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INTRODUCTION

BACKGROUND

Tuberculosis is one of the oldest diseases known to affect man. It is the third most common cause of death worldwide. Every year, more than 9 million people are affected with tuberculosis (TB). Out of which 1.5 million deaths are reported per annum, which contributes to the vast majority of deaths in the developing world. One out of three in this world are affected with latent TB; which has a lifelong risk of acquiring active TB.

Around 350 million people are Diabetes. The prevalence of which is similar in both developed and developing countries. Around Eighty percentage (80%) of deaths due to diabetes is seen in low and middle-income countries. Estimation made that Universal Diabetes prevalence rise by 50% by 2030.

- People with chronic diseases such as diabetes are immune deficient so there is increased risk of progressing from latent to active TB.

- Diabetics have a 2-3 times increased risk of TB compared to non-diabetics.

- Around 10% of TB cases globally are found to be associated with diabetes.
Huge percentage of people who have diabetes and TB are either not diagnosed or diagnosed too late. Early diagnosis will help in improve care and control of both.

Each TB patients should be screened for diabetes.

( WHO Recommendation )

In high prevalent areas screening for TB in diabetic patients should be considered as a priority ( WHO Recommendation ).

Diabetics diagnosed with TB have a greater risk of death at the time of TB treatment or due to TB relapse after completion of treatment.

Treatments should be adequately emphasized for both TB and diabetes.
AIM OF THE STUDY

- To Study the prevalence of Tuberculosis among Diabetic patients.

- To study the pattern, presentation of tuberculosis and the factors influencing the prevalence among Diabetic patients.
REVIEW OF LITERATURE

Diabetes mellitus encloses a group of common metabolic disorders that have the common phenotype of hyperglycemia.

Diabetes mellitus is sub divided on the basis of the pathological process that leads to hyperglycemia

Classification

Type 1 Diabetes Mellitus

Type 1 A: Diabetes mellitus occurs due to autoimmune β cell destruction, which leads to insulin deficiency.

Type 1 B: Diabetes mellitus patients lack immunologic markers that signifies an autoimmune mediated destruction of β cells. Insulin deficiency in them occurs by unknown mechanisms and they are more prone for developing ketosis.
Type 2 Diabetes Mellitus

It encloses insulin resistance; increased glucose production, impaired insulin secretion. Both metabolic and genetic defects contribute for the development of common phenotype of hyperglycemia.

Other Specific Types of Diabetes Mellitus

1. Diseases of exocrine pancreas – pancreatitis, pancreatectomy, neoplasia etc.
2. Endocrine disorders – acromegaly, cushing’s syndrome, glucagonoma, etc.
3. Drug or chemical induced – vacor, pentamidine
4. Infections – CMV, congenital rubella, coxsackie.
5. Genetic syndromes – Turners, Down’s syndrome, klinefelter syndrome, Wolfram’s, etc.
6. Genetic defects of β cell functions with certain mutations.

Gestational Diabetes Mellitus

Maturityonset diabetes of the young (MODY)- characterized by Autosomal dominant inheritance, impairment of insulin production and early onset hyperglycemia.

Symptoms

❖ Polydipsia.
❖ Polyuria
Polyphagia

Fatiguability, irritability

Weight loss/gain

Blurring of vision

Pruritis vulvae, balanitis

Nausea, headache

Poorly controlled diabetes are associated with higher risk for infection and patients are prone to develop skin sepsis (boils) and genital-candidiasis and pruritis vulvae or balanitis.

Patients with type 2 DM have various clinical signs. More than 70% are overweight, and Obesity less common - developing countries. Hypertension is present in 50% of patients with type II diabetes mellitus.

**Diagnosis**

The National Diabetes Data Group and World Health Organization (WHO) on the basis of the spectrum of Fasting plasma glucose (FPG) and the response to an oral glucose load has issued a diagnostic criteria for diabetes mellitus.

Criteria for the diagnosis of DM:
- Symptoms of diabetes plus random blood glucose concentration (RBS) ≥ 200 mg/dl or
- Fasting plasma glucose (FPG) ≥ 126 mg/dl or
- 2 hour plasma glucose (PG) ≥ 200 mg/dl during an oral glucose tolerance test.

Glucose tolerance is subdivided into three (3) groups on basis of FPG.
- (FPG) < 100 mg/dl is considered as normal.
- (FPG) ≥ 100 mg/dl but (FPG) < 126 mg/dl - as Impaired fasting Glucose
- (FPG) ≥ 126 mg/dl- indicative of diabetes mellitus.

IGT - explained by the criteria as plasma glucose levels in persons between - 140 & 200 mg/dl- 2 hours after a 75 g oral glucose load.

Persons with IFG or IGT are at risk to develop - type 2 diabetes mellitus (>40% risk over the next five years) and coronary artery disease.

