received widespread acceptance in the United States, Great Britain, and Germany.

**Treatments**[23]

As the century progressed, some surgical interventions, including the pneumothorax or plombage technique - collapsing an infected lung to "rest" were used to treat tuberculosis. In 1696, Giorgio Baglivi reported a general improvement in tuberculosis sufferers after they received sword wounds to the chest. F. H. Ramage induced the first successful therapeutic pneumothorax in 1834, and reported subsequently the patient was cured. The search for a medicinal cure, however, continued in earnest.

In 1944 Albert Schatz, Elizabeth Bugie, and Selman Waksman isolated Streptomyces griseus or streptomycin, the first antibiotic and first antibacterial agent effective against M. tuberculosis. Isoniazid was the first oral mycobactericidal drug. The advent of Rifampin in the 1970s hastened recovery times, and significantly reduced the number of tuberculosis cases until the 1980s.

**Tuberculosis resurgence**[23]

Hopes that the disease could be completely eliminated were dashed in the 1980s with the rise of drug-resistant strains. Due to the elimination of public health facilities in New York and the emergence of HIV, there was a resurgence of tuberculosis in the late 1980s. The number of patients failing to complete their course of drugs is high.

In response to the resurgence of tuberculosis, the WHO issued a declaration of a global health emergency in 1993. Every year, nearly half a million new cases of multidrug-resistant tuberculosis (MDR-TB) are estimated to occur worldwide.

**EPIDEMIOLOGY:**

TB occurs in every part of the world. About one third of the world's population is infected with tuberculosis. It is a treatable and curable disease that kills almost 2 million people every year. It is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent.2 Effective drugs to treat and cure the disease have been available for more than 50 years, yet every 15 seconds, someone in the world dies from TB. Even more alarming: a person is newly infected with M. tuberculosis every second of every day. Left untreated, a person with active TB will infect an average of 10 to 15 other people every year.[4] The number of new cases that occur each year also continues to grow.

**Incidence**[24]

- ✓ Globally, an estimated 9.27 million new cases (15% amongst HIV +ve) occurred in 2007; mostly in Asia (55%) and Africa (31%).
- ✓ The maximum number of cases occurred in India (2.0 million), China (1.3 million), Indonesia (0.53 million), Nigeria (0.46 million) and South Africa (0.46 million).
- ✓ There were about 1.75 million TB deaths; over 25% occurred in HIV positive persons.
- ✓ The incidence decreased marginally from 142 per 100 000 in 2004 to 139 per 100,000 population in 2007; prevalence and mortality rates also falling globally in all six WHO regions.
- ✓ Tuberculosis was the most common cause of death among people living with HIV/AIDS in 2007. HIV-positive people are about 20 to 37 times more likely to develop tuberculosis.
- ✓ There were an estimated 0.5 million cases of MDR -TB in 2007 with maximum number from India (131,000). Extensively drug resistant tuberculosis (XDR -TB) has been reported from 55 countries.
- ✓ In 2007, 5.5 million tuberculosis cases (2.6 million smear-positive) were notified by Directly Observed Treatment – Short Course (DOTS) Programs (99% of total case notifications). The case detection rate of new smear-positive cases under DOTS was 63%; seven percent short of the target of 70% or more for 2005.
- ✓ Globally, the rate of treatment success for new smear-positive cases treated in DOTS programs in 2006 reached the target of 85%.

- ✓ In 2009, a total of US$ 3.0 billion was available for tuberculosis control in 94 countries which account for 93% of the world's tuberculosis cases as against the requirement of US$ 4.2 billion. Most of the extra funding required was for MDR -TB diagnosis and treatment in India and China, and for DOTS and collaborative tuberculosis and/or HIV activities in Africa.

**Global TB disease burden**

Following neglect of disease during the 1980s[25,26] TB control has been high on international agenda since 1990s. In 1993, WHO declared TB a global public health emergency.

WHO has published a global report on TB every year since 1997. The 2011 edition of WHOs annual global TB report – is 16th in the series.[1]

- ✓ Global incidence estimated at 8.8 million cases.
- ✓ Most of them occurred in Asia (59%) and Africa (26%)
- ✓ The 22 high tuberculosis burden countries that have been given highest priority at the global level since 2000 accounted for 81% of all estimated cases worldwide.
- ✓ The five countries with the largest number of incident cases in 2010 were India (2.0 –2.5 million), China (0.9 –1.2 million), South Africa, Indonesia and Pakistan.
- ✓ India and China combined accounted for 38% of all cases.
- ✓ Estimated 12.0 million prevalent cases of TB.
- ✓ Of the 8.8 million incident cases, 1.0 – 1.2 million (12–14%) were among people living with HIV.
- ✓ The proportion of TB cases co-infected with HIV is highest in countries in the African Region( accounted for 82% ).

- ✓ Approximately 1.4 million deaths (1.1 million cases in HIV negative cases of TB and an additional 0.3 million in HIV positive cases of TB)

**Other notable findings[2]**

- ✓ Tuberculosis mostly affects young adults, in their most productive years. However, all age groups are at risk.
- ✓ Over 95% of cases and deaths are in developing countries.
- ✓ It is among the top three causes of death for women aged 15 to 44.
- ✓ About half a million children (0-14 years) fell ill with TB, and 64 000(a range of 58 000 to 71 000) children died from the disease in 2010.
- ✓ In 2009, there were about 10 million orphan children as a result of TB deaths among parents.
- ✓ People infected with TB have a lifetime risk of TB of 10%.
- ✓ Persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk.
- ✓ At least one-third of the 34 million people living with HIV worldwide are infected with TB bacteria, although not yet ill with active TB. People living with HIV and infected with TB are 21 to 34 times more likely to develop active TB disease than people without HIV.

**Burden of TB**

India accounts for one of the global TB burden i.e.2.2 million out of 9.6 million new cases annually in India. more than 40 % of population is infected ( prevalence of infection) with Mycobacterium tuberculosis. it is estimated that there are 2.5 million prevalence cases of all forms of TB disease. it is also estimated that about 2.2 lakhs people die due to TB anually (mortality). the table below shows the

estimated figures for TB burden globally and for India provided by WHO for the year 2014.

| | **Incidence** | **Prevalence** | **Mortality** |
|---|---|---|---|
| **Global** | 9.6 million (176/lakh/year) | 13 million (227/lakh/year) | 1.1 million (21/lakh/year |
| **India** | 2.2 million (167/lakh/year) | 2.5 million (195/lakh/year) | 2.2 lakh (17/lakh/year) |

TB now ranks alongside HIV as leading cause of death worldwide. TB kills more adults in India than any other infectious disease,

In India, every day :

- ✓ More than 6000 develop TB disease.
- ✓ More than 600 people die of TB (i.e. 2 death every 5 minutes).

India has highest burden of both TB and second highest HIV associated TB based on estimates reported in global TB report 2015. An estimated 71,000 cases of MDR-TB emerge annually from the notified cases of pulmonary TB in India. based on sub-national DR surveys carried out in three states of India, -3 % among new TB cases and 12 % - 17 % among previously treated TB cases have MDR-TB. India bears second highest number of estimated HIV associated TB in world. An estimated 1.1 lack HIV associated TB occurred in 2014 and 31,000 estimated number of patients died among them.[22]

**TB Burden in India**

Though India is the second-most populous country in the world, India has more new TB cases annually than any other country.[27] In 2010 of estimated 8.8 million cases India had 2.0-2.5 million cases accounting for one quarter (26%) of cases worldwide.1 It is estimated that about 40% of Indian population is infected with TB bacillus.[2]

**Estimates of TB burden: WHO global report - 2014 [Rates/ 1 Lakh population]**[1]

| Variables | World | India |
|---|---|---|
| Incidence | 128 | 185 |
| Prevalence(Including HIV) | 178 | 256 |
| Mortality(Including HIV) | 15 | 26 |

**ETIOLOGY AND PATHOPHYSIOLOGY**[9] :

Tuberculosis is a constitutional disease caused by infection with Mycobacterium tuberculosis, characterized by the production of tubercles in the internal organs, especially in the lungs, where it constitutes the most common variety of pulmonary phthisis.

If properly treated it is curable in virtually all the cases, if untreated the disease may be fatal within five years in more than half the cases. Pulmonary tuberculosis is the one involving the lung with progressive wasting of the body.

Mycobacterium belongs to the family Mycobacteriaceae and order Actinomycetales. They are rod shaped, non-spore forming thin aerobic bacteria measuring 0.5 μm by 3 μm. They do not stain by gram method of stain, faintly gram positive, but once stained cannot be decolorized by acid alcohol hence classified as

acid fast bacilli-acid fastness is due to the organisms' high content of mycolic acids, long chain cross linked fatty acids and other cell wall lipids.

The interaction of M. tuberculosis with human host begins when droplet nuclei (less than 10 μm in diameter) which are aerosolized by coughing, sneezing or speaking from an infectious patient are inhaled. While the majority of the inhaled bacilli are trapped in the upper airways and expelled by ciliated mucosal cells, a fraction reaches the alveoli.

The risk of developing the disease after being infected depends on factors like individual's innate susceptibility to the disease and level of cell mediated immunity. Clinical illness directly following infection is classified as primary tuberculosis. Among the infected individuals the incidence is highest during late adolescence and early adulthood peaks between 25 to 34 years of age. In children and in persons with impaired immunity (for example, malnutrition or HIV infection) the disease may progress rapidly to clinical illness.

**Risk Factors for active tuberculosis among persons who have been infected with tubercle bacilli.[9]**

| Risk Factor | Relative risk/ Odds |
|---|---|
| Recent Infection (less than one year) | 12.9 |
| Fibrotic lesion spontaneously healed | 2.30 |
| Comorbidity | |
| HIV Infection | 100 |
| Silicosis | 30 |
| Chronic renal failure / Hemodialysis | 10-25 |
| Diabetes | 2-4 |
| Intravenous drug use | 2-4 |
| Immunosuppressant treatment | 10 |
| Gastrectomy | 2-5 |
| Jejunoleal bypass | 30-60 |
| Post transplantation period | 20-70 |
| Malnutrition and underweight | 2 |

In the initial stage of host bacterium interaction, either the host macrophages contain bacillary multiplication by producing proteolytic enzymes and cytokines or the bacilli begin to multiply. If the bacilli multiply, their growth quickly kills the macrophages which lyse. The balance between the bactericidal activity of the macrophage and the number and virulence of the bacilli determines the events following phagocytosis.

After about two to four weeks after infection, two additional host responses to M. tuberculosis develop a tissue damaging response and a macrophage activating response.

The tissue damaging response is result of delayed type hypersensitivity (DTH) reaction to various bacillary antigens; it destroys non activated macrophages. The macrophage activating response is a well mediated phenomenon resulting in activation of macrophages that ingest and kill the bacilli.

With the development of specific immunity the accumulation of large number of activated macrophages at the primary sites, granulomatous lesions are formed. These lesions are comprised of lymphocytes, epitheloid cells and giant cells. Initially the newly developed tissue damaging response is the only event capable of limiting mycobacterial activity. This not only destroys the macrophages but also produces early solid necrosis in the centre of the tubercle of these lesions, some may heal by fibrous calcification while others may undergo further evolution where cell mediated immunity is critical at this early stage.

In the majority of infected individuals, local macrophages are activated when bacillary antigens processed by macrophages stimulate T lymphocytes to release a variety of lymphokines.

In a minority of cases the macrophage activating response is weak and mycobacterial growth can be inhibited only by intensified DTH reaction which leads to tissue destruction. Bronchial walls and blood vessels may be invaded and destroyed leading to spread into the airways and dissemination through blood vessels.Hematogenous dissemination may result leading to military tuberculosis or tuberculous meningitis.

**Classification of tuberculosis[9]**:

1. Pulmonary tuberculosis
   - ✓ Primary disease
   - ✓ Post primary (Secondary)
2. Extrapulmonary tuberculosis
3. HIV associated tuberculosis

**Pulmonary tuberculosis**

**Primary disease**

Results from an initial infection with tubercle bacilli. Common in persons with impaired immunity (for example, malnutrition and HIV infection) and may progress rapidly to clinical illness. The lesion forming after the infection is usually peripheral accompanied by hilar or paratracheal lymphadenopathy called Ghon's lesion.

**Post Primary (secondary)**

Results from endogenous reactivation of latent infection, localized to apical and posterior segments of lung. May lead to cavitation or become fibrotic and undergo calcification and may undergo spontaneous remission or proceed along a chronic debilitating course.

**Extra-pulmonary tuberculosis**

Commonly involve the lymphnodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, pericardium. It occurs due to hematogenous spread of infection.

**Human immunodeficiency virus associated tuberculosis**

Tuberculosis is an important opportunistic disease among HIV infected persons, worldwide. A person with skin test documented M. tuberculosis infection

who acquires HIV infection has three to fifteen percent annual risk of developing active tuberculosis.

Tuberculosis can appear at any stage of HIV infection and its presentation varies with the stage. When cell mediated immunity is only partially compromised, pulmonary tuberculosis present as a typical pattern of upper lobe infiltrates and cavitation, without significant lymphadenopathy or pleural effusion.

In late stages of HIV infection a primary tuberculosis like pattern with diffuse interstitial or miliary infiltrates, little or no cavitation and intrathoracic lymphadenopathy is more common.

Overall, sputum smears may be positive less frequently among tuberculosis patients with HIV infection than among those without; thus the diagnosis of tuberculosis may be unusually difficult, especially in view of the variety of HIV related pulmonary conditions mimicking tuberculosis.

Extrapulmonary tuberculosis is common among HIV infected patients. The most common forms are lymphatic, disseminated pleural and pericardial.

The diagnosis may be difficult not only because of increased frequency of sputum negativity but because of atypical radiographic findings, a lack of classic granuloma formation and negative results in PPD skin tests.

**Natural history of tuberculosis**

Tuberculosis can affect any organ in the body. Pulmonary tuberculosis is the most frequent site of involvement; extrapulmonary tuberculosis is less frequent. Only pulmonary tuberculosis is infectious.[28]

TB is a disease with an inter-human transmission. Tuberculous bacilli are spread out by infected patients (Flugge's droplets - small aerodynamic particles) coughing, sneezing, or speaking, and they can be inhaled by another individual in

close contact. The inhalation of these sprays, presents a risk of infection. These particles can also remain in the air and play the role of reservoir.[29] Once the infectious particles are inhaled, only those with two or three bacilli can reach the bronchial cells, the largest ones are stopped upstream and eliminated.[30] The success of such infection and the development of the pulmonary form of TB depend on four successive stages: bacilli phagocytosis, intracellular multiplication, the stationary stage, and the pulmonary form of TB.[29]

i. **Bacilli phagocytosis** This step takes place in first week following inhalation, and it depends on two main factors: the bacillus virulence and the bactericidic activity of the macrophage. In general, the phagocytosed bacteria are destroyed by the alveolar macrophages and the infection is stopped at this stage, otherwise they begin an intracellular cycle of multiplication.[31]

ii. **Intracellular multiplication** This second stage occurs between the 7th and the 21st day. It corresponds to intracellular bacilli multiplication in the macrophage alveoli and is also called the symbiotic stage. They are released after cellular lysis, and can thus infect other circulating macrophages and continue their multiplication. At the end of this stage, a huge number of macrophages and bacilli are concentrated at the level of early pulmonary lesions.[31]

iii. **Stationary stage:** Following the induction of the immune response of the host, particularly cell-mediated immunity bacterial growth becomes stationary.[32] This is the third stage of the infection called primary infection. Because of a delayed-type hypersensitivity, the macrophages in which bacilli multiply are destroyed. Bacterial toxins and cellular products are released, and this leads to the formation of solid caseous necrosis,[33] where a pseudo-

equilibrium settles between inactivated and mature macrophages. At this stage, either the number of infected cells in the caseous center decreases if the released bacilli are phagocyted by the mature macrophages or it increases if the bacilli multiply in the inactivated macrophages. Thus, the progression of the disease depends on which macrophage type prevails.[34] At this stage, bacilli may become dormant and never induce TB at all, which is referred to as a latent infection that is detected only by a positive tuberculin skin test; or the latent organisms can eventually begin to grow, with clinical disease, known as TB reactivation.

iv. **Pulmonary form of TB (PTB):** When the equilibrium between the inactivated and mature macrophages is broken, the infection reaches the last stage, the disease, PTB. This step is characterized by the liquefaction of the caseous center, leading to the formation of a cavity detected by pulmonary radiography. The liquefied material present in this cavity constitutes an excellent growth media for the bacteria, and macrophages do not survive in this environment. At this stage of the disease, the person becomes contagious by releasing the bacilli into the air. Furthermore, without treatment, this individual can develop a chronic TB, presumably leading to death.[29]

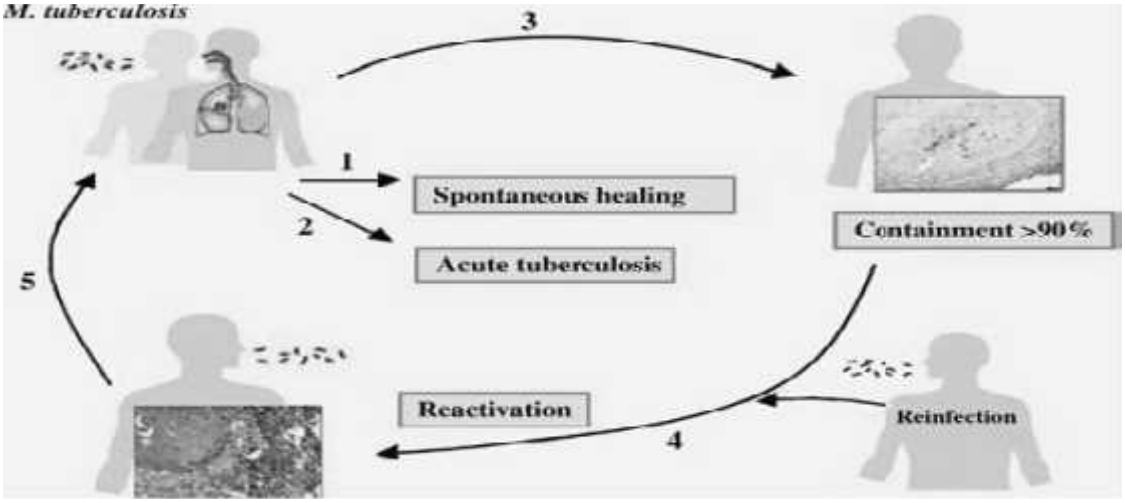
These different stages can evolve into different outcomes: spontaneous healing, acute tuberculosis, latent infection, and reactivation or re-infection.[29]

**Factors that increase the likelihood of becoming infected with tuberculosis**[28]

a) Increases in the intensity and/or duration of exposure.
b) Overcrowding, in buildings that are poorly ventilated.

c) Conditions leading to immune deficiency such as HIV infection, malnutrition, diabetes, or long-term treatment with corticosteroids or immunosuppressive medications.