**DIABETES AND INFECTION**

Before the introduction of modern antimicrobial therapy, infection accounts for most of the mortality in diabetes. In the pre insulin era (from 1914 – 1922, 17.6% ) of death among diabetic patients were reported due to infection. With the advent of chemotherapeutic and antimicrobial agents, fewer and fewer deaths were considered to be due to infection. As for as morbidity is
concerned, diabetic patients are particularly more susceptible to respiratory tract infection, urosepsis and dermatological manifestation

**FACTORS CONTRIBUTING TO INFECTION**

With good control of diabetes, resistance to infection, seems to be normal. If blood sugar is controlled poorly, for eg. in the presence of diabetic ketoacidosis, the resistance is lowered due to impaired leukocyte function. In 1960, there was a report done by Priscilla White regarding 478 patients who lived 30 or more years with juvenile diabetes had high incidence of infections skin infection 55%, urinary tract infection in 28%, pulmonary tuberculosis in 6%

**BLOOD GLUCOSE EFFECT ON INFECTION**

In beginning of 20th century Lassar postulated that” infections were more Prevalent among diabetics because bacteria thrive in a high glucose medium”. Recent studies confirmed that some gram positive cocci prefer high concentration of glucose for growth. There is a definite correlation between presence of infection and mean level of plasma glucose.

Diabetes Mellitus, is said to be a secondary immune deficiency disorder by WHO, as the disease has the following characters:
1. Causes recovery when once the underlying disease is treated

2. Recurrent, extensive and chronic infections.

3. Cause impairment of at least one defence mechanism (e.g. polymorphonuclear leucocytes or lymphocyte response), that results in acquiring infection.

ALTERED IMMUNE MECHANISM IN DIABETES MELLITUS

CHEMOTAXIS:
Chemotaxis is a process in which polymorphonuclear cells migrate to the site of infection as a response to chemotactic substances secreted by microorganisms. In DM patients, there is a diminished chemotaxis that seems to correlate well with the glycemic status of the patients.

PHAGOCYTOSIS:
Phagocytosis is impaired in long standing uncontrolled diabetics, and it is associated with intrinsic defect of polymorphs due to increase in sialidase enzyme production and decrease in the sialic acid. When sugar is high it saturates lectin receptors and it fails to initiate phagocytosis.

KILLING ACTIVITY:
Killing activity are due to lysosomal enzymes, from the polymorphs after the formation of phagolysosome and it is due to both oxid’ative and nonoxidative metabolism. Uncontrolled blood sugar results in
impairment of killing activity and its killing activity is regained once the insulin therapy is started.

Lymphocyte Function:

In type 1 diabetes, there will be decreased no of lymphocytes, especially of (CD4 helper cells) and it may occurs due to decrease in insulin secretion or due to inefficacy. Normalization of blood sugar will reverses this effect. Due to deficiency of CD4, the individuals exhibit impairment in the antibody production against viral infection- eg. Hepatitis b

IMMUNOGLOBULINS:

In Diabetic patients low level of Ig particularly IgG and IgA are seen

COMPLEMENT

In Type 1 diabetes mellitus, 25% of cases found to have decreased C4 levels in relation with C4A null gene. Impairment or defect in other complements like C3 and C1q are also associated with diabetes
Is Local causes plays a significant role in infection in diabetics?

1. Hyperglycemia- causes dysfunction of endothelium and oxidative stress which plays a significant role in fungal and bacterial infection

2. Micro and Macrovascular causes anoxia and it results in proliferation of micro organism, which impairs the oxygen (02) dependent PMN (polymorphonucleocytes) function and impairs the functions of antimicrobial drugs.

**ENDOCRINE SYSTEM INFLUENCE ON INFECTION:**

The relationship of diabetes to endocrine glands other than the pancreas and the role of other hormones apart from insulin in host resistance to infection are extremely important. The anti-inflammatory effect of adrenal steroids attributed to

- decreased permeability of microvasculature,
- diminished antibody response and
- altered function of the reticuloendothelial system.

The precise role of thyroid hormones is not fully worked out.

**Vascular Insufficiency:**

Impairment in circulation contributes to significant level for infection of foot. The normal response to infection is increased local circulation. The response in the presence of vascular insufficiency is thrombosis and necrosis. It can lead to arteriosclerotic gangrene.
Effect of Malnutrition:

In diabetics, there is some degree of malnutrition at the cellular level due to metabolic effects. Perhaps the hepatic dysfunction with its consequent hypovitaminosis contributes for causation of pulmonary tuberculosis among diabetics. Depletion of liver glycogen content may play a role in increased intensity.

INFECTIVE COMPLICATIONS OF DIABETES MELLITUS:

*Urinary tract infections:* Urinary tract infections in diabetics include

- Asymptomatic bacteriuria,
- pyelonephritis,
- cystitis.
- Less common infections are perinephric abscess, renal papillary necrosis secondary to infection, renal tuberculosis and emphysematous pyelonephritis.

*Skin Infections:* Diabetics are more prone to skin infection, particularly those caused by staphylococcus aureus are common in poorly controlled diabetics. These are probably due to number of factors including

- peripheral neuropathy and
- peripheral vascular disease.
Other Infections:

- Osteomyelitis
- Periodontal infection
- Postoperative infection
- Bacterial pneumonia
- Septicemia

Infections peculiar in diabetes are:

- Mucormycosis
- Malignant otitis externa
- Emphysematous cholecystitis
- Necrotizing cellulitis and fascitis

Management of Diabetes:

- For the control of diabetes when it is associated with pulmonary tuberculosis, *insulin* is the main stay of treatment. Nowadays DNA recombinant technology is used for the production of insulin.

Insulin preparations available:

Ultra short:

- Lispro
- Insulin aspart

Short acting
- Regular

Intermediate acting
- NPH
- Lente

Long acting
- Ultra lente
- Glargine

Combinations
- 70/30 – 70% NPH, 30% regular
- 50/50 – 50% NPH, 50% regular

- **Insulin Regimens:**
  - In all regimens, intermediate or long acting insulins (NPH, Lente, Ultralente) supply basal insulin, whereas regular, insulin aspart or lispro provides prandial insulin.

One popularly used regimen consists of an intermediate acting insulin (NPH or lente) given as twice daily injections mixed with a short acting insulin before the morning and evening meal. Such regimens usually prescribe 2/3 of the total daily insulin dose in the morning (with about 2/3 given as intermediate acting and 1/3 as short acting) and 1/3 dose before the evening meal (with approximately one half given as intermediate acting and one half as short acting).
Oral hypoglycemic agents in Type-II Diabetes

1. Insulin secretagogues: Insulin secretagogues act by ↑ insulin secretion. Mechanism of action is to act on ATP sensitive potassium channels in β cells of pancreas. These drugs are efficient in individuals with type 2 diabetes mellitus of recent onset (< 5 years), who tends to be obese and have residual endogenous insulin production.

Example: Sulfonylureas
- Glibenclamide.
- Glimepride
- Glipizide
- Glyburide

Insulin secretagogues: Nonsulfonylurea-↑ Insulin secretion- Nateglinide, repaglinide, mitiglinide.

2. Biguanides: It cause reduction in glucose formation in the liver and it increases the peripheral need for blood glucose.

Example: Metformin

FPG and insulin levels are reduced by biguanides that improves the dyslipidemia (lipid profile), and had neutral effect on weight. Dose 500 – 3000 mg once or twice daily.
2. *Alpha Glucosidase Inhibitors*: They reduce postprandial hyperglycemia by decreasing the rate of (absorption of glucose).

   Example: Acarbose

   Miglitol

   Therapy should be initiated at a low dose (25 mg of Acarbose or Miglitol) with the evening meal and may be increased to a maximal dose over weeks to months. Adverse effects (diarrhoea, flatulence, abdominal distention) is due to increase in delivery of oligosaccharides to the large bowel.

4. Thiazolidinediones: It reduces insulin resistance and increases glucose utilisation

   Example: Pioglitazone: 15 – 45 mg/day single daily dose

   Rosiglitazone: 2 – 8 mg/day

5. Sodium-glucose2 inhibitors-acts by ↑ Urinary glucose excretion -examples

Canagliflozin, dapagliflozin, empagliflozin

6. Dipeptidyl peptidase IV inhibitors-acts by Prolonging endogenous GLP-1 action eg. Alogliptin, Anaglptin, Gemigliptin, linagliptin, saxagliptin, sitagliptin, teneligliptin, vildagliptin.

7. GLP-1 receptor agonists- acts by ↑ Insulin & ↓ glucagon, secretion, slows gastric
emptying, satiety ex. Exenatide, liraglutide, dulaglutide

**Insulin therapy in Type 2 diabetes:**

Insulin used as first line in therapy in type 2 diabetes, in following conditions

- hospitalized / acutely ill patients
- patients having loss of weight,
- Renal or Liver disease

Insulin is usually initiated in a single dose of intermediate or long acting insulin (0.3 – 0.4 units/kg/day) given either before breakfast or just before bed time. Insulin can be used in combination with any of the oral agents in patients who fail to reach the glycemic target. The daily insulin dose required can become quite large (1 – 2 unit/kg/day) as endogenous insulin production falls and insulin resistance persists. Patients who require more than 1 unit/kg/day of intermediate acting insulin should be considered for combination therapy (Metformin or Thiazolidinedione) can reduce insulin requirement in patients with type 2 diabetes.
HISTORICAL BACKGROUND OF PULMONARY TUBERCULOSIS

Tuberculosis has been in existence through the ages. There is evidence to show that it was prevalent even in the prehistoric times in the neolithic and Paleolithic era. Sushrutha describe the disease and had found that it was difficult to treat and his treatment was based mainly on hygiene and diet.

Various names had been given to the disease, the most notable was, Pthisis by Hippocrates. Laennaec described it as tubercle, from which the present day term of tuberculosis is derived. Rudolf Virchow first described the development of caseation in tuberculous tissue.
The concept that tuberculosis is infectious was first proved by Villemin and Koch in the 19th century and was followed by the discovery of the tubercle bacilli in 1882 by Robert Koch. Flugge in 1887 demonstrated that the main channel of infection was by inhalation of the bacilli.