**Mycobacterium tuberculosis enters the host within inhaled droplets.**




Different outcomes are possible

- ✓ Immediate eradication of MTB by the pulmonary immune system.
- ✓ Infection transforms into active tuberculosis.
- ✓ Infection does not transform into disease because MTB is contained inside granulomas.
- ✓ After a latency phase, MTB can become active after either an endogenous reactivation or an exogenous re-infection or both.
- ✓ At this stage, there is dissemination and transmission of MTB.[35]

**Virulence Mechanisms**

The basis for M. tuberculosis virulence is largely unknown. Cell wall components such as LAM have been implicated in binding to alveolar macrophages, utilizing surface fibronectin, mannose, or complement receptors. Once inside, multiple factors contribute to survival and continued multiplication. A number of genes have been identified that are linked to virulence by enhancing survival in the

macrophage or by influencing the physical and chemical conditions(low pH, high lactic acid, high CO2) present in developing lesions, but their function remains unknown. Mycolic acids, sulfolipids, LAM, and proteins have been shown to disrupt phagosome–lysosome interactions and interfere with oxidative killing. LAM has also been shown to modulate cytokine production and down-regulate other aspects of T-cell function including antigen presentation.[36]

**IMMUNITY**

Humans generally have a high innate immunity to development of disease. This was tragically illustrated in the Lubeck disaster of 1926 where infants were administered M. tuberculosis instead of an intended vaccine strain. Despite the large dose, only 76 of 249 died and most of the others developed only minor lesions.[36]

Approximately 10% of immunocompetent persons infected with M. tuberculosis will develop active disease any time in their life. There is epidemiologic and historic evidence for differences in the immunity.[36]

DTH to tuberculoprotein and CMI to M. tuberculosis develop 2 to 6 weeks after primary infection. The subsequent course of the infection depends on the balance between these two defensive mechanisms.[36]

DTH, through the mediation of natural killer cells, destroys the inactivated macrophages as well as the surrounding tissues, releasing still viable mycobacteria into an area of necrosis unsuitable for bacterial multiplication.[36]

CMI develops when competent T lymphocytes recognize mycobacterial antigen complexes on the surface of M. tuberculosis– containing macrophages. In the presence of macrophage-produced interleukin-1, the activated lymphocytes respond to the presented antigens with the elaboration of several cytokines. Some of these proteins attract circulating monocytes. Others, including interferon and possibly

tumor necrosis factor, activate local tissue macrophages and the recruited monocytes to enhanced destruction of ingested mycobacteria, resulting in a slowing or discontinuation of intracellular bacterial growth. Nitrous oxide or other reactive nitrogen intermediates probably mediate the destruction of the mycobacteria. Another cytokine, interleukin- 2, induces clonal expansion of the activated lymphocytes, thus amplifying the host's immunologic response. Still others stimulate accumulation of fibroblasts and deposition of collagen, which help wall off the area of infection and prevent further dissemination.[36]

Acquired immunity is cell mediated but incomplete. Both helper–inducer (CD4+) and cytotoxic (CD8+) T lymphocytes are involved. Two to three weeks after infection, macrophages are activated at the site of infection by a network of pro- and anti-inflammatory cytokines and chemokines from antigen-stimulated CD4+ T lymphocytes, macrophages, and dendritic cells. This interaction between M. tuberculosis and the host is what eventually limits its multiplication and spread. Cytotoxic T cells release bacilli from inactivated phagocytic cells and allow them to be ingested and handled by the activated macrophages. The concomitant DTH to tuberculoprotein plays an important part in immunity to reinfection by mobilizing immune cells and macrophages to the site of deposition of tubercle bacilli. In the past, it was believed that re-infection from external sources was extremely rare, but it is now clear that loss of hypersensitivity and CMI can occur over time and that re-infection can develop into clinical tuberculosis.[36]

The role of DTH in immunity of established tuberculosis is complex, because high degrees of sensitivity can precipitate caseous necrosis and lead to spread of the disease. The importance of CMI and hypersensitivity in modulating the course of tuberculosis is, perhaps, most dramatically illustrated in patients with AIDS. Those

with minimal impairment of cellular immune responses develop typical tubercles containing relatively few bacilli. Those with advanced impairment demonstrate abundant acid-fast bacilli without epithelioid cell accumulation or associated tissue necrosis.[36]

Emboldened by its achievements, the programme in 12th five year plan (2012-2017) as articulated national strategic plan with a vision of TB free India. the goal of the NSP is to achieve universal access to quality TB diagnosis and treatment for all TB patients in the community. The objective of The national strategic plan are :

- ✓ To achieve 90% notification rate for all cases.
- ✓ To achieve 90% success rate for all new and 85% for re-treatment cases.
- ✓ To significantly improve the successful out comes of treatment of DR- TB cases.
- ✓ To achieve decreased morbidity and mortality of HIV- associated TB .
- ✓ To improve out comes of TB care in the private sector.[22]

**Clinical and subclinical infection**

The term "TB infection'' refers to a positive TB skin test with no evidence of active disease; this state is also called latent infection . "TB disease'' refers to cases that have a positive acid-fast smear or culture for MTB or radiographic and clinical presentation of TB.32 Only some people develop active TB disease after infection, almost all TB infections are asymptomatic and remain latent.[37]

**Active disease**

A patient with PTB presents with the symptoms of chronic or persistent cough and sputum production. If the disease is at an advanced stage, the sputum will contain blood, and the patient will also have lack of appetite, weight loss, fever, night sweats etc.[29]

Patients with PTB are classified in different categories because a specific treatment is needed for each category. The main categories are as follows: [29]

**New case:**

TB in a patient who either has never received anti-tuberculous treatment or started a treatment for less than 1 month.

**Relapse:**

TB already treated and declared cured after sufficient treatment time, which has become active again.

**Chronic TB:**

A case of relapse from which the microscopic exam of expectoration remains positive after a second complete treatment.

**Primary resistance case:**

This characterizes the bacilli that are resistant to treatments, although patients have never been treated by anti-tuberculous drugs Multi-resistance case: MTB resistant at least to both major anti-tuberculous drugs (isoniazid and rifampicin)

**Latent infection**

Latent TB is the product of a complex set of interactions between MTB and the host immune response. The bacilli remain dormant until the host defenses are impaired by a disorder such as HIV infection. MTB subsequently reactivate to cause active disease. The latent state of infection is a major obstacle for eradicating TB. In latent TB, the host immune response is capable of controlling the infection but fails to eradicate the pathogen. One-third of the world population is estimated to be infected with the pathogen in the latent stage.[29]

**Symptoms and signs of pulmonary tuberculosis**[9]

In the early course of disease, symptoms and signs are non specific and insidious, consisting of night sweats and fever, weight loss, anorexia, general malaise and weakness.

Cough eventually develops initially, non productive but subsequently accompanied by production of purulent sputum. Blood streaking of sputum is frequently documented.

Massive hemoptysis may ensue. Pleuritic chest pain sometimes develops in patients with subpleural parenchymal lesion. It may also be result of muscle strain due to persistent coughing. Extensive disease may produce dyspnoea and acute respiratory distress syndrome.

**Physical findings**9

May have no abnormalities detectable by chest examination while other have detectable rales in the involved areas. Occasionally rhonchi due to partial bronchial obstruction and classic amphoric breath sounds in areas of large cavities are heard.

Systemic features include fever (low grade intermittent) and wasting and in some cases pallor and finger clubbing may develop.

The following factors increase the likelihood that a patient will have tuberculosis (TB):

- ✓ HIV infection.
- ✓ History of a positive PPD test result.
- ✓ History of prior TB treatment.
- ✓ TB exposure.
- ✓ Travel to or emigration from a TB endemic area.
- ✓ Homelessness, shelter-dwelling, incarceration.

**Classic features associated with active TB are as follows:**

- ✓ Cough.
- ✓ Weight loss/anorexia.
- ✓ Fever.
- ✓ Night sweats.
- ✓ Hemoptysis.
- ✓ Chest pain.

With regard to chest pain, a dull aching consistent with pericardial TB can lead to cardiac tamponade or constriction and presents similarly to congestive heart failure.

Genitourinary symptoms are less common in patients with TB. In women, dysuria, hematuria, and frequent urination may be present. In men, painful scrotal mass, prostatitis, orchitis, and epididymitis may be present.

Signs and symptoms of extrapulmonary TB may be nonspecific. They can include leukocytosis, anemia, and hyponatremia due to the release of ADH (antidiuretic hormone)-like hormone from affected lung tissue

Elderly individuals with TB may not display typical signs and symptoms of TB infection because they may not mount a good immune response. Active TB infection in this age group may manifest as nonresolving pneumonitis.

**Tuberculous meningitis**

Patients with tuberculous meningitis may present with a headache that is either intermittent or persistent for 2-3 weeks. Subtle mental status changes may progress to coma over a period of days to weeks. Fever may be low-grade or absent.

**Skeletal TB**

The most common site of skeletal TB involvement is the spine. Symptoms include back pain or stiffness. Lower-extremity paralysis occurs in up to half of

patients with undiagnosed Pott disease. Tuberculous arthritis usually involves only 1 joint. Although any joint may be involved, the hips and knees are affected most commonly, followed by the ankle, elbow, wrist, and shoulder. Pain may precede radiographic changes by weeks to months.

**Gastrointestinal TB**

Any site along the gastrointestinal tract may become infected. Symptoms of gastrointestinal TB are referable to the site infected, including the following: nonhealing ulcers of the mouth or anus; difficulty in swallowing (with esophageal disease); abdominal pain mimicking peptic ulcer disease (with stomach or duodenal infection); malabsorption (with infection of the small intestine); and pain, diarrhea, or hematochezia (with infection of the colon).

**Physical Examination**

Physical examination findings associated with TB depend on the organs involved.

Patients with pulmonary TB have abnormal breath sounds, especially over the upper lobes or involved areas. Rales or bronchial breath signs may be noted, indicating lung consolidation.

Signs of extrapulmonary TB differ according to the tissues involved. Signs may include confusion, coma, neurologic deficit, chorioretinitis, lymphadenopathy, and cutaneous lesions.

Lymphadenopathy in TB takes occurs as painless swelling of one or more lymph nodes, usually bilaterally; typically, anterior or posterior cervical chain or supraclavicular may be present.

The absence of any significant physical findings does not exclude active TB. In high-risk patients, classic symptoms are often absent, particularly in patients who

areimmuno compromised or elderly. Up to 20% of patients with active TB may deny symptoms. Therefore, sputum sampling is essential when chest radiography findings are consistent with TB.

**Diagnosis**[9]

Following laboratory tests are helpful in the diagnosis:

- ✓ Sputum for acid fast smear and culture.
- ✓ Complete blood count (CBC) .
- ✓ Chemistries, including alanine aminotransferase (ALT) or aspartate aminotransferase (AST).
- ✓ Alkaline phosphatase.
- ✓ Total bilirubin.
- ✓ Uric acid.
- ✓ Creatinine.
- ✓ HIV serology in all patients with TB and unknown HIV status.

For congenital TB, the best diagnostic test is the examination of the placenta for pathology, histology, and culture. Mycobacterial blood cultures of the newborn may also be helpful. Treatment may be necessary until placental culture results are negative.

If chest radiography findings suggest TB and sputum smear is positive for acid-fast bacilli, initiate treatment for TB.

Ziehl-Neelsen staining of sputum is a simple 5-step process that takes approximately 10 minutes to accomplish. While highly specific for mycobacteria, this stain is relatively insensitive, and detection requires at least 10,000 bacilli per mL; most clinical laboratories currently use a more sensitive auramine-rhodamine fluorescent stain (auramine O).

Routine culture uses a nonselective egg medium (Lowenstein-Jensen or Middlebrook 7H10) and often requires more than 3-4 weeks to grow because of the 22-hour doubling time of M tuberculosis. Radiometric broth culture (BACTEC radiometric system) of clinical specimens significantly reduced the time (10-14 d) for mycobacterial recovery. Newer broth culture media and systems for isolation are available for use in clinical laboratories based on a fluorescent rather than a radioactive indicator. The indicator is inhibited by oxygen; as mycobacteria metabolize substrates in the tubes and use the oxygen, the tube begins to fluoresce.[38]

Deoxyribonucleic acid (DNA) probes specific for mycobacterial ribosomal ribonucleic acid (RNA) identify species of clinically significant isolates after recovery. In tissue, polymerase chain reaction (PCR) amplification techniques can be used to detect M tuberculosis -specific DNA sequences and thus, small numbers of mycobacteria in clinical specimens.[39,40]

Extrapulmonary involvement occurs in one fifth of all TB cases, although 60% of patients with extrapulmonary manifestations of TB have no evidence of pulmonary infection on chest radiograph or sputum culture. Ocular TB can be especially difficult to identify, owing to its mimicry and its lack of accessible sampling; a high index of suspicion is required.

The hallmark of extrapulmonary TB histopathology is the caseating granuloma, consisting of giant cells with central caseating necrosis. Rarely, if ever, are any TB bacilli seen.

Altered mental status, neck stiffness, decreased level of consciousness, increased intracranial pressure, and cranial nerve involvement can indicate tuberculosis meningitis or tuberculoma. TB can directly seed the meninges and, if suspected, performing a lumbar puncture for evaluation of the cerebrospinal fluid is necessary. In

addition, a tuberculoma can be substantiated based on an increase in intracranial pressure and computed tomography (CT) scanning/magnetic resonance imaging (MRI).

If vertebral involvement (Pott disease) or brain involvement is suspected, it is important to consider that a delay in treatment could have severe repercussions for the patient (compression of the spinal cord and/or paraplegia); further evaluation is necessary with CT scanning or MRI.

**Tuberculin sensitivity**

Tuberculin sensitivity develops 2-10 weeks after infection and usually is lifelong.

**Cultures**

Patients suspected of having TB should submit sputum for smear and culture. Sputum should be collected in the early morning on three consecutive days. In hospitalized patients, sputum may be collected every eight hours. However, the absence of a positive smear result does not exclude active TB infection.

Approximately 35% of culture-positive specimens are associated with a negative smear result.

In patients without spontaneous sputum production, sputum induction with hypertonic saline should be attempted.[41] Early-morning gastric aspirate may also produce a good specimen, especially in children. Patients diagnosed with active TB should undergo sputum analysis for M tuberculosis weekly until sputum conversion is documented. Monitoring for toxicity includes baseline and periodic liver enzymes, CBC count, and serum creatinine.

Another option is fiberoptic bronchoscopy with transbronchial biopsy and bronchial washings. Biopsy of bone marrow, liver, or blood cultures is occasionally necessary and may be helpful.

Traditional mycobacterial cultures require weeks for growth and identification. Newer technologies, including ribosomal RNA probes and DNA PCR, allow identification within 24 hours. The DNA probes are approved for direct testing on smear-positive or smear-negative sputum. However, smearpositive specimens yielded higher sensitivity.

Culture for acid-fast bacilli (AFB) is the most specific and allows direct identification and susceptibility of the causative organism; however, access to the organisms may require lymph node/sputum analysis, broncho alveolar lavage, or aspirate of cavity fluid or bone marrow. Unfortunately, obtaining the test results is slow (3-8 wk), and they have a very low positivity in some forms of disease.

AFB stain is quick but requires a very high organism load for positivity. This is more useful in patients with pulmonary disease, but a delay in diagnosis can increase mortality, as other diagnostic testing may need to be considered.

Blood cultures using mycobacteria-specific, radioisotope-labeled systems help to establish the diagnosis of active TB. Mycobacterial bacteremia (bacillemia) is detectable using blood cultures only if specialized systems are used. The bacilli have specific nutrient growth requirements not met by routine culture systems.

Such blood cultures should be used for all patients with HIV who are suspected of having TB, because bacillemia is particularly prevalent in this population. If available, such cultures should be used for any patient highly suspected of having active TB. One study found an incidence of 88% mycobacterial infection (66% TB, 22% Mycobacterium avium complex [MAC]) detected by blood culture in stage IV HIV disease).

**Drug Susceptibility Testing**

Because conventional drug susceptibility tests for drug-resistant M tuberculosis take at least 3-8 weeks, Choi et al39 recommend direct DNA sequencing analysis as a rapid and useful method for detecting drug-resistant TB. In their clinical study of the use of direct DNA sequencing analysis for detecting drug-resistant TB, turnaround time of the direct DNA sequencing analysis was 3.8 +/- 1.8 days.

A total of 113 sputum specimens from 111 patients in the study were tested for genes conferring resistance to isoniazid, rifampin, ethambutol, and pyrazinamide, and the results were compared with drug susceptibility tests. The sensitivity and specificity of the assay were 63.6% and 94.6% for isoniazid, 96.2 and 93.9% for rifampin, 69.2% and 97.5% for ethambutol, and 100% and 92.6% for pyrazinamide, respectively.[42]

An automated molecular test that uses sputum samples for the detection of M tuberculosis and resistance to rifampin has been developed. In studies conducted in low-income countries, the sensitivity for TB was 98.3% (CI, 97- 99%) using a single smear-positive sputum sample and 76.9% (CI, 72.4-80.8%) using a single smear-negative sputum sample. Sensitivity from smear-negative sputum samples increased to 90.2% when 3 samples were tested. The test correctly identified 94.4% (CI, 90.8-96.6%) of rifampin-resistant organisms and 98.3% (CI, 97.1-99%) of rifampin-sensitive organisms.[43,44]

Microscopic-observation drug susceptibility (MODS) and thin-layer agar (TLA) assays are inexpensive, rapid alternatives to conventional methods or molecular methods for TB drug susceptibility testing. WHO endorsed the MODS assay, as a direct or indirect test, for rapid screening of patients with suspected MDR-TB. The evidence is insufficient to recommend the use of the TLA assay for rapid

screening, but this assay is a promising diagnostic technique. Further research is encouraged.[45]

**Alternative Diagnostic Tests**

Jafari et al found that an M tuberculosis –specific ELISpot assay can be used to differentiate TB cases with sputum smear negative for AFB from latent TB infection. In a prospective study of 347 patients suspected of having active TB who were unable to produce sputum or who had AFB-negative sputum smears, ELISpot testing of bronchoalveolar lavage fluid displayed a sensitivity and specificity of 91% and 80%, respectively, for the diagnosis of active pulmonary TB.[46]

Other rapid tests are also available, such as BACTEC-460 (Becton-Dickinson), ligase chain reaction; and luciferase reporter assay (within 48 h). These tests have been developed for rapid drug-susceptibilities testing, which can be available within 10 days.

Drug resistance tests such as the FASTPlaque TB-RIF for rifampicin resistance can be used after growth in semiautomated liquid cultures such as BACTEC-460; rifampicin resistance can be used as a surrogate marker for isoniazid resistance.

Xpert MTB/RIF (Xpert), a fully automated amplification system, has shown good results in the diagnosis of pulmonary TB in highly endemic countries, and has been shown to have high sensitivity in diagnosing extrapulmonary TB in a low-incidence setting, although the authors caution that the test's ability to rule out TB is suboptimal.[47]

**Chest Radiography**

Obtain a chest radiograph to evaluate for possible associated pulmonary findings (demonstrated in the images below). A traditional lateral and PA view should

be ordered. In addition, an apical lordotic view may permit better visualization of the apices and increase the sensitivity of chest radiography for indolent or dormant disease.

The chest film is also useful to screen for sarcoidosis, which closely imitates the clinical course of ocular TB. Radiologists look more decisively for signs of TB or sarcoid if the requesting physician simply asks to rule out sarcoid or TB.

Chest radiographs may show a patchy or nodular infiltrate (as seen in the image below). TB may be found in any part of the lung, but upper-lobe involvement is most common. The lordotic view may better demonstrate apical abnormalities.

Primary TB is more likely to mimic the appearance of routine community-acquired pneumonia on chest radiography, in contrast to reactivation TB. Studies have shown that either may be associated with pleural effusion or cavitation.