With the discovery of X-ray by Roentgen in 1895, radiological examination became a valuable diagnostic tool. The first significant step in the treatment of the disease was the sanitorium therapy suggested by George Bodington. BCG vaccination was introduced as a preventive measure in 1921.

The first specific drug to combat tuberculosis was streptomycin discovered in 1944 by Waksman. This was followed by PAS, INH and other drugs.

The conquest of tuberculosis will be one of the greatest steps forward for the attainment of our goal of positive health. The conquest of tuberculosis will be one of the greatest steps forward for the attainment of our goal of positive health.

**Pathology:**

Diabetes mellitus, when associated with pulmonary tuberculosis shows special features of large confluent, sometimes transient infiltrations which tend to liquify extensively.

Experimentally, it has been suggested that dogs lose their natural resistance to tuberculosis after pancreatectomy. Similarly, the natural resistance of
The albino rat is lowered by induced hyperglycemia, the tubercles being more confluent, more widespread and richer in rats infected with tubercle bacilli than among controls.

The morphology of lungs in patients with TB and DM showed that the combined affection is characterized by a progressive course of tuberculosis with involvement of bronchi. Specific features of tissue reactions pertinent to this combined pathology comprises of defective defence mechanisms, generalized affection of pulmonary vessels, intensive fibre formation and disorganization of the forming connective tissue.

Decreased production of interferon γ by CD4 + T cells plays an important role in increased susceptibility to infection among diabetics. Tuberculous patients had low Interferon γ at diagnosis irrespective of their diabetic status.

Among diabetic patients, IFN-γ was found to be more lower in uncontrolled diabetics than in controlled diabetics. After 6 months of treatment for diabetes, IFN-γ will becomes normal only in those individuals, who had good glycemic control.

There was higher incidence of sputum positivity and higher incidence of lung involvement, particularly cavitations in comparison with other
lung changes. Early studies show that lower lobe involvement is higher among diabetics but recent studies show that similar pattern of lung involvement among diabetics and non-diabetics.

Pulmonary Alveolar macrophages (PAM) along with lymphocytes play a major role in elimination of mycobacterial infections. Hypodense PAM (less than 1030 gm/ml) fraction is less in diabetic pulmonary tuberculosis than in pulmonary tuberculosis alone. PAM in tuberculous patients who are associated with diabetes mellitus seems to be less activated, and its contributes for the development of mycobacterial infections.

*Factors responsible for increased susceptibility to tuberculosis in diabetics are as follows:*

1. Impairment in the function of Neutrophils.
2. Interleukin1β and TNFα synthesis is reduced more among the Uncontrolled diabetic patients.
3. Lung capacity, total diffusion capacity and elastic recoil effect of lungs is decreased due to thickening of alveolar epithelium and basal lamina.
4. Diabetic autonomic neuropathy leads to reduced bronchial dilation and reactivity.
Relapse rate is more common with resistant strains among diabetics and has a worse prognosis inspite of similar bacteriological conversion rate among diabetics and non diabetics.

As patients with poor glycemic control are more prone to develop tuberculosis, patients affected with TB also have a higher prevalence of diabetes mellitus with prevalence rate ranging between (1.8 – 40%) in various studies.

**Probable factors for prevalence of diabetes mellitus in tuberculosis are:**

- Reciprocal worsening of disease by each other.
- Malnourishment and low Body Mass Index.
- Pancreatic tuberculosis (rarely).
- Stress induced diabetes mellitus as a result of tuberculosis.
- Adrenal gland, pituitary- hyperactivity.
- Deficiency of vitamin D

In a study on 927 cases of culture positive tuberculosis, diabetes mellitus was detected in 12.4 percent of individuals. As shown in the above study the symptoms of TB are not altered by diabetes. It does not change the drug response or resistance or distributive pattern of the lesion in the lung.

Lower lung involvement is significantly high among individuals above 40 years and in female sex. In Tuberculous diabetic patients cavity, opacity
and involvement of pleura were higher in comparison with reticulonodular pattern. Type 1 diabetics are more prone for cavitating lesions than type 2 diabetic patients (DM 1> 2). Inspite of higher bacterial population in cavitary lesions less smear positivity is seen among diabetic patients which can be due to weakness of muscles caused by poor glycemic control and weak expectoration. Increased incidence of lower lobe involvement may be due to (1) Increased incidence of primary tuberculosis or impairment in the immunological status, (2) increased oxygen pressure in lower lobe alveoli. MDR tuberculosis is more common in diabetics than in non-diabetics. (MDR-Diabetics>Non diabetics)

.Reactivation of the primary or post primary lesion :

In a patients life reactivation can occur at any point of time. Reactivation of lesion which was acquired many years previously is the major cause of post primary pulmonary tuberculosis among adult men/women. Immunosuppression at any point of time in his/her life can result in post primary PTB.

Steroid and other Immunosuppressant drugs :

Reactivation of TB may occur in patients who has been receiving corticosteroids or other immunosuppressant drugs for treatment of disease or for the suppression of transplant rejection.
Immunodeficiency states like acquired immune deficiency syndrome (AIDS), Hodgkin’s disease, leukemia & lymphoma increase the susceptibility to reactivation.

Smear positivity and predisposition to tuberculosis is more among diabetics.

**Incidence of Tuberculosis**

Diabetics are 5-10 times more prone for infection with TB which is usually asymptomatic and diagnosed late and is commonly because of reactivation of latent infection.

**Reasons for incidence of tuberculosis is more common in diabetes?**

Probable reasons are:

- Hyperglycemia favours the growth, viability and propagation of tuberculosis bacilli.
- Decreased opsonic index.
- Pituitary or adrenocortical hyperactivity.
- Hypovitaminosis A and C.
- Impaired phagocytosis.
- Decreased neutralising antibody in bronchial secretions.
- Decreased resistance - due to vascular damage to lung tissue.
Peculiarities of Tuberculosis in DM

Unique features of TB in diabetics:

- Relative absence of symptoms and diagnosed at late stage.
- Cavitary lesions with caseation are more in number.
- Minimal involvement of pleura.
- Have increased hemoptysis.
- Decreased incidence of extra pulmonary and endobronchial tuberculosis.
- Higher smear positivity.

In a study done on 2434 cases of pulmonary tuberculosis, it showed that 62.8% were males and 37.2% were females and 39.7% were in age group 45 years and above. There were 138 cases of diabetes, 100 were males and 38 were females.

Prevalence in males was 6.4% and in females 4.3%.

Most of the diabetic cases were in the age of 45 years and above (82.6%).

In 4349 cases of diabetes studied between 1967 and 1974, 179 cases were found to have pulmonary tuberculosis. 135 cases were males and 44 were females. Maximum cases occurred in age groups of 50-60 years.

Research Committee of the Tuberculosis Association of India conducted a study in 7 centers in India. It consisted of 935 pulmonary
tuberculosis patients and 9.7% had diabetes. Of the 602 patients in the age group less than 40 years, 29 had diabetes mellitus (4.8%). Of the 333 patients belonging to greater than 40 years, 62 had diabetes mellitus (18.6%). The overall rate was males 10% against 8.7% in females.

Clinical Manifestations:

Tuberculosis supervening on patients having preexisting diabetes often is devoid of the early warning signs and symptoms. The patient may attribute to malaise, loss of appetite and weight loss to an exacerbation of his diabetic state. The patient usually attributes “cough with expectoration and fever” to frequent respiratory tract infection he is prone to develop. Eventually, the patients with diabetes attributes these alterations to improper control of diabetes mellitus and the onset of tuberculosis is masked long enough until the disease to get established & the florid signs and symptoms become manifest. Similarly tuberculosis patients attribute their worsening of their conditions to tuberculosis and hence they fail to suspect diabetes mellitus.
Tuberculosis should be suspected in patients with diabetes who has fever, weight loss, generalised fatiguability that cannot be fully explained by poor diabetic control alone.

Tuberculosis can involve any organ system, but most common organ for primary lesion is lung and it is the principle organ involved. Symptoms may be absent during the early phase of development of lesion as well as in advanced disease. Appearance of symptoms depends not only on the extent of the disease, but primarily on the

- host-parasite relationship,
- the state of natural resistance
- the number and virulence of the infective organism

General or constitutional symptoms occurs due to release of products from the diseased foci into the bloodstream and include lassitude, loss of appetite and weight, anaemia, sweating, tachycardia, pyrexia, digestive disturbances. The other common symptoms of tuberculosis include cough, hemoptysis, chest pain and dyspnoea.
Common presentation of pulmonary tuberculosis:

- Symptoms free and radiologically diagnosed.
- Productive or non productive cough.
- Generalised fatiguability.
- Loss of weight.
- Repeated attacks of URI.
- Tuberculous pneumonia.
- Hemoptysis

Duration of Diabetes:

The time gap between diagnosis of diabetes and the onset of symptoms of pulmonary tuberculosis was found to range from several months to 16 years with a mean interval of 7 years. One other study also noted similar relation between diabetes and onset of pulmonary tuberculosis.

In 26.7% cases, tuberculosis is diagnosed before DM, in 46.7% cases after diabetes mellitus and in 18.6% at the same time. Younger individuals with less BMI, uncontrolled type 1 diabetes are prone to develop TB.

However, some studies didn’t show any relationship between onset of pulmonary TB and duration of diabetes.
Cigarette Smoking:

In Tuberculous patients of age more than 40 years, there are increased number of smokers than non-smokers.

Clubbing and Pulmonary Tuberculosis

The prevalence of clubbing in pulmonary tuberculosis, as reported by various studies varied from less than 1% to 90%.. Finger clubbing was shown to accompany with extensive- pulmonary damages evidenced by larger cavities on the chest X-ray and had more chance of hemoptysis. Gross clubbing only occurs in patient with long standing tuberculosis.