Various patterns may be seen, as follows (these are further discussed below):

- ✓ Cavity formation - Indicates advanced infection and is associated with a high bacterial load.
- ✓ Noncalcified round infiltrates - May be confused with lung carcinoma.
- ✓ Homogeneously calcified nodules (usually 5-20 mm) - Tuberculomas; represent old infection rather than active disease.
- ✓ Miliary TB - Characterized by the appearance of numerous small, nodular lesions that resemble millet seeds on chest radiography.

Chest radiography consistent with TB indicates active disease in the symptomatic patient even in the absence of a diagnostic sputum smear. Similarly, normal chest radiographic findings in the symptomatic patient do not exclude TB, particularly in a patient who is immunosuppressed.

In primary active TB, radiographic features of pulmonary tuberculosis are nonspecific, sometimes even normal. The chest radiograph typically shows a pneumonia-like picture of an infiltrative process in the middle or lower lung regions, often associated with hilar adenopathy and/or atelectasis.

In classic reactivation TB, pulmonary lesions are located in the posterior segment of the right upper lobe, apicoposterior segment of the left upper lobe, and apical segments of the lower lobes. Cavitation is most common; healing of tubercular regions results in the development of a scar with loss of lung parenchymal volume and calcification.

In the presence of HIV or another immunosuppressive disease, lesions are often atypical. Up to 20% of patients who are HIV positive with active disease have normal chest radiographic findings.

Old, healed TB presents differently, with dense pulmonary nodules found, with or without calcifications, in the hilar or upper lobes. Smaller nodules, with or without fibrotic scars, can be seen in the upper lobes. Nodules and fibrotic lesions are well demarcated, have sharp margins, and are dense. Persons with nodular or fibrotic scars with positive chest radiographic findings and positive PPD results should be treated as latent carriers. Calcified nodular lesions (granulomas) or apical pleural thickening has a lower risk of conversion.

In disseminated/miliary tuberculosis, the chest radiograph commonly shows a miliary pattern, with 2-mm nodules that are histologically granulomas disseminated like millet seeds throughout the lung; however, chest radiographic patterns can vary and can include upper lobe infiltrates with or without cavitation.

In pleural tuberculosis, the pleural space can be involved in 2 ways: a hypersensitivity response with pleuritic pain and fever, or an empyema that can be seen on chest radiograph with associated pleural effusions.

An in vitro blood test based on interferon-gamma release assay (IGRA) with antigens specific for M tuberculosis can also be used to screen for latent TB infection and offers certain advantages over tuberculin skin testing.[48,49] Currently available tests include QuantiFERON-TB Gold In-Tube (QFT-GIT), an enzymelinked immunosorbent assay or ELISA based on ESAT-6, CFP-10, and TB 7.7 antigens and T-SPOT.TB, an enzyme-linked immunospot (ELISpot) assay based

on ESAT-6 and CFP-10 antigens. Both tests measure in vitro T-cell interferon (IFN)-gamma in response to antigens highly specific for M tuberculosis and absent from the BCG vaccine and M avium.[50]

Overall, sensitivity and specificity of IGRA are comparable to those of tuberculin skin testing; however, unlike tuberculin skin testing, a second encounter for reading is unnecessary. Results are reported as positive, negative, or indeterminate. Patients with an indeterminate result may have evidence of immunosuppression and may be nonreactive on skin testing.[51]

Neither tuberculin skin testing nor IGRA testing is sufficiently sensitive to rule out TB infection.[52] Approximately 20% of patients with active TB, particularly those with advanced disease, may have normal PPD test results.

Limited data exist on the sensitivity of TST and IGRA tests in some situations; caution is recommended on the interpretation of these tests in infants and patients with immunosuppressive conditions.[50]

A systematic review of QUANTIFERON-TB Gold (QFT-G)/Gold in-Tube (QFT-G-IT) and T-SPOT.TB by Chang and Leung concluded that QFT-G had the

highest positive likelihood ratio (48.1) for latent TB infection and TSPOT. TB had the best negative likelihood ratio (0.10). A negative T-SPOT.TB result in middle-aged and older patients makes active TB very unlikely.[53]

Results from a study by Leung et al indicated that tuberculin skin testing was not predictive of the subsequent development of active TB.[54] The authors followed 308 males with increased risk of TB due to a diagnosis of silicosis. A positive T-SPOT.TB finding was associated with a relative risk of 4.5 for subsequent TB in the group overall and a relative risk of 8.5 among the men who did not receive preventive treatment for latent TB. CFP-10 spot count was more predictive than the ESAT-6 spot count.

In a separate study by Diel et al,[55] all subjects who developed active tuberculosis within 4 years after exposure to a smear-positive index case had positive results using QuantiFERON-TB Gold in-tube.

In a study of kidney-transplant recipients, isoniazid therapy was given to all patients with a significant TST reaction or risk factors for TB infection. ELISPOT assay was performed on all patients. No patients who were treated with isoniazid developed active TB. Among 71 patients with positive ELISPOT who did not receive isoniazid, 4 (6%) subsequently developed active TB after kidney transplantation.[56]

A systematic review of QuantiFERON-TB Gold (QFT-G)/Gold in-Tube (QFT-G-IT) and T-SPOT.TB by Chang and Leung concluded that, at a 90% certainty threshold, latent TB infection is best diagnosed with QFT-G/QFT-G-IT and best excluded with T-SPOT.TB. Neither test can diagnose TB disease, but TSPOT. TB can exclude it in middle-aged and older patients.[53]

**Urinalysis**

Urinalysis and urine culture can be obtained for patients with genitourinary complaints. Patients are often asymptomatic; however, significant pyuria and/or hematuria with no routine bacterial organisms should prompt urine culture for acid-fast bacilli.

**HIV Testing**

All patients who are diagnosed with active tuberculosis (TB) and who are not known to be HIV positive should be considered for HIV testing. In recent years, strong evidence has been gathered to confirm a link between TB and yet another disease diabetes mellitus. That link had been suspected for centuries.[8]

## Dosage for DR-TB for Adults[22]

| Sl/No | DRUGS | 16 - 25 kgs | 26 - 45kgs | 46 - 70kgs | >70kgs |
|---|---|---|---|---|---|
| 1 | Rifampicin* | 300 | 450 | 600 | 600 |
| 2 | Isoniazid$ | 200 | 200 | 300 | 450 |
| 3 | Ethambutol | 400mg | 800mg | 1200mg | 1600mg |
| 4 | Pyrazinamide | 500mg | 1250mg | 1500mg | 2000mg |
| 5 | Kanamycin | 500mg | 500mg | 750mg | 1000mg |
| 6 | Levofloxacin | 250mg | 750mg | 1000mg | 1000mg |
| 7 | Ethionamide | 375mg | 500mg | 750mg | 1000mg |
| 8 | Cycloserine | 250mg | 500mg | 750mg | 1000mg |
| 9 | Na-PAS (80% weight /vol)[1] | 7.5gm | 10gm | 12gm | 16gm |
| 10 | Pyridoxine | 50mg | 100mg | 100mg | 100mg |
| 11 | Moxifloxacin(Mfx) | 200mg | 400mg | 400mg | 400mg |
| 12 | Capreomycin(Cm) | 500mg | 750mg | 1000mg | 1000mg |
| 13 | Amikacin(Am) | 500mg | 500mg | 750mg | 1000mg |
| 14 | High dose INH(high dose-H) | 400mg | 600mg | 900mg | 900mg |
| 15 | Clofazimine(Cfz) | 100mg | 200mg | 200mg | 200mg |
| 16 | Linezolide(Lzd) | 300mg | 600mg | 600mg | 600mg |
| 17 | Amoxyclav(Amx/Clv)(In child : WHO 80mg/kg in 2 divided doses | 875/125mg BD | 875/125mg BD | 875/125mg 2 morn + even | 875/125mg 2 morn + even |
| 18 | Clarithromycin(CLr) | 250mg BD | 500mg BD | 500mg BD | 750mg BD |

## DIABETES MELLITUS:

### Historical review

Diabetes is perhaps as old as mankind. Cognizance of symptoms related to diabetes and recognition of the disorder was confined to a few geographic and cultural locations in the Ancient Era (up to 600 AD).

The knowledge acquired during this period was lost sight of and progress was tardy and indiscrete during the medieval period (600 to 1500 AD).

With the advent of modern age (1500 to 1758 AD) and its progression to renaissance and industrial revolution (1750 to 1850 AD), certain key features of diabetes were rediscovered and some new information was generated which stand out as landmarks in characterizing diabetes.

During the later decades of the 19th and first half of the 20th century, all round progress was achieved in the knowledge of pathology, predisposing factors, management, course and complications of diabetes mellitus. Growth of knowledge has been very fast in course of the second half of the last century (contemporary period) involving epidemiology, genetics, immunology and molecular biology which has led to accumulation of voluminous information on various aspects of this versatile disorder.[57,58]

Some key developments in scientific and clinical understanding of diabetes may be summarized as follows:

The earliest mention of diabetes like illness characterized by polyuria can be traced to Egyptian Papyrus dating back to around 1550 B.C.[58]

- ✓ The sweet taste of diabetic urine was noted in the 5th and 6th century AD by the Indian physicians and in the 17th century by Thomas Willis. The term 'Diabetes mellitus', an allusion to the honeyed taste of urine, was first used in

the late 18th century by John Rollo and others, to distinguish it from other polyuric states in which urine was tasteless.[58]

- ✓ In 1776, Matthew Dobson discovered that diabetic serum as well as urine contained sugar, and concluded that diabetes was a systemic condition rather than a disease of kidneys.[58]
- ✓ Claude Bernard made numerous discoveries in the field of metabolism and diabetes during the mid to late 19th century, describing the storage of glucose in the liver as glycogen and hyperglycemia in experimental animals.[58]
- ✓ In 1889, Oskar Minkowski and Josef Von Mering observed that total pancreatectomy produced diabetes in dogs.[58]
- ✓ In 1893, Edovard Laguesse named that pancreatic islets after Paul Langerhans, who had described them in 1869, and suggested that they produced a glucose lowering substance. This then hypothetical hormone was named 'insulin' by Jean de Meyer in 1909, over a decade before its discovery.[58]
- ✓ Various workers, including George Zueler (Germany) and Nicolas Paulesco (Romania), isolated active but impure hypoglycemic extracts from the pancreas during the first two decades of the 20th century; but toxic side effects precluded their formal testing in diabetic patients.[58]
- ✓ Insulin was discovered at the University of Toronto in 1921, through collaboration between Frederick G. Banting, Charles H. Best, James B. Collip and J.J.R. Macleod. Insulin was extracted from chilled pancreas in an acid / ethanol mixture; the extracts were found to lower blood glucose levels in pancreatectomized dogs and were first tested in a human diabetic in January 1922.[58]

- ✓ Major advances in the understanding of diabetes and metabolism have included:
- ➢ The sequencing of insulin in 1955 by Frederick Sanger and elucidation of its three dimensional structure in 1969 by Dorothy Hodgkin.
- ➢ The measurement of insulin concentration using the first radio immunoassay by Solomon Berson and Rosalyn Yalow in 1959.
- ➢ The isolation of proinsulin in 1967 by Donal Steiner's group.
- ➢ Identification of specific insulin receptors by Pierre Freychet and colleagues in 1971.
- ➢ The sequencing of the insulin receptor in 1985.

Diabetes mellitus refer to a group of common metabolic disorder that shares the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[9,59]

The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. In the United States, DM is the leading cause of end-stage renal disease (ESRD), non traumatic lower extremity amputations, and adult blindness. It also predisposes to cardiovascular diseases. With an increasing incidence worldwide, DM will be leading cause of morbidity and mortality for the foreseeable future.[9,57,58-60]

## CLASSIFICATION OF DIABETES MELLITUS

DM is classified on the basis of the pathogenic process that leads to hyperglycemia, as opposed to earlier criteria such as age of onset or type of therapy. The two broad categories of DM are designated as[57]

- Type 1
- Type 2

Both types of diabetes are preceded by a phase of abnormal glucose homeostasis as the pathogenic processes progresses. Type 1 diabetes is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycemia in type 2 DM and have important potential therapeutic implications now that pharmacologic agents are available to target specific metabolic derangements. Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).[57]

**Etiologic classification of diabetes mellitus**[57]

**I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)**

A. Immune-mediated

B. Idiopathic

**II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)**

**III. Other specific types of diabetes**

**A. Genetic defects of β-cell function characterized by mutations in :**

1. Hepatocyte nuclear transcription factor (HNF) 4α maturity onset diabetes of young (MODY) 1
2. Glucokinase (MODY 2)
3. HNF – 1α (MODY 3)
4. Insulin promoter factor (IPF) 1 (MODY 4)
5. HNF – 1β (MODY 5)
6. Neuro D1 (MODY 6)
7. Mitochondrial deoxyribo nucleic acid (DNA)
8. Sub units of adenosine triphosphate (ATP) – sensitive potassium channel.
9. Proinsulin or insulin conversion

B. **Genetic defects in insulin action**.

1. Type A insulin resistance
2. Leprechaunism
3. Rabson-Mendenhall syndrome
4. Lipodystrophy syndromes.

C. Diseases of the exocrine pancreas – pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculouspancreatopathy.

D. Endocrinopathies – acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma

E. Drug or chemical induced – Vacor, pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, beta-adrenergic agonists, thiazides, phenytoin, α– interferon, protease inhibitors, clozapine, beta blockers.

F. Infections – congenital rubella, cytomegalovirus, coxsackie.

G. Uncommon forms of immune-mediated diabetes – “stiff-man” syndrome, anti-insulin receptor antibodies.

H. Other genetic syndromes sometimes associated with diabetes – Down’s syndrome, Klinefelter’s syndrome, Turner’s syndrome, Wolfram’s syndrome, Friedreich’s ataxia, Huntington’s chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome.

**IV. Gestational diabetes mellitus (GDM) Epidemiology**

Diabetes is fast becoming the epidemic of the 21st century. Type 2 diabetes, which is more prevalent (more than 90% of all diabetes cases) and the main driver of the diabetes epidemic, now affects 5.9% of the world's adult population with almost 80% of the total in developing countries.[61]

Nowhere is the diabetes epidemic more pronounced than in India as the WHO reports show that 32 million people had diabetes in the year 2000. World Health Organization reported that, 346 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of high blood sugar. More than 80% of diabetes deaths occur in low- and middle-income countries. WHO projects that, diabetes deaths will double between 2005 and 2030.[62]

**Race**

The prevalence of type 2 diabetes mellitus varies widely among various racial and ethnic groups. Type 2 diabetes mellitus is becoming virtually pandemic in some groups of Native Americans and Hispanic people. The risk of retinopathy and nephropathy appears to be greater in blacks, Native Americans, and Hispanics.[63]

**Sex**

Type 2 DM is slightly more common in older women than men.[63]

**Age**

While type 2 diabetes mellitus traditionally has been thought to affect individuals older than 40 years, it is being recognized increasingly in younger persons, particularly in highly susceptible racial and ethnic groups and the obese. In some areas, more type 2 than type 1 diabetes mellitus is being diagnosed in prepubertal children, teenagers, and young adults. Virtually all cases of diabetes mellitus in older individuals are type 2.[63]

**Indian scenario**

India is in the midst of an ever-increasing epidemic of diabetes mellitus. Data on type 1 diabetes mellitus from our country is scant. Clinic based data from the mid sixties to the eighties reported the prevalence of childhood diabetes with onset below 15 years of age as being one to four percent of all the diabetic subjects attending clinics in different parts of the country.[57,59]

According to recent study also, almost 95% of childhood diabetes reportedly belongs to Type 1 DM. Early onset type 2 diabetes, MODY, fibrocalculous pancreatic diabetes and diabetes associated with genetic syndromes accounted for the remaining cases.[57]

Type 2 DM accounts for more than 90% of all patients with diabetes in India. According to WHO there were an estimated 19.4 million diabetes individuals in 1995, and this number is projected to increase in 80 million by 2030. The ICMR study (1972 to 1975) was the first systematic nationwide collaborative study on the prevalence of diabetes mellitus.[57,59]

The prevalence of diabetes was found to be 2.8% in rural and five percent in the urban population above the age of 40 years. The prevalence of Diabetes in India Study (PODIS) carried out in 77 centres recently reported a standardized prevalence

rate for DM, in the total urban and rural population of 4.3, 5.9 and 2.7% respectively.[57]

Several epidemiological studies in migrant Indians and India itself show that, the population has a high genetic predisposition for diabetes, which is precipitated by environmental factors such as urbanization.60 The prevalence of diabetes is four to six fold lower in rural areas, which is probably attributed to a conventional lifestyle which has beneficial effect on glucose tolerance (IGT). National Urban Diabetes Survey done in six cities, found age standardized prevalence rates of 12% for diabetes; with a slight male preponderance and 14% for impaired glucose tolerance. Subjects under the age of 40 years, had a prevalence of five percent for DM and 13% prevalence of impaired glucose tolerance.

The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025.[64] It is clear that in the last two decades, there has been a marked increase in the prevalence of diabetes among both urban as well as the rural Indians, with a suggestion that Southern India has seen the sharpest increase. Subsequent studies confirmed this high prevalence of diabetes in urban south India. Although in rural India the prevalence of diabetes is much lower than in the urban population, even here the prevalence rates are rapidly rising, though clearly more studies are needed. Variations in the prevalence rates of diabetes in different urban populations of India are expected because of the large variation in the prevalence of cardiovascular risk factors in different regions and states. It is evident that there is a shift in age of onset to younger age groups, which is alarming and this could have adverse effects on the nation's economy. Hence, the early identification of at-risk individuals and appropriate intervention to increase physical activity, bring about

changes in dietary habits could to a great extent help to prevent/ delay, the onset of diabetes and thus reduce the burden due to its associated complications in India.[61]

The world wide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, more than 360 million individuals will have diabetes by the year 2030. Although the prevalence of both type 1 and type 2 DM is increasing world wide, the prevalence of type 2 DM is rising much more rapidly because of increasing obesity and reduced activity levels as countries become more industrialized. This is true in most countries, and 6 of the top 10 countries with the highest rates are in Asia. In the United States, the CDC estimated that 20.8 million persons, or seven percent of the population, had diabetes in 2005 (30% of individuals with diabetes were undiagnosed).[57,59]

The prevalence is similar in men and women throughout most age ranges but is slightly greater in men more than 60 years. World wide estimates project that in 2030 the greatest number of individuals with diabetes will be 45 to 64 years of age.[59]

**Causes for diabetic**

The type 2 DM epidemic is tightly and consistently linked to that of obesity, both geographically and chronologically. Many factors like, urbanization and mechanization, together with globalized pattern of western pattern of lifestyle, together with poverty, lack of education and low socio-economic status and inner city deprivation are emerging as significant risk factors for DM. Lack of breast feeding, low birth weight is associated with insulin resistance and type 2 DM in adult life (especially in subjects who become obese) due to long term metabolic response during poor fetal nutrition.[65]

**Obesity**

Prevention of obesity, in women of child bearing age, is another primary goal because exposure to environment of a diabetic pregnancy places the fetus at increased risk for future onset diabetes. About 80% of patients are obviously obese at the time of diagnosis, usually with a central fat distribution in and around the abdominal cavity. In addition, many of those who are not traditionally obese, by weight criteria have increased percentage of fat predominantly distributed in the abdominal region. It is the most obvious target to prevent DM.

**CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS**[58,59]

- ✓ Symptoms of diabetes plus random blood glucose concentration more than 11.1 mmol/L (200 mg/dL).
- ✓ Fasting plasma glucose more than 7.0 mmol/L (126 mg/dL).
- ✓ Two-hour plasma glucose more than 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test

**Note:**

In the absence of unequivocal hyperglycemia and acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day.

- ➢ Random is defined as without regard to time since the last meal.
- ➢ Fasting is defined as no caloric intake for at least 8 h.
- ➢ The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; not recommended for routine clinical use.

**SCREENING**[9]

Diabetes was originally identified by the presence of glucose in the urine. Almost 2,500 years ago it was noticed that ants were attracted to the urine of some individuals. In the 18th and 19th centuries the sweet taste of urine was used for diagnosis before chemical methods became available to detect sugars in the urine. Tests to measure glucose in the blood were developed over 100 years ago, and hyperglycemia subsequently became the sole criterion recommended for the diagnosis of diabetes. Initial diagnostic criteria relied on the response to an oral glucose challenge, while later measurement of blood glucose in an individual who was fasting also became acceptable.

The most widely accepted glucose-based criteria for diagnosis are fasting plasma glucose (FPG) ≥126 mg/dL or a 2-h plasma glucose ≥200 mg/dL during an oral glucose tolerance test (OGTT) on more than one occasion. In a patient with classic symptoms of diabetes, a single random plasma glucose ≥200 mg/dL is considered diagnostic. Before 2010 virtually all diabetes societies recommended blood glucose analysis as the exclusive method to diagnose diabetes. Notwithstanding these guidelines, over the last few years many physicians have been using hemoglobin A1C to screen for and diagnose diabetes. Although considered the "gold standard" for diagnosis, measurement of glucose in the blood is subject to several limitations, many of which are not widely appreciated. Measurement of A1C for diagnosis is appealing but has some inherent limitations.[66]

These issues have become the focus of considerable attention with the recent publication of the Report of the International Expert Committee that recommended the use of A1C for diagnosis of diabetes,[67] a position that has been endorsed (at the time of writing) by the ADA,[68] the Endocrine Society, and in a more limited fashion

by American Association of Clinical Endocrinologists/American College of Endocrinology.[69]

**Current criteria for the diagnosis of diabetes**[70]

- ✓ A1C ≥6.5%. The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP)- certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay
- ✓ Fasting plasma glucose (FPG) ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.
- ✓ 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT). The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
- ✓ In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).
- ✓ In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

**Oral glucose tolerance test**

The OGTT evaluates the efficiency of the body to metabolize glucose and for many years has been used as the "gold standard" for diagnosis of diabetes. An increase in postprandial glucose concentration usually occurs before fasting glucose increases. Therefore, postprandial glucose is a sensitive indicator of the risk for developing diabetes and an early marker of impaired glucose homeostasis. Published evidence suggests that an increased 2-h plasma glucose during an OGTT is a better predictor of both all-cause mortality and cardiovascular mortality or morbidity than the FPG.[66]

The OGTT is accepted as a diagnostic modality by the ADA, WHO/International Diabetes Federation (IDF),67 and other organizations. However, extensive patient preparation is necessary to perform an OGTT. Important conditions include, among others, ingestion of at least 150 g of dietary carbohydrate per day for 3 days prior to the test, a 10- to 16-h fast, and commencement of the test between 7:00 a.m. and 9:00 a.m.[66]

In addition, numerous conditions other than diabetes can influence the OGTT. Consistent with this, published evidence reveals a high degree of intraindividual variability in the OGTT, with a CV of 16.7%, which is considerably greater than the variability for FPG.[66] These factors result in poor reproducibility of the OGTT, which has been documented in multiple studies.[71] The lack of reproducibility, inconvenience, and cost of the OGTT led the ADA to recommend that FPG should be the preferred glucose-based diagnostic test.[67]

**Advantages**

- Sensitive indicator of risk of developing diabetes.
- Early marker of impaired glucose homeostasis

**Disadvantages**

- Lacks reproducibility.
- Extensive patient preparation.
- Time-consuming and inconvenient for patients.
- Unpalatable .
- Expensive.
- Influenced by numerous medications.
- Subject to the same limitations as FPG, namely, sample not stable, needs to be performed in the morning, etc.

WHO Diabetes criteria - Interpretation of Oral Glucose Tolerance Test [72]

| Glucose levels | Normal | | Impaired fasting glyeaemia | | Impaired glucose tolerance (IGT) | | Diabetes Mellitus (DM) | |
|---|---|---|---|---|---|---|---|---|
| VENOUS PLASMA | Fasting | 2hrs | Fasting | 2hrs | Fasting | 2hrs | Fasting | 2hrs |
| (mmoi/L) | <6.1 | <7.8 | ≥6.1 & < 7.0 | <7.8 | <7.0 | ≥7.8 | ≥7.0 | ≥11.1 |
| (mg/dL) | <110 | <140 | ≥110& <126 | <140 | <126 | ≥140 | ≥126 | ≥200 |

ADA criteria for diagnosis of diabetes mellitus[68]

The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus of the American Diabetes Association stated that diabetes can be provisionally diagnosed with any one of the three criteria listed below. In the absence of unequivocal hyperglycemia with acute metabolic decompensation the diagnosis should be confirmed, on a subsequent day, by any one of the same three criteria.

- ✓ A fasting plasma glucose of >126 mg/dl (after no caloric intake for at least 8 hours) or,
- ✓ A casual plasma glucose >200 mg/dl (taken at any time of day without regard to time of last meal) with classic diabetes symptoms: increased urination, increased thirst and unexplained weight loss or,
- ✓ An oral glucose tolerance test (OGTT) (75 gram dose) of >200 mg/dl for the two hour sample. Oral glucose tolerance testing is not necessary if patient has a fasting plasma glucose level of >126 mg/dl.

The Committee states that the fasting plasma glucose is the preferred test and

recommends moving toward its universal use for testing and diagnosis because of its ease of administration, convenience, acceptability to patients, and lower cost in comparison to the OGTT.

Summarized Interpretation of Oral Glucose Tolerance Test (OGTT)

- 2 hour postload glucose of < 140 mg/dl = normal glucose tolerance .
- 2 hour postload glucose between 140 mg/dl and 199 mg/dl = impaired glucose tolerance.
- 2 hour postload glucose > 200 mg/dl = provisional diagnosis of diabetes (Must be confirmed on a subsequent day by any of the above criteria for diagnosis of Diabetes Mellitus.)

## PATHOGENESIS

### Type 2 DM

Insulin resistance and abnormal insulin secretion are central to the development of type 2 DM. Although the primary defect is controversial, most studies support the view that insulin resistance precedes an insulin secretory defect but that diabetes develops only when insulin secretion becomes inadequate.

### Genetic Considerations

Type 2 DM has a strong genetic component. 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. The disease is polygenic and multifactorial since in addition to genetic susceptibility, environmental factors (such as obesity, nutrition, and physical activity) modulate the phenotype. The genes that predispose to type 2 DM are incompletely identified, but recent genome-wide association studies have identified several genes that convey a relatively small risk for type 2 DM (relative risk of 1.1 to 1.5). Most prominent is a variant of the transcription factor 7 like 2 gene that has been associated with type 2 diabetes in several populations and with impaired glucose tolerance in one population at high risk for diabetes. Genetic polymorphisms associated with type 2 diabetes have also been found in the genes encoding the peroxisome proliferators-activated receptor-r, inward rectifying potassium channel expressed in beta cells, zinc transporter expressed in beta cells, IRS, and calpain 10. The mechanisms by which these genetic alterations increase the susceptibility to type 2 diabetes are not clear, but

several are predicted to alter insulin secretion. Investigation using genome-wide scanning for polymorphisms associated with type 2 DM is ongoing.[9]

**PATHOPHYSIOLOGY**

Type 2 DM is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production, and abnormal fat metabolism. Obesity, particularly visceral or central (as evidenced by the hip-waist ratio), is very common in type 2 DM. In the early stages of the disorder, glucose tolerance remains near-normal, despite insulin resistance, because the pancreatic beta cells compensate by increasing insulin output.

As insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to sustain the hyperinsulinemic state. IGT, characterized by elevations in postprandial glucose, then develops. A further decline in insulin secretion and an increase in hepatic glucose production lead to overt diabetes with fasting hyperglycemia. Ultimately, beta cell failure may ensue.[9]

**Pulmonary tuberculosis and diabetes mellitus**

Overall TB continues to infect an estimated one-third of the world's population, to cause disease in 8.8 million people per year, and to kill 1.6 million of those afflicted. The global burden of diabetes mellitus (DM) is expected to rise from an estimated 180 million prevalent cases currently to a predicted 366 million by 2030, with the greatest increase projected in the developing world.[73]

Experts have raised concerns about the twin epidemics of DM and TB, especially in low to middle income countries like India and China that are of TB in the world.[74] Several recent studies suggest that DM increases the risk of active TB with an approximately three fold risk of developing active TB been reported.[75] Recent papers have also reflected increasing concern among tuberculosis field workers, that

DM may be a major force in converting latent infection into overt disease. Thus the link between DM and TB has occupied the center stage of discussion.[73]

Since the early part of the 20th century, clinicians have observed an association between DM and TB, although they were often unable to determine whether DM caused TB or whether TB led to the clinical manifestation of DM.[76-80] The mid 20th century saw a few reports documenting such a link and speculating on its significance.

More recently, multiple rigorous epidemiological studies investigating the relationship, have demonstrated that DM is indeed positively associated with TB.[81,82] McCornick and colleagues from the University of Texas school of Public Health, in 2007 explored the association between the two conditions in over 5000 TB patients on the two sides of the Rio Grande River. Using retrospective data they found that the co morbidity of TB-DM exceeded that of TB-HIV. Patients with TB and DM were older, more likely to have hemoptysis and pulmonary cavitations, be smear positive at diagnosis, and remain positive at the end of the first and second month of treatment. Type 2 DM was the major factor associated with TB in both Mexicans and the Hispanic Americans. These observations raise important scientific and public health questions concerning possible immunological impairment in DM, the importance of DM control in exposed individuals and the control of tuberculosis in communities with an increasing prevalence of DM.[73]

The recent studies predict that in India 18.4% (12.5% to 29.9%) of people with pulmonary tuberculosis (both smear-positive and smear-negative) have diabetes and that in the smear-positive group diabetes prevalence is 23.5% (12.1% to 44%).[73]

Studies conducted after the introduction of the glucose tolerance test in 1950s, have shown high prevalence of impaired glucose tolerance test in patients with

tuberculosis with rates ranging from 2% to 41%.[83]

The use of different criteria for diagnosis of diabetes mellitus makes comparisons between the results of the studies almost impossible. There have been reports of high prevalence rates of diabetes in cases of pulmonary tuberculosis (4-20%) and rates are higher for impaired glucose tolerance test (16-29%). Interestingly, after antituberculosis therapy, 50% of these patients had normalization of their glucose tolerance.

Some investigators have reported an association between severity of tuberculosis and abnormal glucose tolerance. However, no association has been found with age, family history of tuberculosis, ethnicity or duration of treatment.[84]

Case series by Deshmukh et al[85] with 138 TB-DM patients revealed that 82.6% of the study population was above 45 years of age and there was a male preponderance. 43.4% of TB patients gave history of DM and 56.6% were detected subsequently on the examination of urine, confirmed by blood sugar examination. In this study, the authors observed that, when a known case of diabetes presents with symptoms of general ill-health like fever, weakness, apathy, cough, haemoptysis, and chest pain; investigations may reveal the presence of tuberculosis. They also noted that in a few cases a rapid deterioration of health took place with persistent fever, loss of weight, and investigations revealed presence of co-existent diabetes and pulmonary tuberculosis. Sometimes in the study population a patient who has been put on anti-tuberculosis treatment failed to respond adequately in a given period of time and further investigations revealed the presence of diabetes.[85]

In another study by Tripathi et al,[86] the authors observed 55% of TB-DM group were underweight and this group was mostly more than 40 years of age.

Experienced clinicians observe that patients with both diabetes and

tuberculosis usually have a prolonged duration of fever and more significant weight loss with co-existent disease than with diabetes or pulmonary tuberculosis alone.[85-87]

Diabetes may be diagnosed for the first time when blood sugars are initially sent off in the patient with pulmonary TB and found to be high. We would advocate checking fasting and post-prandial sugars in all newly diagnosed TB patients. However, there are recent reports that show no significant difference in the mean duration of symptoms between the TB-DM patients and the TB patients without DM. Low grade fever and productive cough were the most common symptoms and were observed with almost equal frequency in both groups.[88] Taken together these studies suggest that the clinical spectrum of this group of patients with co-existent pulmonary tuberculosis and diabetes mellitus is quite varied.[73]

A study by Jain MK et al**,** reported that out of the 106 patients of pulmonary tuberculosis (all aged 30 years and above) 18 (16.98 %) had abnormal Glucose Tolerance Test (GTT) of which 2 (1.88%) had impaired fasting glycemia, 11 (10.34 %) had impaired glucose tolerance and 5 (4.7 %) were frankly diabetic.[18]

Yamagishi et al,[89] reported 14.1% patients diagnosed pulmonary tuberculosis had impaired glucoce tolerance test.

Firsova et al,[90] reported 10.8% patients of pulmonary tuberculosis had impaired glucoce tolerance test.

Guptan et al,[91] reported 9.7% patients of pulmonary tuberculosis had impaired glucoce tolerance test.[4]

Roy Choudary et al,[92] reported 27.25%patients of pulmonary tuberculosis had impaired glucose tolerance test.

If diabetes can predispose a patient to tuberculosis, can infection with tuberculosis lead to diabetes mellitus? Infections, including tuberculosis, often worsen

glycaemic control in diabetic patients, and poorly controlled diabetes might in turn augment the severity of infections.[93]

Some studies suggest that tuberculosis can even cause diabetes in those not previously known to be diabetic. Many studies have used oral glucose tolerance testing to show that patients with tuberculosis have higher rates of glucose intolerance than community controls.[94-96] Whereas the high incidence of abnormal oral glucose tolerance found in tuberculosis patients is of concern, it is unclear whether glucose intolerance or diabetes mellitus was truly incident, or whether prevalent diabetes mellitus was being newly diagnosed in patients receiving expanded medical services related to tuberculosis treatment. Also, the implications of these findings depend on whether diabetes mellitus persists in these patients, and whether its presence is substantially more common with tuberculosis than with other infectious diseases.[15]

In a study in Nigeria, tuberculosis patients with impaired glucose tolerance had normal tests after 3 months of tuberculosis treatment.[97]

In Turkey, oral glucose tolerance tests were given to 58 patients with active tuberculosis and 23 patients with community-acquired pneumonia.[98] Of those with tuberculosis, 10% were glucose intolerant and 9% had diabetes; of patients with community-acquired pneumonia, none had glucose intolerance and 17% were diabetic. All patients had normal tests 3 months and 2 years after the start of treatment. The latter two studies suggest that infection causes reversible glucose intolerance and that this effect is not specific to tuberculosis. In Indonesia, 13% (60 of 454) of patients with tuberculosis had diabetes, compared with 3·2% (18 of 556) of age-matched and sex-matched controls from the same residential unit; for 60% of these patients, diabetes was a new diagnosis.[99] Whereas impairment of glucose metabolism probably preceded tuberculosis in these patients rather than the reverse,

these data underscore the importance of screening tuberculosis patients for diabetes.[15]

With increasing rates of obesity and diabetes worldwide and continued high rates of tuberculosis in low-income countries, we can expect that the number of individuals who have both tuberculosis and diabetes mellitus will increase markedly in the coming decades. More research in this largely neglected area would therefore be beneficial.

**Double burden of tuberculosis and diabetes**

The burden of communicable diseases is concentrated in low-income countries. However, non-communicable diseases, which represented 47% of the disease burden in 1990 in low-income countries, have been predicted to rise to 69% by 2020[100].

**Effect of diabetes on tuberculosis risk and severity**

Historically, the incidence of tuberculosis in patients with diabetes has been high. In 1934, a treatise on the association between diabetes and tuberculosis was written by Howard Root (a physician at the Deaconess Hospital, Boston, MA, USA), described the epidemiology, pathology, and clinical course of dually affected patients. In his studies, tuberculosis in adults with diabetes was more common than expected, and risk was particularly high in schoolchildren and adolescents with diabetes. Tuberculosis developed most frequently in patients with poor diabetic control. Furthermore, they found that diabetic patients who needed more than 40 units of insulin per day were twice as likely to develop tuberculosis as those using lower doses, thus linking severity of diabetes mellitus with risk of tuberculosis[100].

**Tuberculosis incidence in patients with diabetes**

The risk of developing active tuberculosis is a two-step process, beginning with initial exposure to and infection by Mycobacterium tuberculosis followed by

subsequent progression to disease. Studies of diabetes mellitus and tuberculosis generally focus on active tuberculosis disease. Several case–control studies have shown that the relative odds of developing tuberculosis in diabetic patients ranges from 2·44 to 8·33 compared with non-diabetic patients. Although there is no reason, a priori, to expect an association with diabetes mellitus and drug resistance, two studies have shown that diabetic patients are more likely to develop multidrug-resistant tuberculosis than those without diabetes[100].

**How might diabetes mellitus lead to tuberculosis?**

Poorly controlled diabetes can lead to multiple complications, including vascular disease, neuropathy, and increased susceptibility to infection. The mechanisms include those directly related to hyperglycaemia and cellular insulinopenia, as well as indirect effects on macrophage and lymphocyte function, leading to diminished ability to contain the organism[101].

The most important effector cells for containment of tuberculosis are phagocytes (alveolar macrophages and their precursor monocytes) and lymphocytes. Diabetes is known to affect chemotaxis, phagocytosis, activation, and antigen presentation by phagocytes in response to M tuberculosis. In diabetic patients, chemotaxis of monocytes is impaired, and this defect does not improve with insulin. In their role as antigen-presenting cells for the initiation of lymphocyte activation, phagocytes bind and then internalize antigen for processing and presentation via their Fc receptors; once activated, they produce interleukin 2, enhancing T-cell proliferation. Insulin deficiency can cause impaired internalization of Fc-receptor-bound material. Diabetes might adversely affect T-cell production of interferon γ, and T-cell growth, function, and proliferation. Interferon γ potentiates the nitric-oxide-dependent intracellular killing activity of macrophages[100].

**Does tuberculosis lead to diabetes?**

Infections, including tuberculosis, often worsen glycaemic control in diabetic patients, and poorly controlled diabetes might in turn augment the severity of infections. Some studies suggest that tuberculosis can even cause diabetes in those not previously known to be diabetic. Many studies have used oral glucose tolerance testing to show that patients with tuberculosis have higher rates of glucose intolerance than community controls[100].

The present study was aimed to find the incidence of OGT and it's clinical profile in patients with pulmonary tuberculosis. Method: Study included 75 patients with positive sputum smear for acid fast bacilli and chest x-ray. Results: AFB findings showed positive in 73.33% in sample 1 and 76% in sample2.on chest x-ray almost half(49.33%) of the patients had infiltration. No statistically significant association of sex, age and chest x-ray findings was seen in patients with pulmonary tuberculosis and diabetes mellitus.