The individuals having finger clubbing are undernourished compared with the individuals not having. It is due to the severity of infection resulting in protein catabolism.. Immunodeficiency due to malnutrition cause damage to the lung, due to extensive TB or due to secondary infection. Clubbing of fingers is a marker of destructive disease in PTB.

Haematology in Pulmonary Tuberculosis:

A normocytic, normochromic anaemia was a predominant feature in pulmonary tuberculosis. A study done in Kashmir, it is found that 87.76%
of TB patients were anaemic. (14.26% - mild anaemia, 16.34% -moderate and 57.16% -severe anaemia.) Anaemia was normocytic hypochromic and normocytic normochromic type. Haemoglobin range was from 4 gm/dl to 13.4 gm/dl.

Erythrocyte sedimentation rate (ESR) is a non-specific reaction and is a general manifestation of disease or tissue destruction. It is therefore, not of specific diagnostic value in tuberculosis. Rate of ESR indicates only the degree of activity of the infectious process. Repeated value of ESR has more significance than a single value and is a prognostic indicator in chronic PTB on treatment.

WBC – Widespread pulmonary shadows on a chest x ray with normal WBC suggests a diagnosis of PTB than a lung abscess or pneumonia.

**Severity of Diabetes**

A correlation between the severity of diabetes mellitus and the presence of active tuberculosis is suggested by the fact that 5.3% of those whose had diabetes required more than forty (40) units of insulin daily had the disease in active form. Diabetics with severe degree of hyperglycemia was shown to increase the incidence of pulmonary tuberculosis.
In patients of diabetes having pulmonary tuberculosis, majority had moderate or severe type of diabetes.

A study of 170 cases of Diabetes, 30.6% incidence of pulmonary tuberculosis was found. Greater than 100 units of insulin daily dose was required in 87.7% of tuberculous diabetics and in 24.2% of non-tuberculous diabetics.

**Lower Lung Field Tuberculosis:**

Lower lungfield TB are classified as tuberculous disease seen below the imaginary line traced across the hila and including the parahilar region on a standard PA chest radiograph.

Reason for developing for lower lung field tuberculosis are transbronchial perforation of hilar lymphnode, and disseminates to adjacent structure.

Thus, lower lung field disease occurs due to continuation of the primary tuberculous infection or soon afterwards in the pathogenesis of lower lung field tuberculosis.

It can also results from (1) poor ventilation, (2) coastal breathing and (3) retrograde lymphatic flow from the involved hilar nodes. The first site of disease is the apical segment of lower lobe and upper and posterior part of lower lobe are second most vulnerable site.
The percentage of lower zone TB in diabetics with tuberculous was 13.91%. Right lower lobe was found to be involved more common than the left.

Radiology in Pulmonary Tuberculosis with Diabetes Mellitus:

Tuberculous involvement tend to be more severe in diabetics compared to non-diabetics. Most tuberculous diabetics are admitted for treatment in the advanced stage of tuberculosis.

In a study, it was observed that 77.8% of patients had severe stage of tuberculosis, 18.5% had moderately severe and only (3.9%) had minimal lesion. Uncontrolled cases of diabetes mellitus with tuberculosis, number of zone in the lung involved was higher as compared to control series31.

The cavitary lesions were observed in 70% of tuberculous diabetics as compared to non-tuberculous diabetics. In 76.3% tuberculous diabetics with cavity, the evidence of activity was noted. Fibrosis and calcification were seen in significantly less number of tuberculous diabetics cases. Coexistence of diabetes with pulmonary tuberculosis causes the flaring of lesions and also interferes in healing process
Diagnosis of Pulmonary Tuberculosis:

1. Sputum examination: Is of more significance
   - In PTB diagnosis
   - For monitoring treatment response
     Sputum examination can be done by Ziehl-Neilsen method /fluorescence method of which the fluorescence method is used for quick screening of more number of samples. Advanced disease and patients with multiple cavities show more sputum smear positivity than in less advanced PTB.

2. Sputum culture: Culture is positive after 3 – 8 weeks (Lownstein –Jensen medium). Bactec a radiometric culture method allows for rapid diagnosis within 2-6 days. Sputum culture should be carried out in whom the diagnosis of TB is doubtful.

3. Radiological features indicative of tuberculosis: Following are the features of PTB on chest X-ray:
   - Upper zone opacities.
   - Nodular / patchy opacities
   - Calcification
   - Cavity
Bilateral upper zone opacities.

Persistent opacities (several weeks)

**Characteristic Radiographic Appearances:**

Shadows that are soft confluent are due to an exudative process and mimic a simple pneumonia. Fibrosis is suggested by linear shadows that cause distortion of mediastinum, trachea, fissures and diaphragm. A common finding on chest X-ray is presence of fibrotic shadows in bilateral upper zone, elevation of pulmonary hila and shrinkage of upper lobes.

Healed disease is indicated by calcification although reactivation can occur in old calcification. Upper lobe apical and posterior segment is most commonly involved but rarely the disease can be limited to the upper lobe anterior segment.

**Cavitation:**

A draining bronchus with a valvular process results in cavity whose wall is initially irregular with caseous material that later on transforms into thin smooth walled cavity as the caseous material is reabsorbed or coughed out.