The link between Diabetes mellitus & Tuberculosis has been recognizing for centuries. Recently Tuberculosis has re-emerged as a major health concern. There is growing evidence that Diabetes mellitus with Tuberculosis may affect disease presentation and treatment. The Tuberculosis also influences glucose intolerance and influences the glycaemic control in the people with Diabetes mellitus. Approximately 2 Million persons worldwide died of Tuberculosis and 9 Million become infected each year. (CDC, 2007)1**.** With the convergence of tuberculosis and diabetes Mellitus epidemic, co-affliction with the two diseases is on the rise. The observational study was conducted with 100 patients. The patients with Pulmonary Tuberculosis sputum positive/negative with radiological lesions was admitted in medicine wards of our hospital between years 2009-2011. The aim of our study is to find out the prevalence

of GTT in patients of Pulmonary Tuberculosis Age, sex distribution of impaired Glucose Tolerance Test (GTT) in Patients with pulmonary tuberculosis and study the correlation between impaired GTT with Sputum positivity and also radiological extent of disease. The patients were subjected to oral GTT and results were evaluated according to the WHO criteria and the statistical analysis was done to determine the P value and significance on the basis Chi-square test. The results found in the studied patient were that prevalence of abnormal GTT in Pulmonary Tuberculosis patients was found to be 22% (P=0.07). Abnormal GTT was more common in males as compared to females and this was found to be significant (P=0.692). Sputum positive Pulmonary Tuberculosis is strongly associated in patients with abnormal GTT (P=0.03), and bilateral lung involvement was more common among Pulmonary Tuberculosis patients with abnormal GTT.

The frequency of glucose intolerance was studied in 106 patients with pulmonary tuberculosis attending Nazimabad Chest Clinic. Diagnosis was based on X-ray and a positive sputum smear. An oral glucose tolerance test (OGTT) was performed and evaluated according to the WHO criteria. Glucose intolerance was detected in 52(49%) patients, 31 Impaired Glucose Tolerance (IGT), 21 Diabetes Mellitus (DM). After adequate antitubercular therapy and sputum conversion, the OG1'T was repeated in 23 cases. Of these 13 (56.5%) patients had a normal glucose tolerance indicating that glucose intolerance observed during active pulmonary tuberculosis improves or normalizes after adequate therapy (JPMA 45:237, 1995).

The coexistence of diabetes and tuberculosis is common and challenge to the community. Diabetes predisposes to tuberculosis and treatment often become complicated. Though the prevalence of tuberculosis is decreasing due to success of combination chemotherapy but coexistence of diabetes with tuberculosis poses a

threat to success of anti-tubercular program. India has huge burden of the both diabetes and tuberculosis. We did a prospective study to know the prevalence of diabetes in tuberculosis patients in a tertiary care hospital. Out of total 419 patients who were included in the study 135 patients were found to be diabetic. A prevalence of 32.2% was found in the study.

Tuberculosis is one of the world's deadliest infectious diseases which infects one third of the world's population and kill 1.6 million people each year. On the other hand global burden of diabetes mellitus is going to increase from estimated 180 million currently to 366 million by the year 2030. Both diseases are very common in developing countries like India and Pakistan. Since centuries it was observed that pulmonary tuberculosis is more common in Diabetes Mellitus patients. Recently inverse relation is also observed i.e.-e high prevalence of impaired glucose tolerance in tuberculosis. 136 patients of pulmonary tuberculosis were selected irrespective age sex and duration of symptoms. OGTT was done in all selected patients, Glucose tolerance test was abnormal in 22 out of 136 patients of pulmonary tuberculosis. Abnormal glucose tolerance is more common in older people (>50 years) and males. It is also seen that abnormality is more common in obese and socioeconomically poor patients who are living in rural areas.

As the pulmonary tuberculosis is still rampant in our country inspite of directly observed treatment short course( DOTS). Recently it has been observed that diabetic patients having pulmonary tuberculosis have more morbidity and mortality hence it gives us the impetus to know whether pulmonary tuberculosis is leading to development of diabetes**.** Hence we had undertaken this study to know the prevalence of diabetes in these early diagnosed pulmonary tuberculosis patients and assessing the pattern of drug resistance. Acute severe stress, fever, and malnutrition stimulate the

stress hormones which is the cause of increased blood sugar level. The prevalence of group B and C were 22.5% and 7.5% respectively.The development of multi drug resistance (MDR) tuberculosis accounted for nearly 37.5% in diabetics which is significantaly greater in comparison to IGT (33.3%) and nondiabetics (1.2%).

Association between tuberculosis and diabetes mellitus is known since ancient times. Tuberculosis is more frequent (four to five times) among diabetics but there are conflicting views on increased prevalence of diabetes & prediabetes in tuberculosis patients. Presently developing nations are facing epidemic of both diseases. It becomes important to screen diabetes mellitus among tuberculosis patients as both diseases have adverse effects on each other outcomes. 8.2% & 12.3% patients had diabetes & prediabetes respectively. Prevalence of TB diabetics increases with age and was more in males compared to females. TB diabetics had more symptoms and far advanced disease which were statistically significant.

India being Diabetic Capital with largest number of tuberculosis patients. Several studies have highlighted that Diabetes as a risk factor for TB. TB in Diabetic patients tend to have more cavitatory, less sputum positive with paucity in symptoms and signs. Hence We would like to highlight the varied pulmonary manifestations through our study. Out of 50,36(72%) males & 14(28%). Maximum incidence of TB was seen in >50 years with peak incidence in 51-60 & 61-70.Mean age for males was 52.8 and females was 55.6 years. Symptoms noted were cough(92%), Fever(80%), Anorexia(58%), Loss of weight(56%), Dyspnea(42%), Hemoptysis(20%), Chest pain(20%),night sweats(20%). Duration of Diabetes were <1y(22%),2-5y(42%),6-10y(32%),>10y(4%). Mean FBS was 241 mg/dl and PPBS was 316 mg/dl.

Sputum positive cases <50y(16/20) and >50y(21/30) with P=0.182. Cavitatory lesions were noted in 38% followed by non homogenous opacities in 22% of patients.

The present research was focused to estimate the occurrence of Diabetes mellitus. in pulmonary tuberculosis and to study the clinical and radiological profile of pulmonary tuberculosis with Diabetes mellitus. Proven cases of patents with pulmonary tuberculosis were screened for the presence of. Diabetes mellitus. Treatment was instituted for both diabetes and pulmonary tuberculosis and followed up. Antitubercular therapy was extended beyond six months for most patients. 50% of the patients could be maintained on oral hypoglycemics alone. In conclusion, it is recommended that sputum positive cases of tuberculosis be screened for. Diabetes mellitus., since the prevalence of diabetes in pulmonary tuberculosis is quite high.

Tuberculosis and Diabetes mellitus are two public health problems which not only often coexist but have serious implications on each other.DM has an impact on symptomatology, radiological manifestation, diagnosis, and management of TB.TB has significant impact on DM, causing unmasking of DM and poor control because of stress or because of drug treatment for TB. Present study attempts to asseses this coexistence with regard to the age predisposition, sex preponderance, duration and glycemic control of diabetes and the radiological manifestation. It was found that majority were males(52 /84).The age group most commonly involved was the 40-60 year group (64 /84).Majority had their diabetes diagnosed before diagnosis of tuberculosis (48 /84), 19 had diagnosis after TB diagnosis .Out of these 48 diagnosed diabetes,9 had controlled diabetes whereas 39 had uncontrolled diabetes.26 patients had the typical radiological lesions while 58 had atypical radiological manifestation with either patchy opacity or cavitations fanning out from hilar region, lower lobe involvement and multi lobe involvement.

The link between tuberculosis (TB) and diabetes mellitus (DM) has occupied the center stage of discussion. Experts have raised concern about the merging

epidemics of tuberculosis and diabetes particularly in the low to medium income countries like India and China that have the highest burden of TB in the world, and are experiencing the fastest increase in the prevalence of DM. There is good evidence that DM makes a substantial contribution to TB incidence. The huge prevalence of DM in India, may be contributing to the increasing prevalence of TB.

This review looks at the link between these two merging epidemics. We discuss the epidemiology, clinical features, microbiology and radiology, and management and treatment outcomes of patients with tuberculosis and diabetes mellitus.

The present work conducted showed that the prevalence of diabetes among the coastal region of Andhra Pradesh, India is as high as 14.5% of the total patients screened around six hundred. During the survey it was observed the 2% of the patients suffering with tuberculosis in all the age groups. In the age group among 31-40 years the prevalence of tuberculosis along with the diabetes is of 2% where estimation of HbA1c is very high. Normally, the prevalence of recognized diabetes mellitus below the 20 years age group is around 06% but between 21-30 years 16%, the highest incidence 30% was observed between 31-40 years. Further with the increase of the age of the people the incidence of diabetes mellitus abnormality reduced from 24% to 4% between 41-60 years of age. In the Group-C all the 50 patients 15 are identified with the diabetes mellitus with highest incidence of 30%. HbA1c in the group-C patients 8.92% having mean blood glucose 270 mg/dl gives a chance of reducing the immune system gives an opportunity to the TB germs to the establish. In the patient C13 age about 38 years and the intensity of tuberculosis is also high.

Tuberculosis and diabetes are major health problems in developing country like ours. Patients with diabetes mellitus are at a higher risk of developing tuberculosis. Presentation of tuberculosis in diabetes varied. Thus clinician should have strong degree of suspicion and investigate accordingly to institute early treatment. Objectives: To study clinical profile of pulmonary tuberculosis in diabetic patients. To study the radiographic patterns of pulmonary tuberculosis in diabetic patients. Total population studied was 100, with male preponderance of 72% with mean age group 54.9 years. Anorexia and cough were predominant symptoms with 59% and 51% respectively. Mean duration of diabetes was 6.6 years. Mean FBS was 234.4 mg/dl and PPBS being 345.5 mg/dl. Sputum positivity was less in age group >40 years. Cavitatory lesions were seen in 53% and fibrosis in 32%. There was a linear relation between the duration of diabetes mellitus and the development of tuberculosis. Poorly controlled hyperglycemia is associated with development of tuberculosis. Lower lung field tuberculosis was more common in diabetics. All the diabetics with abnormal weight loss, unexplained cough or sudden increase of insulin requirement should have sputum examination and chest x-ray done thus helping in early diagnosis and treatment.

The link between diabetes mellitus never occupied the centre-stage of discussions. Presently, an epidemic of diabetes is on both in developed and developing nations. With the recognition of this explosive, increase in the the world, a whole new field of issues related to interaction between diabetes and pulmonary tuberculosis has been thrown open. diabetes mellitus in TB patients was 21.69%. T whereas in non diabetic TB patent was 42.4 }13.4. Majority of the patients in DM with Tb and non diabetic TB group were on category I treatment (75.61% and 77.03%). Family history of diabe Alcoholism was observed commonly in diabetic

patients as compared to non diabetic patients with statistically significant difference. 31.71% diabetics were either overweight or obese whereas only 14.19% non diabetic overweight or obese.

Tuberculosis (TB) remains one of the leading killers among bacterial diseases worldwide. In the Philippines, the prevalence of culture-positive TB is estimated to be 5 per 1000 and that for sputum smear-positive pulmonary TB is 2 per 1000 based on the 2007 National Prevalence Survey. In addition, the prevalence of metabolic syndrome among Filipinos is 5% or approximately 5 million people have diabetes (DM) in the Philippines. With the Philippines being endemic for TB, compounded by an upward trend of DM, there is a need to jointly address this tandem disease interaction. This study aims to mount a coordinated response to TB/DM with the following expectations: 1) improve the case detection rate for TB, 2) facilitate early management among patients, and 3) prevent a significant number of severe disease

and deaths. A mixed methods are used to achieve the objectives including a systematic review and gray literature to estimate the magnitude of co-morbidity with TB and DM, records review specifically medical records on clinical charts of patients, cross-sectional survey on knowledge, attitudes and practices of health care providers on TB/DM screening and care, focus group discussions comprising of program managers and technical advisors of the National Tuberculosis Program, and costing exercise on bidirectional screening of TB in diabetic patients and vice-versa. Given the government's commitment to the nationwide control of TB, the under-explored frontier of TB among diabetic patients can be among the stretch goals towards increased case detection, management and prevention efforts. Likewise, the increasing prevalence of diabetes in the country and the associated risk of TB transmission in a TB endemic population suggest the need for raising awareness on the need for TB

screening. However, there is a body of programmatic and operational research questions to answer before an integrated approach to bidirectional screening can actually be implemented.

# MATERIALS AND METHODS

## 1. SOURCE OF DATA:

- Data is collected from patients who are attending OPD and admitted in BLDEU'S Shri B.M.Patil's medical college hospital and research centre, Bijapur.
- Period of study is from December 2014 to June 2016.

## 2. METHOD OF COLLECTION OF DATA:

**Inclusion Criteria:**

Patients of who will be attending OPD and who will be admitted in BLDEU`s Shri B M Patil medical college hospital Bijapur between December 2014 to June 2016.

- Patients with positive sputum smear for acid fast bacilli.
- Clinical symptoms and signs suggestive of pulmonary TB and evidence of chest x-ray, suggestive of pulmonary TB.

**Exclusion criteria:**

- Type 1 diabetes mellitus.
- Patients with diabetes mellitus.

## 3. TYPE OF STUDY

Cross sectional study

## 4. SAMPLE SIZE:

With 95%level of confidence, expected prevalence of Pulmonary Tuberculosis (based on review of literature) as 25%[6].The minimum sample size coming out to be 71 at ±10% margin of error

N=73 approx. 75

The formula used in the calculation[7]

$$N=\frac{Z^2 P*(1-P)}{D^2}$$

Where Z=1.96 at 95% level of confidence

P=prevalence of pulmonary tuberculosis.

D=margin of error

**Statistical Method**

1. Mean ± SD
2. Graphical presentation
3. $\chi^2$ test of association
4. Student t test

**INVESTIGATIONS**

CBC- Hb%, Tc, Dc, ESR

Urine Examination

Sputum smears for acid fast bacilli

Chest x ray

Oral glucose tolerance test

# RESULTS

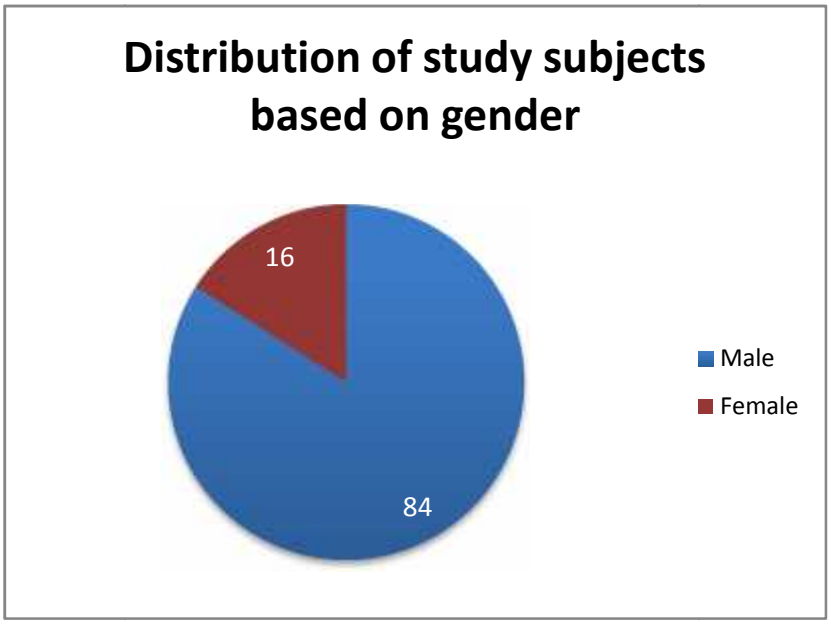
The present cross sectional study was conducted in the Department of Medicine , SHRI B M PATIL MEDICAL COLLEGE, VIJAYAPURA on patients with pulmonary tuberculosis. A total of 75 patients with positive sputum smear for acid fast bacilli or chest x-ray features suggestive of pulmonary tuberculosis aged more than 18 years and less than 65 years were selected for the study.

The data obtained was coded and entered into Microsoft Excel Worksheet. The data was analysed and the final results were tabulated as below.

**Table 1: sex distribution**

| Gender | Number | Percentage |
|---|---|---|
| Male | 63 | 84 |
| Female | 12 | 16 |

**GRAPH 1 : SEX DISTRIBUTION**

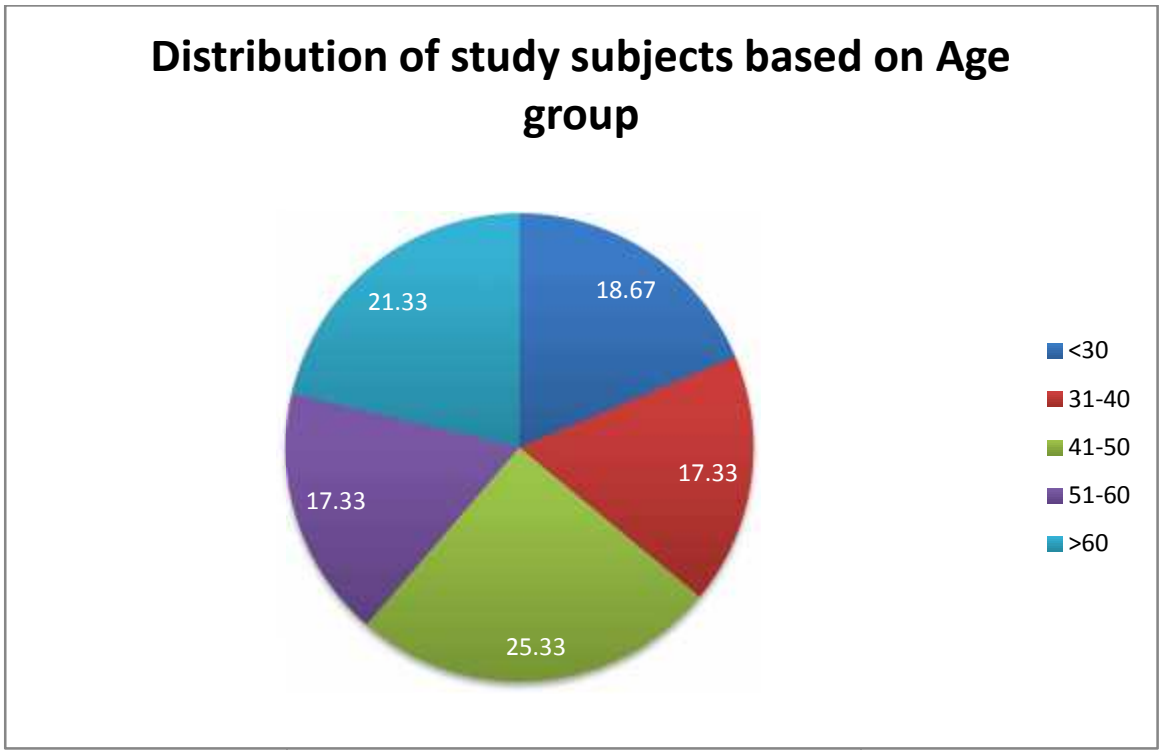



In this present study 84% patients were males and 16% were female with male to female ratio of 5.25:1

**TABLE 2 : AGE DISTRIBUTION**

| Age group | Number | Percentage |
|---|---|---|
| <30 | 14 | 18.67 |
| 31-40 | 13 | 17.33 |
| 41-50 | 19 | 25.33 |
| 51-60 | 13 | 17.33 |
| >60 | 16 | 21.33 |

**GRAPH 2: AGE DISTRIBUTION**

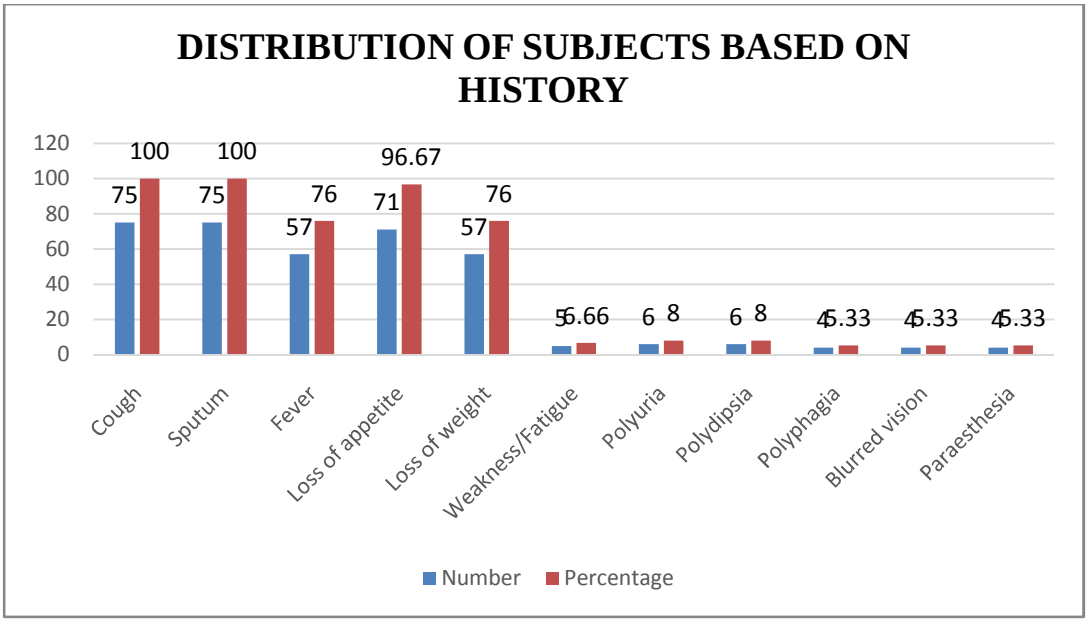



In this study the commonest age group was 41-50 (25.33%) followed by >60yeras (21.33%). However 18.67% and 17.33% patients had age between <30years and both 31-40 and 51-60 years respectively.

**TABLE 3 : HISTORY**

| History | Number | Percentage |
|---|---|---|
| Cough | 75 | 100 |
| Sputum | 75 | 100 |
| Fever | 57 | 76 |
| Loss of appetite | 71 | 96.67 |
| Loss of weight | 57 | 76 |
| Weakness/fatigue | 5 | 6.66 |
| Polyuria | 6 | 8 |
| Polydipsia | 6 | 8 |
| polyphagia | 4 | 5.33 |
| Blurred vision | 4 | 5.33 |
| Paraesthesia | 4 | 5.33 |

**GRAPH 3: HISTORY**

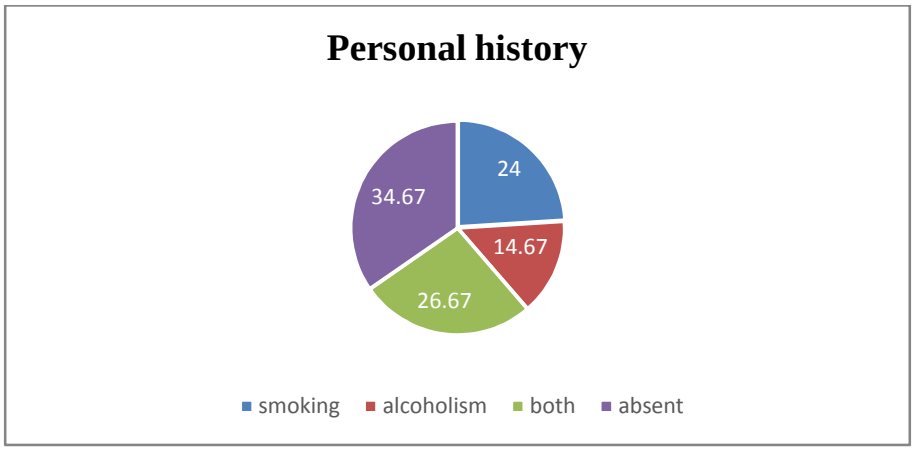



In the present study most of the patients presented with cough (100%) and expectoration (100%) followed by loss of appetite (96.67%), fever (76%), loss of weight (76%) and weakness and fatigue (6.66%). Among the diabetic symptoms 8% of patients presented with polyuria and polydipsia. The other diabetic symptoms were polyphagia, blurred vision, paresthesia (5.33% each).

**TABLE 4: PERSONAL HISTORY**

| Personal history | Number | Percentage |
|---|---|---|
| Smoking | 18 | 24.00 |
| Alcohol consumption | 11 | 14.67 |
| Both | 20 | 26.67 |
| No habits | 26 | 34.67 |
| Total | 75 | 100 |

**GRAPH 4: PERSONAL HISTORY**

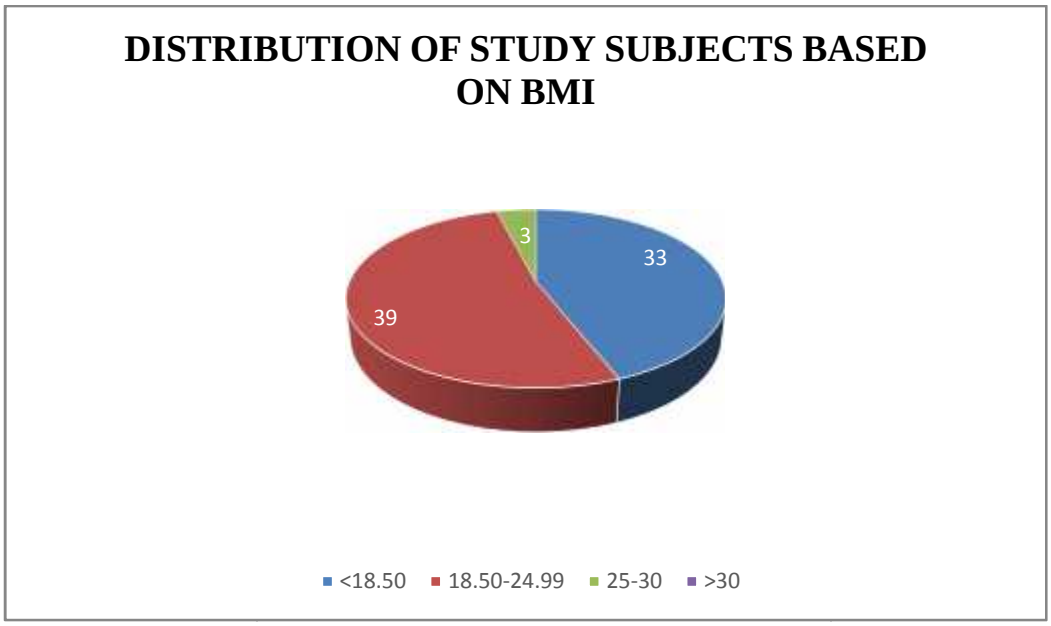



In the present study 24% were smokers and 14.67% consumed alcohol and in 26.67% had history of consumption of alcohol and smoking. However in 34.67% of patients had no habits of smoking and alcohol consumption.

**TABLE 5: BODY MASS INDEX**

| Body mass index | Number | Percentage |
|---|---|---|
| <18.50 | 33 | 44 |
| 18.50-24.99 | 39 | 52 |
| 25.00-30.00 | 3 | 4 |
| >30 | 0 | 0 |

**GRAPH 5: BODY MASS INDEX**




In this study among 52% of patients had normal BMI (18.5-24.9kg/$m^2$) and where as 4% were overweight (25-30kg/$m^2$).44% of patients were underweight (<18.50kg/$m^2$).

**TABLE 6: VITALS**

| Vitals | Mean | SD | Median | Minimum | Maximum |
|---|---|---|---|---|---|
| Pulse | 83.44 | 13.06 | 80.00 | 64 | 140 |
| SBP | 106.42 | 10.59 | 100 | 90 | 150 |
| DBP | 70.05 | 7.10 | 70.00 | 60.00 | 100 |

Overall the mean pulse of the study population was 83.44 ± 13.06 bpm and the median pulse was 80 bpm with range being 64 bpm as minimum and 140 bpm as maximum.

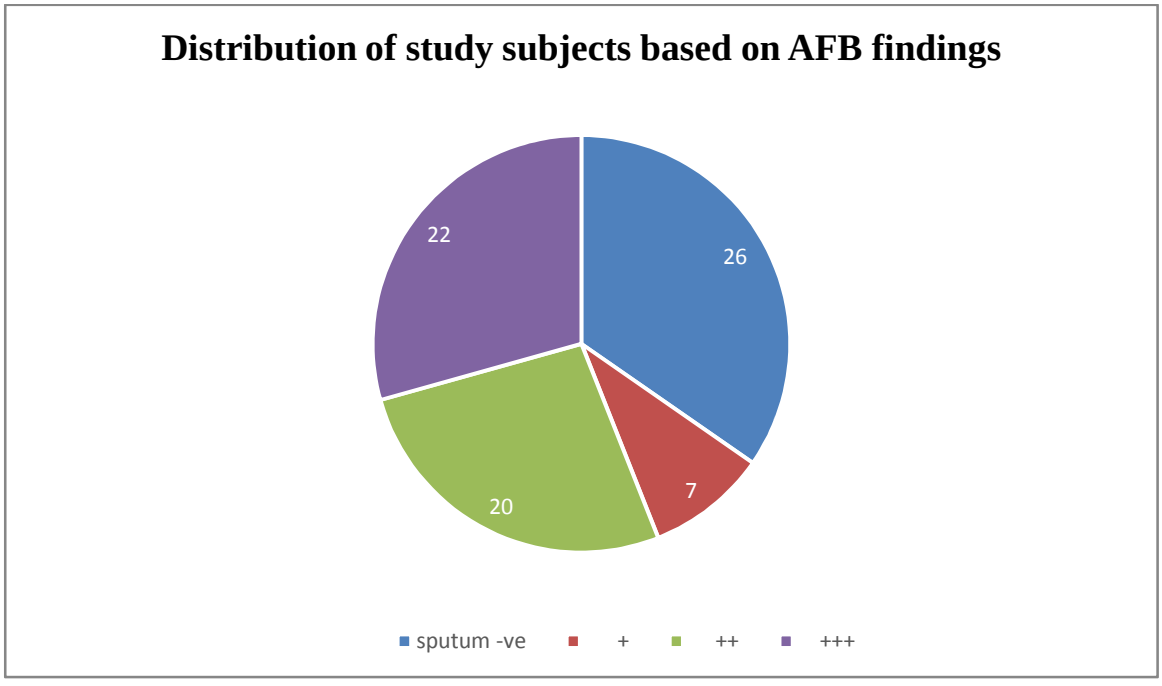
The systolic blood pressure was 106.42 ± 10.59 mm Hg. The median systolic blood pressure was 100 mm Hg with range being 90 mm Hg as minimum and 150 mm Hg as maximum.

The diastolic blood pressure was 70.05 ± 7.10 mm Hg and median systolic blood pressure was 60 mm Hg with range being 60.00 mm Hg as minimum and 100 mm Hg as maximum.

**TABLE 7: SPUTUM FOR ACID FAST BACILLI**

| AFB findings (sputum) | Number | Percentage |
|---|---|---|
| Sputum –ve | 26 | 34.66 |
| + | 7 | 9.33 |
| ++ | 20 | 26.67 |
| +++ | 22 | 29.33 |

**GRAPH 6: SPUTUM FOR ACID FAST BACILLI**

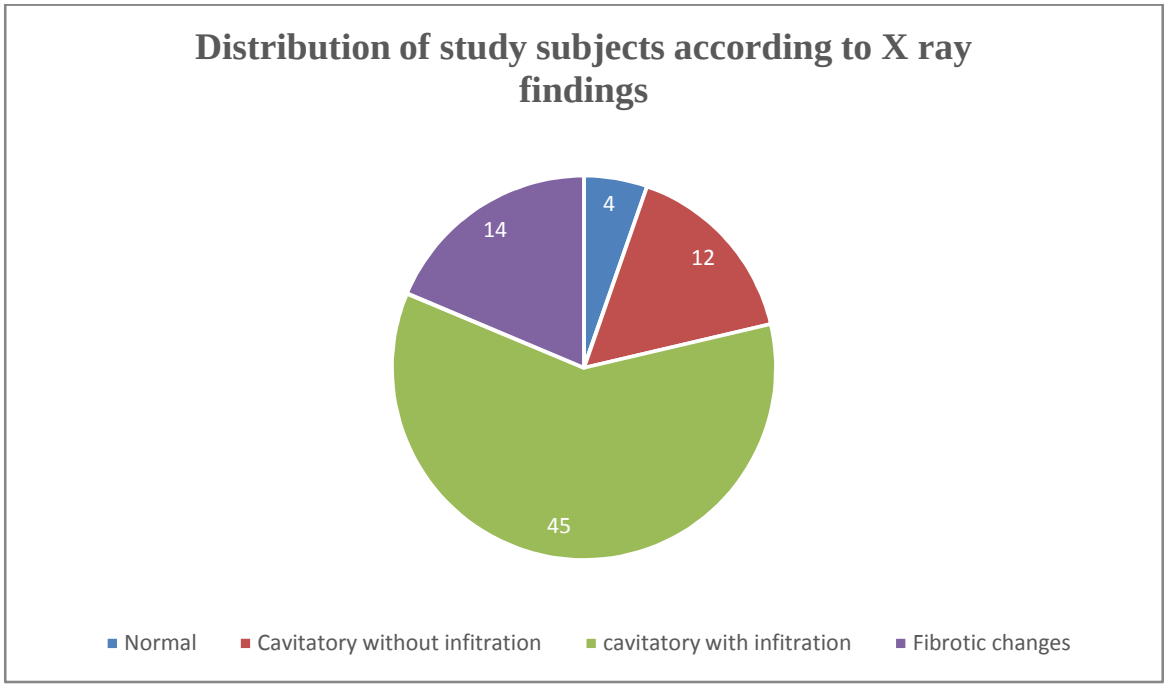



In this study AFB findings showed + in 9.33% patients, ++ in 26.67% and +++ in 29.33%. 34.66% patients were negative for acid fast bacilli.

**TABLE 8: X RAY FINDINGS**

| X ray findings | Number | Percentage |
|---|---|---|
| Normal | 4 | 5.33 |
| Cavitatory without Infiltration | 12 | 16 |
| Cavitatory with infiltration | 45 | 60 |
| Fibrotic changes | 14 | 18.67 |

**GRAPH 7: X-RAY FINDINGS**

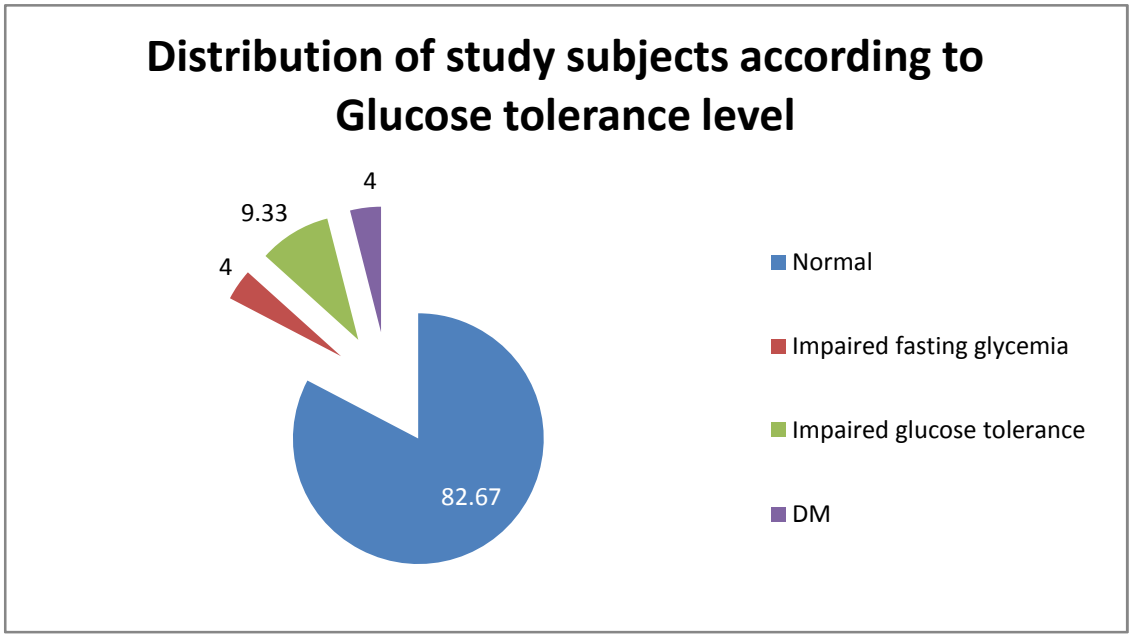



In the present study on chest x-ray almost 16 % of the patients had cavitatory lesions without infiltration. In 18.67% and 60% of patients fibrotic changes and cavitatory lesions with infiltration were noted. However, in 5.33% patients, chest x-ray was normal.

**TABLE 09: GLUCOSE TOLERANCE TEST**

| Glucose tolerance | Number | Percentage |
|---|---|---|
| Normal | 62 | 82.67 |
| Impaired fasting glycemia | 3 | 4 |
| Impaired glucose tolerance | 7 | 9.33 |
| DM | 3 | 4 |

**GRAPH 8: GLUCOSE TOLERANCE TEST**




In the present study 82.67% patients GTT was normal (fasting <110mg/dl and 2hrs <140mg/dl). In 9.33% patients have impaired glucose tolerance test and 4% patients had impaired fasting glycemia and other 4% have diabetes milletus was diagnosed.