Tuberculoma results when a cavity is blocked and filled up with caseous purulent material. Persistent cavities can be present despite chemotherapy and get transformed into an aspergiloma. Prolonged illness and presence of nodular or
patchy infiltrates and areas of atelectasis helps differentiate tuberculous and non-tuberculous cavities.

CT helps in confirming the diagnosis on the basis of presence of cavity and satellite lesions and detecting calcifications in a doubtful lesion.

**Assessment of Activity:**

It is tough to determine if a lesion needs treatment or further assessment.

1. Sputum positivity suggests active lesion and treatment is absolute.

- A radiographically detected lesion associated with symptoms of hemoptysis, weight loss, fatiguability, loss of appetite and cough indicates an active lesion.

- Persistent crepitations suggest an active lesion.

- Cavity or a soft shadow that is widespread and that extends on serial chest films is highly indicative of activity.

**Treatment of Pulmonary Tuberculosis**

First line drugs in the management of PTB are Isoniazid, Rifampicin, Ethambutol Pyrazinamide. These drugs were advised on basis of their lower rate of causing drug resistance, bactericidal and sterilizing activity.

Recommended dosage of drug for initial treatment of tuberculosis in adults:

- **Isoniazid** 5 mg/kg, maximum 300 mg
✓ Rifampicin 10 mg/kg, maximum 600 mg
✓ Pyrazinamide 20 – 25 mg/kg, maximum 2 gm
✓ Ethambutol 15 – 20 mg/kg.

Second line drugs are used only in resistant cases due to their low efficacy and higher side effects.

Second line drugs include:
✓ Streptomycin
✓ Kanamycin
✓ Amikacin
✓ Capreomycin
✓ Ethionamide, Cycloserine, PAS
✓ Fluoroquinolone antibiotics has become the most commonly used second line drugs.

Six months regimens (short course) is subdivided into an initial/bactericidal phase and continuation/sterilizing phase. In the bactericidal phase, most of tubercle bacilli is destroyed and symptoms recovers and the patients are non infectious.
Continuation phase is needed for eradicating persistent mycobacteria and for preventing relapse. The treatment regimen of choice for virtually all forms of tuberculosis consists of a two months bactericidal phase of isoniazid, rifampicin, pyrazinamide and ethambutol followed by a four months continuation phase of isoniazid and rifampicin.

Treatment is prolonged for a period of 9 months in those who show sputum culture positivity after 2 months of treatment and in cavitary PTB. In those who are prone for vitamin B 6 deficiency such as pregnant and lactating mothers, chronic diseases (diabetes, renal failure, HIV), malnourishment and alcoholics pyridoxine (10 – 25 mg/day) is added in order to avoid INH induced neuropathy.

**Multidrug Resistant Tuberculosis And Its Association With DM**

In a study conducted in Bellevue chest hospital, New York, it was reported that is significant relation between DM and multidrug resistant tuberculosis. 3.6% (17cases) of the cases with tuberculosis diabetic patients has MDR TB compared to Ten % (10 cases) in control group.

In a study conducted in Chennai, it was reported that 26% of cases had multidrug resistant tuberculosis. Single drug resistance occurs due to direct monotherapy (ingestion of only one drug) or indirect monotherapy (multiple
drugs of which the bacilli is sensitive to only one). Individuals with secondary type of drug resistance can transmit the bacilli to others who are then referred as primary drug resistance. This type of transmission is favoured by HIV in which deficient infection control measures and late diagnosis leads to rapid progression of the disease.

Treatment is to be started with 3 drugs that are sensitive against the bacilli if chance of multi drug resistance is high (eg. Immigrant from high drug resistant country, contact with an MDR TB patient, relapse patient)

Sputum culture negativity at 6 or 12 months is required to stop therapy.

**Special aleration in treatment of Tuberculosis and Diabetes:**

1. Protein and calorie rich diet (2150 - 2500 cal/day)
   - To meet the need for negative nitrogen balance.
   - To avoid reactivation or infection.
   - To increase insulin production.

2. Effect of anti-tuberculosis drugs in diabetes mellitus.
   - Rifampicin
     - Interacts with P450 cytochrome oxidase enzyme and accentuates sulphonylurea metabolism.
Insulin need is increased

Absorption of glucose in intestine is increased

- INH
  - Opposes sulphonylurea action
  - Rare incidence of pancreatitis.

- Biguanides
  - Weight loss and Appetite loss
  - Glucose malabsorption.

3. Selection of anti-diabetic drugs:

To counteract the calorie rich diet and also due to incidence of pancreatic TB, Oral hypoglycemic (Biguanides and sulphonylurea) that are pancreatic stimulants are avoided.

To lower any degree of blood sugar within short interval of time Insulin is the best choice because hyperglycemia will affect the anti-tuberculosis response.

Insulin also helps has anti-inflammatory response and helps in healing process.
MATERIALS AND METHOD

DURATION OF STUDY: 1 year (October 2015 - September 2016)

POPULATION TO BE STUDIED: 100

STUDY GROUP: 10 to 75 years age group.