**TABLE 10: FINAL DIAGNOSIS OF DM BASED ON FBS AND PPBS**

| Diagnosis | Number | Percent | Number | Percent |
|---|---|---|---|---|
| Confirmed | 3 | 100.00 | 3 | 100.00 |
| Not confirmed | 0 | 0.00 | 0 | 0.00 |

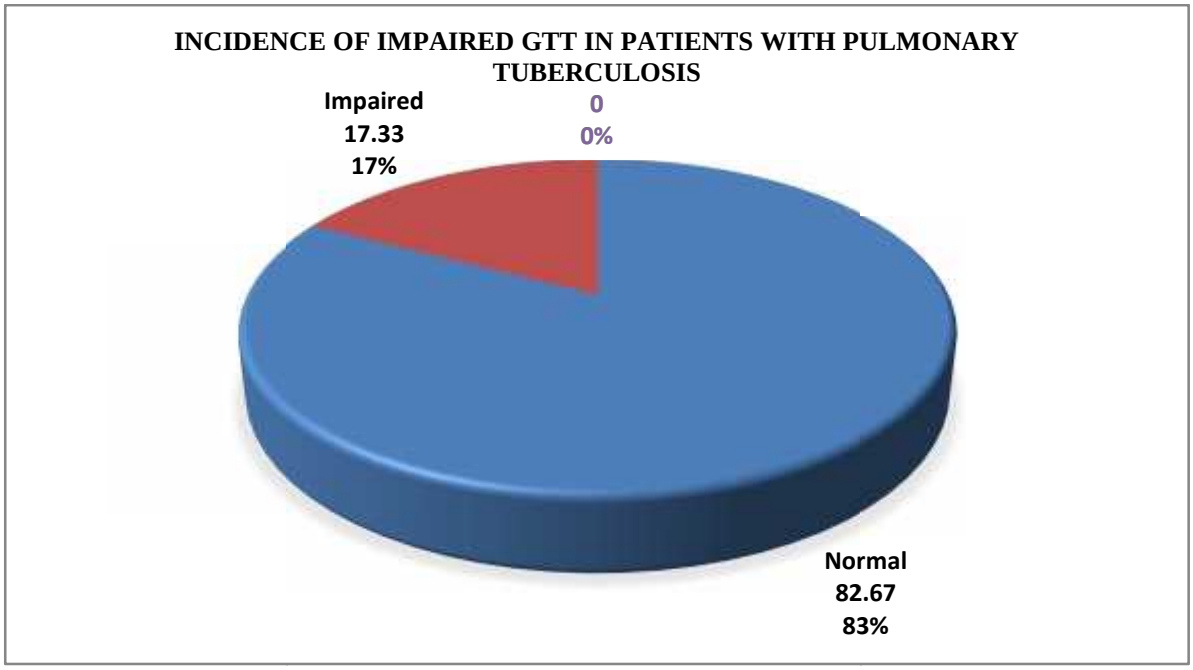
In the present study 4% patients with diabetes mellitus (Fasting > 126 mg/dL and 2 hours > 200 mg/dL) based on glucose tolerance test were subjected to FBS and PPBS. These test confirmed diagnosis of diabetes mellitus among all the (100%) patients.

**TABLE 11. INCIDENCE OF IMPAIRED GLUCOSE TOLERANCE IN PATIENTS WITH PULMONARY TUBERCULOSIS**

Distribution (n=75)

| Glucose tolerance | Number | Percentage |
|---|---|---|
| Normal | 62 | 82.67 |
| Impaired | 13 | 17.33 |
| Total | 75 | 100.00 |

**GRAPH 09. INCIDENCE OF IMPAIRED GLUCOSE TOLERANCE IN PATIENTS WITH PULMONARY TUBERCULOSIS**

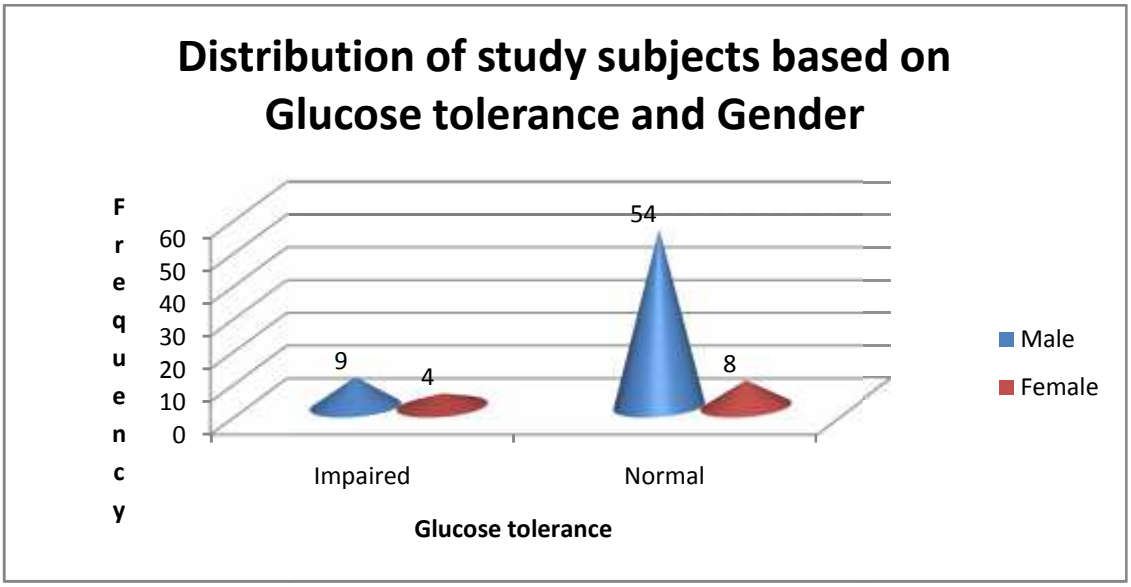



In the present study overall incidence of impaired glucose tolerance and DM was 17.33% (including 3 cases of confirmed diabetes mellitus)

**TABLE 12:ASSOCIATION OF IMPAIRED GLUCOSE TOLERANCE WITH SEX**

| Gender | Impaired | Normal |
|---|---|---|
| Male | 9 | 54 |
| Female | 4 | 8 |
| Chi square | 2.55 | |
| P value | 0.1101 | |

**GRAPH 10: DISTRIBUTION OF STUDY SUBJECTS BASED ON GLUCOSE TOLERANCE AND GENDER**

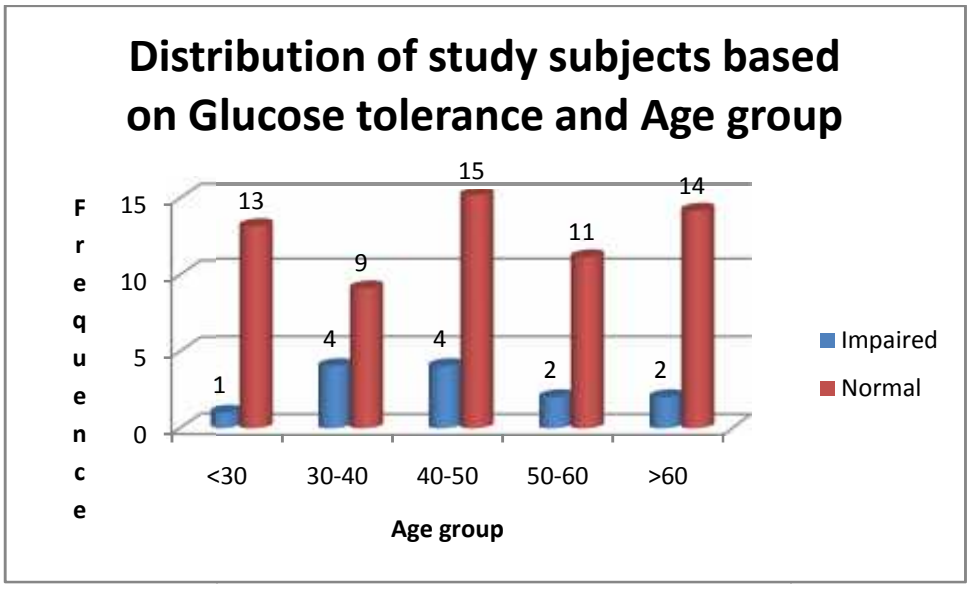



In the present study 53.33% of female had impaired glucose tolerance compared 12% males. Though females showed higher impaired glucose tolerance compared to males, this difference was statistically not significant (p=0.11).

**TABLE 13: ASSOCIATION OF IMPAIRED GLUCOSE TOLERANCE WITH AGE**

| Age group | Impaired | Normal |
|---|---|---|
| <30 | 1 | 13 |
| 30-40 | 4 | 9 |
| 40-50 | 4 | 15 |
| 50-60 | 2 | 11 |
| >60 | 2 | 14 |
| Chi square | 3.13 | |
| Df | 4 | |
| P value | 0.5361 | |

**GRAPH 12: ASSOCIATION OF IMPAIRED GLUCOSE TOLERANCE WITH AGE**

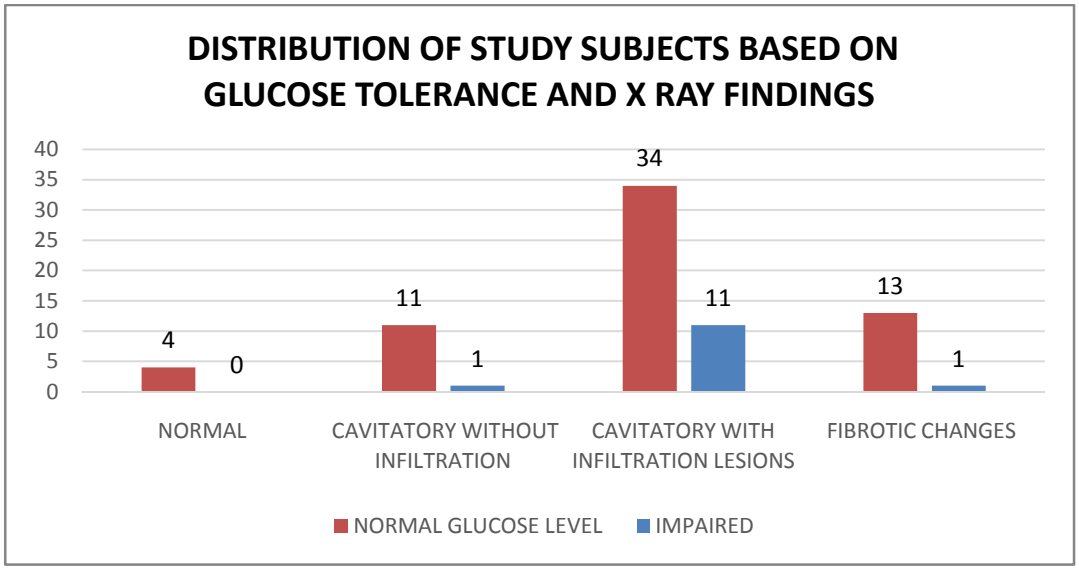



In the present study, 1.33%, 5.33%, 5.33% ,2.66% and 2.66%patients aged between <30, 30-40,40-50,50-60 and age more than 60 had impaired glucose tolerance. However this difference was statistically not significant (p=0.5361).

**TABLE 14: ASSOCIATION OF IMPAIRED GLUCOSE TOLERANCE WITH XRAY FINDING**

| X ray findings | Impaired | Normal-1Glucose level |
|---|---|---|
| Normal | 0 | 4 |
| Cavitatory without Infiltration | 1 | 11 |
| Cavitatory lesions with Infiltration | 11 | 34 |
| Fibrotic changes | 1 | 13 |
| Chi square | 4.11 | |
| Df | 3 | |
| P value | 0.2488 | |

**GRAPH 12: DISTRIBUTION OF STUDY SUBJECTS BASED ON GLUCOSE TOLERANCE AND X RAY FINDINGS**




In this study 8.33% of patients showing cavitatory lesions without infiltration on chest X-ray had impaired glucose tolerance followed by 7.14% with those having fibrotic changes followed by 24.44% having cavitatory lesions with infiltration changes in x ray. No statistically significant association of chest X-ray findings with impaired glucose tolerance was found in the present study.

# DISCUSSION

A high incidence of glucose intolerance in patients with active tuberculosis has been reported by a number of workers[101,02,03]. Occult glucose intolerance could either be a cause for the development of pulmonary tuberculosis or some endocrine abnormality may predispose to both impaired glucose tolerance and tuberculosis[104]. Tuberculosis and diabetes mellitus are very common diseases of Asia especially India[105]. Higher prevalence of tuberculosis in diabetic patients is well known fact[106,07], the suspected reason being decreased immune response in diabetic patients and hyperglycemia as a good growth medium for tuberculosis bacilli. The impaired glucose tolerance in a tuberculosis population is also being increasingly realized.

The present study was an attempt to find the incidence of impaired glucose tolerance in patients with pulmonary tuberculosis.

The present one year cross sectional study was conducted in the Department of Medicine, Shri B M Patil Medical College Hospital And Research Centre , Vijayapura, on patients admitted with pulmonary tuberculosis. A total of 75 patients with positive sputum smear for acid fast bacilli or chest x-ray features suggestive of pulmonary tuberculosis aged more than 25 years and less than 65 years were selected for the present study.

The present study of 75 cases showed overall incidence of impaired glucose tolerance as 17.33% in patients with pulmonary tuberculosis. Among 82.67% patients GTT was normal (Fasting < 110 mg/dL and 2 hours < 140 mg/dL). In 13.33% of patients impaired glucose tolerance (Fasting < 126 mg/Dl and 2 hours > 140 mg/dL) was observed , impaired fasting glycemia in 4% of patients and among 4% of patients diabetes mellitus (Fasting > 126 mg/dL and 2 hours > 200 mg/dL) was diagnosed.

The 4% patients with diabetes mellitus (Fasting > 126 mg/dL and 2 hours > 200 mg/dL) based on glucose tolerance test were subjected to FBS and PPBS. These tests confirmed diagnosis of diabetes mellitus among all the (100%) patients.

In the present study males outnumbered females (84% males versus 16% females) with male to female ratio of 5.25:1. The most common age group was 41-50 years (25.33%) followed by age >60 years (21.33%). However, the present study showed no statistically significant association of sex and age with impaired glucose tolerance. Overall TB continues to infect an estimated one-third of the worlds population, to cause disease in 8.8 million people per year, and to kill 1.6 million of those afflicted. The global burden of diabetes mellitus (DM) is expected to rise from an estimated 180 million prevalent cases currently to a predicted 366 million by 2030[8], with the greatest increase projected in the developing world. To date very few studies have reported the incidence of diabetes in patients with pulmonary tuberculosis.

A study by Jain MK et al[18]**,** reported that out of the 106 patients of pulmonary tuberculosis (all aged 30 years and above) 18 (16.98 %) had abnormal Glucose Tolerance Test (GTT) of which 2 (1.88%) had impaired fasting glycemia, 11 (10.34 %) had impaired glucose tolerance and 5 (4.7 %) were frankly diabetic. Yamagishi et al[89], reported 14.1% patients diagnosed with pulmonary tuberculosis had impaired glucoce tolerance test. Firsova et al[90], reported 10.8% patients of pulmonary tuberculosis had impaired glucoce tolerance test. Gupta et al[91], reported 9.7% patients of pulmonary tuberculosis with impaired glucoce tolerance. Roy Choudary et al[92], reported 27.25% patients of pulmonary tuberculosis had impaired glucoce tolerance test. These findings were comparable with the present study except the study done by Choudary Roy et al[92].

A case series by Deshmukh et al[85] with 138 TB-DM patients revealed that 82.6% of the study population was above 45 years of age and there was a male preponderance. In another study by Tripathi et al,the authors observed 55% of TB-DM group were underweight and this group was mostly more than 40 years of age. In the present study 52% of patients had normal BMI , 44 % of the patients were underweight and the remaining 4 % were in the overweight category.

The commonest presentation of pulmonary tuberculosis in the present study was Cough and expectoration of sputum (100% each) followed by loss of appetite (96.67% ) followed by fever(76%).History of loss of weight was noted in 76 % of cases .

The diabetic symptoms of polyuria and polydipsia were seen in 8% of patients and other symptoms of polyphagia , blurred vision and paresthesia were noted in 5.33 % of patients .

All the patients in the present study were subjected for sputum examination with 2 samples being taken, one at the time of admission and the other subsequent day early morning. In the present study AFB findings showed + in 9.33 % patients, ++ in 26.67 % patients , +++ in 29.33 % and 34.66% patients were negative for AFB.In the present study , 65.3 % of the patients turned out to be sputum positive for pulmonary tuberculosis .

On examination of the chest x-ray of the subjects, 16 % of the patients had cavitatory lesions without infiltration. In 18.67% and 60% of patients fibrotic changes and cavitatory lesions with infiltration were noted. However, in 5.33% patients, chest x-ray was normal.

In the present study 8.33% of patients showing cavitatory lesions without infiltration on chest X-ray had impaired glucose tolerance followed by 7.14% with

those having fibrotic changes followed by 24.44% having cavitatory lesions with infiltration changes in x ray. However no statistically significant association of chest X-ray findings with impaired glucose tolerance was found in the present study.

The limitations of the present study were smaller sample size and HbA1c was not done to confirm the diagnosis. More research with large sample size and other variables such as HbA1c, duration of symptoms and the presence of other diabetic complications would be more beneficial for better outcome of the study.

# CONCLUSION

The present study of 75 cases showed overall incidence of impaired glucose tolerance as 17.33% in patients with pulmonary tuberculosis. Among 82.67% patients GTT was normal (Fasting < 110 mg/dL and 2 hours < 140 mg/dL). In 13.33% of patients impaired glucose tolerance (Fasting < 126 mg/dL and 2 hours > 140 mg/dL) was recorded and among 4% patients diabetes mellitus (Fasting > 126 mg/dL and 2 hours > 200 mg/dL) was diagnosed. 4% patient had impaired fasting glycemia.

This study showed no statistically significant association of sex, age and chest X-ray findings in patients with pulmonary tuberculosis and diabetes mellitus.

# SUMMARY

The relation of pulmonary tuberculosis and development of altered impaired glucose tolerance are not well documented and very few studies have reported the incidence of diabetes mellitus in patients with pulmonary tuberculosis. The present study was aimed to find the incidence of impaired glucose tolerance in patients with pulmonary tuberculosis.

This one year cross sectional study was conducted in the Department of Medicine, Shri B M Patil Medical College Hospital And Research Centre , Vijayapura, on patients with pulmonary tuberculosis. A total of 75 patients with Patients with positive sputum smear for acid fast bacilli or chest x-ray features suggestive of pulmonary tuberculosis aged more than 25 years and less than 65 years were selected for the study.

The results showed majority of the patients were males (84%) with male to female ratio of 5.25:1. . The most commonest age group was 41-50 years (25.33%) followed by age >60 years (21.33%). The commonest presentation of pulmonary tuberculosis was cough and expectoration of sputum (100% each)followed by loss of appetite (96.67% ) followed by fever(76%). AFB findings showed +++ in 29.33% patients. On chest x-ray almost 60% of the patients had cavitatory lesions with infiltration . In 18.67% and 16% of patients fibrotic changes and cavitatory lesions without infiltration were noted.

This study of 75 cases showed overall incidence of impaired glucose tolerance as 17.33% in patients with pulmonary tuberculosis. Among 82.67% patients GTT was normal (Fasting < 110 mg/dL and 2 hours < 140 mg/dL). In 13.33% of patients impaired glucose tolerance (Fasting < 126 mg/dL and 2 hours> 140 mg/dL) was

recorded and among 4% patients diabetes mellitus (Fasting >126 mg/dL and 2 hours > 200 mg/dL) was diagnosed.

No statistically significant association of sex, age and chest X-ray findings was seen in patients with pulmonary tuberculosis and diabetes mellitus.

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# ANNEXURES

## ETHICAL CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 574/14
Date 21/11/14
B.L.D.E.U's Shri B.M. Patil Medical College.

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

**INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE**

The Ethical Committee of this college met on 22-11-2014 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "A Study of oral Glucose tolerance in pulmonary tuberculosis"

x x x

Name of P.G. student Dr. Sandeep. S. Kavalikai,
Dept of medicine

Name of Guide/Co-investigator Dr M.S. Mulimani
Prof & HOD. Medicine

for
DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL.
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutirization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents

**BLDEU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR- 586103**

**INFORMED CONSENT FOR PARTICIPATION**

**DISSERTATION/ RESEARCH**

I, the undersigned _____ S/O.D/O.W/O _____,aged ____years ordinarily resident of _____do here by state/declare that Dr Sandeep S Kavalikai of Shri B.M.Patil Medical College and Hospital has examined me thoroughly on _____at_____(place) and has explained to me in my own language _____that I am suffering from _____ disease (condition) and this disease/condition mimic following diseases _____Further Dr Sandeep S Kavalikai informed me that she is conducting dissertation/research titled "A STUDY OF ORAL GLUCOSE TOLERANCE IN PULMONARY TUBERCULOSIS" of Shri B.M.Patil Medical College, Bijapur. Under the guidance of Dr M S Mulimani requesting my participation in the study.

Apart from routine treatment procedure of doing the video assisted laproscopic thoracoscopy treatment, the pre operative, operative, post operative and follow up observations will be utilized for the study as the reference data.

Doctor has also informed me that during conduct of this procedure _____ like adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available.

Further Doctor has informed me that my participation in this study help in evaluation of results of the study which is useful reference for treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/video graphs taken upon me by the investigator will be kept secret and not accessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary based on information given to me, I can ask any clarification during the course of treatment/study related to Diagnosis, Procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or investigator can terminate me from the study at any time from the study but not the procedure of treatment & follow up unless I request to discharge.

In the view of anticipated or unexpected complications during the course of study, that I will be treated free of cost, as explained by the investigator.

After understanding the nature of dissertation or research, Diagnosis made, mode of treatment I the under signed Shri/Smt _____under my full conscious state of mind I agree to participate in the said research/Dissertation .

Signature of patient:

Signature of Doctor:

Witness 1

Witness 2

Date: Place:

# PROFORMA

## BLDE'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR

## "A STUDY OF ORAL GLUCOSE TOLERANCE IN PULMONARY" TUBERCULOSIS

Name: IP No:

Address: Date:

Age: Sex:

History

Presenting complaints

Cough:

Sputum:

Fever:

Loss of appetite:

Loss of weight:

Diabetic symptoms

Polyuria:

Polydipsia:

Polyphagia:

Blurred vision:

Parasthesia:

Others:

Personal Habits

Smoking: Alcoholism:

General physical examination

Height (Cms): Weight (Kgs):

Body Mass index:

Pulse rate (bpm):

Blood pressure (mm Hg): SBP: DBP:

**Investigations**

CBC: TC

DC

Hb

ESR

UR: Albumin

Sugar

Pus cells

Epitelial cells

Sputum smear for AFB

Sputum Sample

Chest X-ray

OGTT (mg/dL)

Fasting:

1 hour:

2 hour

## KEY TO MASTER CHART

| | | |
|---|---|---|
| Y | - | Yes |
| N | – | No |
| CXR | – | Chest x-ray |
| AFB | – | Acid fast bacilli |
| N | – | Normal |
| f | – | Fibrosis |
| ci | – | Cavitatory without infiltration |
| ic | - | Infiltration with cavitatory |

**MASTER CHART**

| Serial Number | In /Out patient Number | Sex | Age (Years) | History | | | | | | Diabetic symptoms | | | | | Habits | | General physical examination | | | | | | Investigations | | | | Fasting blood sugar (mg/dL) | Post prandial blood sugar (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Cough | Sputum | Fever | Loss of appetite | Loss of weight | Weakness/fatigue | Polyuria | Polydipsia | Polyphagia | Blurred vision | Parasthesia | Smoking | Alcoholism | Height (Cms) | Weight (Kgs) | BMI (Kg/m 2 ) | (mm Hg) | | Pulse (bpm) | AFB | | | | | |
| | | | | | | | | | | | | | | | | | | | | Systolic | Diastolic | | sputum sample | CXR | fasting | 2 hour | | |
| 1 | 39363 | F | 35 | Y | Y | N | Y | Y | N | Y | N | N | N | N | N | N | 150 | 50 | 22.2 | 110 | 70 | 64 | +++ | n | 120 | 190 | - | - |
| 2 | 1604 | M | 42 | Y | Y | Y | Y | Y | N | N | Y | N | N | N | Y | N | 166 | 45 | 16.3 | 130 | 90 | 110 | +++ | ci | 6 | 106 | - | - |
| 3 | 4351 | M | 78 | Y | Y | N | Y | Y | N | N | N | N | N | N | Y | N | 155 | 45 | 20 | 110 | 70 | 82 | ++ | ci | 91 | 136 | - | - |
| 4 | 4070 | M | 42 | Y | Y | N | Y | Y | Y | N | N | N | N | N | Y | N | 165 | 50 | 18.51 | 90 | 60 | 70 | +++ | ic | 140 | 200 | 150 | 230 |
| 5 | 12595 | M | 55 | Y | Y | Y | Y | Y | N | Y | N | Y | N | N | N | Y | 160 | 56 | 20.12 | 130 | 80 | 84 | +++ | ci | 117 | 105 | - | - |
| 6 | 12329 | M | 43 | Y | Y | Y | Y | Y | N | N | Y | N | N | N | N | Y | 154 | 41 | 17.46 | 100 | 80 | 80 | ++ | ci | 87 | 112 | - | - |
| 7 | 13660 | M | 71 | Y | Y | N | Y | Y | N | N | N | N | N | N | Y | Y | 150 | 46 | 18.56 | 110 | 70 | 80 | +++ | n | 84 | 96 | - | - |
| 8 | 4804 | M | 66 | Y | Y | N | N | N | N | Y | N | N | N | N | Y | N | 170 | 50 | 17.30 | 150 | 100 | 76 | + | ic | 84 | 113 | - | - |
| 9 | 4410 | M | 40 | Y | Y | Y | Y | N | N | N | Y | Y | N | N | Y | N | 166 | 60 | 21.81 | 120 | 70 | 80 | + | ci | 100 | 116 | - | - |
| 10 | 4809 | M | 38 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 166 | 39 | 15.2 | 100 | 70 | 90 | +++ | ic | 90 | 110 | - | - |
| 11 | 4402 | M | 34 | Y | Y | Y | Y | Y | N | Y | N | N | N | N | N | N | 165 | 50 | 25.73 | 110 | 60 | 130 | ++ | ci | 108 | 130 | - | - |
| 12 | 7528 | M | 28 | Y | Y | Y | Y | Y | N | N | Y | Y | N | N | Y | Y | 165 | 70 | 25.73 | 130 | 70 | 76 | ++ | ic | 100 | 90 | - | - |
| 13 | 6060 | M | 70 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | N | 175 | 40 | 13.07 | 100 | 70 | 90 | +++ | ci | 100 | 90 | - | - |
| 14 | 7693 | M | 40 | Y | Y | Y | Y | Y | N | Y | N | N | N | N | Y | N | 171 | 50 | 17.85 | 130 | 80 | 80 | +++ | ic | 110 | 120 | - | - |
| 15 | 7952 | M | 28 | Y | Y | Y | Y | Y | N | N | N | Y | N | N | N | Y | 160 | 55 | 21.15 | 110 | 70 | 80 | ++ | ic | 90 | 110 | - | - |
| 16 | 3896 | F | 45 | Y | Y | Y | Y | Y | N | N | Y | N | N | N | N | N | 158 | 55 | 22.08 | 90 | 60 | 140 | +++ | ic | 122 | 146 | 160 | 226 |
| 17 | 3890 | F | 41 | Y | Y | N | N | N | N | Y | N | N | N | N | N | N | 156 | 50 | 22.22 | 100 | 60 | 96 | ++ | ic | 90 | 140 | - | - |
| 18 | 38870 | F | 29 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 156 | 48 | 22.22 | 110 | 70 | 80 | ++ | ic | 110 | 124 | - | - |
| 19 | 15189 | M | 55 | Y | Y | Y | Y | Y | N | N | Y | N | N | N | Y | N | 170 | 50 | 18.4 | 120 | 70 | 70 | +++ | ci | 80 | 130 | - | - |
| 20 | 19386 | M | 45 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | N | 165 | 45 | 16.54 | 100 | 70 | 72 | + | ic | 85 | 120 | - | - |

| Serial Number | In /Out patient Number | Sex | Age (Years) | History | | | | | | Diabetic symptoms | | | | | Habits | | General physical examination | | | | | | Investigations | | | | Fasting blood sugar (mg/dL) | Post prandial blood sugar (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Cough | Sputum | Fever | Loss of appetite | Loss of weight | Weakness/fatigue | Polyuria | Polydipsia | Polyphagia | Blurred vision | Parasthesia | Smoking | Alcoholism | Height (Cms) | Weight (Kgs) | BMI (Kg/m 2 ) | (mm Hg) | | Pulse (bpm) | AFB | | OGTT (mg/dL) | | | |
| | | | | | | | | | | | | | | | | | | | | Systolic | Diastolic | | sputum sample | CXR | Fasting | 2 hour | | |
| 21 | 16394 | M | 74 | Y | Y | Y | Y | Y | Y | N | N | N | N | N | Y | Y | 160 | 50 | 18.4 | 120 | 70 | 82 | n | ic | 75 | 130 | - | - |
| 22 | 19328 | M | 50 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | Y | 170 | 45 | 15.57 | 110 | 70 | 70 | +++ | ic | 140 | 200 | 160 | 240 |
| 23 | 16837 | M | 35 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 30 | 11.71 | 110 | 60 | 80 | +++ | ci | 100 | 120 | - | - |
| 24 | 13380 | M | 45 | Y | Y | Y | Y | Y | Y | N | N | N | N | N | Y | N | 160 | 47 | 15.8 | 90 | 60 | 80 | n | ic | 116 | 150 | - | - |
| 25 | 15377 | F | 30 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 170 | 34 | 15.2 | 100 | 80 | 98 | n | ic | 80 | 110 | - | - |
| 26 | 21803 | F | 25 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 160 | 45 | 17.57 | 110 | 64 | 104 | n | ic | 100 | 110 | - | - |
| 27 | 21589 | M | 50 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 112 | 70 | 70 | + | n | 90 | 110 | - | - |
| 28 | 24628 | M | 19 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 160 | 40 | 15.62 | 120 | 70 | 78 | n | ci | 140 | 220 | 150 | 272 |
| 29 | 25296 | M | 65 | Y | Y | Y | Y | N | N | N | N | N | N | N | N | N | 165 | 50 | 18.36 | 110 | 70 | 96 | +++ | ic | 118 | 148 | - | - |
| 30 | 24547 | M | 62 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | N | 160 | 40 | 15.62 | 110 | 70 | 72 | +++ | ic | 109 | 80 | - | - |
| 31 | 24852 | M | 66 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 40 | 15.62 | 110 | 70 | 72 | n | ic | 100 | 80 | - | - |
| 32 | 24627 | M | 45 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | N | 160 | 40 | 15.6 | 110 | 70 | 78 | +++ | ic | 100 | 90 | - | - |
| 33 | 24831 | M | 50 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 165 | 45 | 16.54 | 108 | 70 | 80 | +++ | ci | 95 | 85 | - | - |
| 34 | 23205 | M | 65 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | Y | 170 | 45 | 15.57 | 110 | 70 | 78 | n | ic | 110 | 150 | - | - |
| 35 | 22909 | M | 75 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | Y | 175 | 55 | 17.97 | 102 | 60 | 98 | n | f | 63 | 107 | - | - |
| 36 | 21414 | M | 45 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | Y | 150 | 30 | 13.33 | 90 | 60 | 110 | n | ic | 100 | 90 | - | - |
| 37 | 19977 | M | 45 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 110 | 70 | 80 | n | ci | 70 | 126 | - | - |
| 38 | 19834 | M | 50 | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | N | 160 | 50 | 19.53 | 110 | 70 | 110 | - | f | 100 | 90 | - | - |
| 39 | 20094 | M | 70 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 110 | 70 | 80 | n | ic | 103 | 144 | - | - |
| 40 | 825 | M | 45 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 100 | 70 | 70 | n | f | 90 | 118 | - | - |

| Serial Number | In /Out patient Number | Sex | Age (Years) | History | | | | | | Diabetic symptoms | | | | | Habits | | General physical examination | | | | | | Investigations | | | | Fasting blood sugar (mg/dL) | Post prandial blood sugar (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Cough | Sputum | Fever | Loss of appetite | Loss of weight | Weakness/fatigue | Polyuria | Polydipsia | Polyphagia | Blurred vision | Parasthesia | Smoking | Alcoholism | Height (Cms) | Weight (Kgs) | BMI (Kg/m 2 ) | (mm Hg) | | Pulse (bpm) | AFB | | OGTT (mg/dL) | | | |
| | | | | | | | | | | | | | | | | | | | | Systolic | Diastolic | | sputum sample | CXR | Fasting | 2 hour | | |
| 41 | 42045 | M | 40 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 100 | 80 | 70 | n | f | 90 | 100 | - | - |
| 42 | 2196 | F | 63 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 140 | 35 | 23.97 | 100 | 70 | 70 | n | ic | 97 | 105 | - | - |
| 43 | 2089 | M | 26 | Y | Y | N | Y | N | N | N | N | N | N | N | N | N | 170 | 50 | 17.30 | 100 | 70 | 80 | ++ | ic | 90 | 100 | - | - |
| 44 | 2109 | M | 55 | Y | Y | N | Y | N | Y | N | N | N | N | N | N | N | 165 | 45 | 16.5 | 100 | 70 | 72 | ++ | f | 100 | 110 | - | - |
| 45 | 2617 | M | 42 | Y | Y | Y | N | Y | N | N | N | N | N | N | N | N | 165 | 50 | 18.38 | 100 | 70 | 80 | n | ic | 84 | 110 | - | - |
| 46 | 1725 | F | 60 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 138 | 50 | 26.31 | 100 | 70 | 80 | +++ | ic | 100 | 110 | - | - |
| 47 | 2315 | M | 60 | Y | Y | N | Y | N | N | N | N | N | N | N | Y | N | 154 | 50 | 20.04 | 100 | 80 | 70 | ++ | n | 120 | 160 | 166 | 220 |
| 48 | 2056 | M | 40 | Y | Y | Y | N | N | N | N | N | N | N | N | N | N | 158 | 50 | 20.08 | 110 | 80 | 80 | n | f | 100 | 120 | - | - |
| 49 | 6753 | M | 55 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 150 | 50 | 19.53 | 110 | 60 | 80 | +++ | ic | 118 | 164 | - | - |
| 50 | 9167 | M | 63 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 100 | 70 | 80 | +++ | ic | 96 | 100 | - | - |
| 51 | 10593 | F | 21 | Y | Y | N | Y | Y | N | N | N | N | N | N | N | N | 155 | 50 | 20.83 | 100 | 60 | 80 | n | f | 100 | 110 | - | - |
| 52 | 4665 | M | 46 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | Y | 150 | 38 | 16.80 | 90 | 60 | 100 | ++ | ic | 90 | 110 | - | - |
| 53 | 2615 | M | 35 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.53 | 100 | 70 | 80 | ++ | ic | 100 | 80 | - | - |
| 54 | 4168 | M | 30 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.33 | 120 | 70 | 80 | n | ic | 120 | 70 | - | - |
| 55 | 3044 | M | 35 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 168 | 55 | 19.40 | 100 | 80 | 80 | ++ | f | 100 | 90 | - | - |
| 56 | 4983 | M | 32 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 168 | 55 | 20.56 | 110 | 70 | 80 | + | ic | 80 | 120 | - | - |
| 57 | 4776 | M | 25 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | N | 170 | 55 | 19.03 | 100 | 60 | 80 | n | ic | 100 | 110 | - | - |
| 58 | 4625 | M | 45 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 45 | 17.57 | 100 | 60 | 80 | ++ | ic | 100 | 80 | - | - |
| 59 | 3798 | M | 58 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 170 | 50 | 2.89 | 100 | 70 | 80 | ++ | f | 80 | 124 | - | - |
| 60 | 2854 | M | 20 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 170 | 60 | 20.76 | 100 | 70 | 80 | n | ic | 130 | 220 | 186 | 276 |

| Serial Number | In /Out patient Number | Sex | Age (Years) | History | | | | | | Diabetic symptoms | | | | | Habits | | General physical examination | | | | | | Investigations | | | | Fasting blood sugar (mg/dL) | Post prandial blood sugar (mg/dL) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | | | | | (mm Hg) | | | AFB | | OGTT (mg/dL) | | | |
| | | | | Cough | Sputum | Fever | Loss of appetite | Loss of weight | Weakness/fatigue | Polyuria | Polydipsia | Polyphagia | Blurred vision | Parasthesia | Smoking | Alcoholism | Height (Cms) | Weight (Kgs) | BMI (Kg/m 2 ) | Systolic | Diastolic | Pulse (bpm) | sputum sample | CXR | Fasting | 2 hour | | |
| 61 | 3003 | M | 55 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 150 | 38 | 16.89 | 100 | 80 | 100 | n | f | 100 | 110 | - | - |
| 62 | 2972 | M | 55 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 160 | 50 | 19.33 | 100 | 70 | 80 | n | ic | 80 | 90 | - | - |
| 63 | 26190 | M | 35 | Y | Y | N | Y | Y | N | N | N | N | N | N | N | N | 154 | 55 | 18 | 100 | 70 | 80 | n | f | 100 | 112 | - | - |
| 64 | 2789 | M | 32 | Y | Y | Y | Y | Y | Y | N | N | N | N | N | Y | Y | 155 | 55 | 22.91 | 100 | 70 | 90 | ++ | ic | 90 | 100 | - | - |
| 65 | 27660 | M | 65 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | Y | 156 | 50 | 20.57 | 110 | 70 | 80 | n | ic | 82 | 110 | - | - |
| 66 | 27947 | F | 22 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 150 | 40 | 2.25 | 100 | 70 | 80 | ++ | ic | 100 | 136 | 186 | 256 |
| 67 | 19928 | M | 22 | Y | Y | N | Y | Y | N | N | N | N | N | N | N | N | 155 | 50 | 22.22 | 120 | 70 | 80 | + | f | 86 | 124 | - | - |
| 68 | 16282 | M | 52 | Y | Y | N | Y | Y | N | N | N | N | N | N | Y | N | 150 | 45 | 20 | 100 | 80 | 80 | +++ | ic | 86 | 124 | - | - |
| 69 | 23014 | M | 35 | Y | Y | N | Y | N | N | N | N | N | N | N | Y | Y | 154 | 50 | 21.73 | 100 | 70 | 80 | +++ | ic | 80 | 112 | - | - |
| 70 | 24055 | M | 25 | Y | Y | N | Y | Y | N | N | N | N | N | N | N | Y | 154 | 50 | 21.73 | 100 | 70 | 80 | n | ic | 78 | 110 | - | - |
| 71 | 24023 | M | 34 | Y | Y | Y | Y | Y | N | N | N | N | N | N | Y | N | 150 | 50 | 22.22 | 100 | 70 | 80 | +++ | f | 80 | 110 | - | - |
| 72 | 24271 | M | 25 | Y | Y | Y | Y | Y | N | N | N | N | N | N | N | N | 155 | 45 | 18.75 | 110 | 70 | 80 | +++ | ic | 80 | 106 | - | - |
| 73 | 23860 | F | 35 | Y | Y | N | Y | N | N | N | N | N | N | N | N | N | 145 | 40 | 19.04 | 100 | 70 | 90 | + | ic | 125 | 150 | 166 | 236 |
| 74 | 24646 | F | 45 | Y | Y | N | Y | Y | N | N | N | N | N | N | N | N | 140 | 35 | 17.87 | 100 | 70 | 100 | n | ic | 80 | 110 | - | - |
| 75 | 24433 | M | 50 | Y | Y | N | Y | Y | N | N | N | N | N | N | Y | N | 150 | 40 | 17.77 | 100 | 60 | 80 | n | f | 82 | 100 | - | - |