STUDY SETTING: Dept of General Medicine, Chengalpattu Medical College and Hospital Chengalpattu.

INCLUSION CRITERIA

- Includes all old and newly diagnosed cases of diabetes.
- Type 1 and type 2 DM are included.

EXCLUSION CRITERIA

- Diabetic patients with HIV patients are also excluded.
- Other types of Diabetes including GDM.
- Diabetic patients on steroids and immunosuppresants.
- Critically ill patients.
- Patients not given consent.

STUDY POPULATION:
Diabetic patients in diabetic clinic, wards of Department of medicine,

Chengalpattu Medical College and Hospital
RESULTS

Number of TB cases - 100.

Number of males - 70 (70%)

Number of females - 30 (30%)

TABLE 1: SEX WISE DISTRIBUTION

<table>
<thead>
<tr>
<th></th>
<th>MALES</th>
<th>FEMALES</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE LESS THAN 40 YEARS</td>
<td>70</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>AGE MORE THAN 40 YEARS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

M:F Ratio - 2.3:1
Table 2 represents the distribution of patients on the basis of age. The peak occurrence of PTB is noted in age > 50 years. The maximum occurrence is noted in the age group 50-59 years of age and 60-69 years of age.

Mean age among males – 55.9

Mean age among females – 47.0

Table 2 : Age sex distribution

<table>
<thead>
<tr>
<th>AGE GROUPS</th>
<th>MALE</th>
<th>FEMALE</th>
<th>TOTAL</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 - 19</td>
<td>1</td>
<td>1</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>20-29</td>
<td>2</td>
<td>2</td>
<td>04</td>
<td>04</td>
</tr>
<tr>
<td>30-39</td>
<td>9</td>
<td>6</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>50-59</td>
<td>60-69</td>
<td>70-79</td>
</tr>
<tr>
<td>------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>21</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>22</td>
<td>25</td>
<td>24</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>22</td>
<td>25</td>
<td>24</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>Mean age</td>
<td>55.9</td>
<td>47.0</td>
<td>51.4</td>
<td></td>
</tr>
<tr>
<td>± SD</td>
<td>± 11.4</td>
<td>± 13.2</td>
<td>± 12.5</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>34 – 76</td>
<td>19 – 70</td>
<td>19 – 76</td>
<td></td>
</tr>
</tbody>
</table>
Table 3 shows that the predominant clinical features are anorexia (82%), cough (77%), weight loss (44%), pyrexia (42%). Other clinical features are night sweats (31%), hemoptysis (12%), shortness of breath (20%), chest pain (16%).
Table 3: CLINICAL FEATURES

<table>
<thead>
<tr>
<th>CLINICAL FEATURES</th>
<th>M</th>
<th>F</th>
<th>LESS THAN 40 YRS</th>
<th>MORE THAN 40 YRS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANOREXIA</td>
<td>58</td>
<td>26</td>
<td>19(90)</td>
<td>65(82)</td>
<td>84</td>
</tr>
<tr>
<td>COUGH</td>
<td>52</td>
<td>22</td>
<td>13(62)</td>
<td>61(77)</td>
<td>74</td>
</tr>
<tr>
<td>PYREXIA</td>
<td>41</td>
<td>17</td>
<td>16(76)</td>
<td>40(42)</td>
<td>58</td>
</tr>
<tr>
<td>SHORTNESS OF BREATH</td>
<td>18</td>
<td>3</td>
<td>5(23)</td>
<td>16(20)</td>
<td>21</td>
</tr>
<tr>
<td>WEIGHT LOSS</td>
<td>34</td>
<td>13</td>
<td>12(57)</td>
<td>35(44)</td>
<td>47</td>
</tr>
<tr>
<td>HEMOPTYSIS</td>
<td>7</td>
<td>5</td>
<td>3(14)</td>
<td>9(12)</td>
<td>12</td>
</tr>
<tr>
<td>CHEST PAIN</td>
<td>15</td>
<td>4</td>
<td>7(33)</td>
<td>12(16)</td>
<td>19</td>
</tr>
<tr>
<td>NIGHT SWEATS</td>
<td>23</td>
<td>12</td>
<td>10(47)</td>
<td>25(31)</td>
<td>35</td>
</tr>
</tbody>
</table>
In Table 4, 20% of cases had a old history of TB. 15% of cases were hypertensives and 8% of cases had IHD.

Table 4: Past history
<table>
<thead>
<tr>
<th></th>
<th>MALE</th>
<th>FEMALE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>ISCHEMIC HEART DISEASE</td>
<td>5</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>HYPERTENSION</td>
<td>11</td>
<td>4</td>
<td>15</td>
</tr>
</tbody>
</table>

Family h/o tuberculosis-15%

In table 5, out of the 70 males, 48 patients (68.5%) are smokers.

<table>
<thead>
<tr>
<th>TOTAL NO.OF CASES</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL NO OF CASES</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>TOTAL NO OF</td>
<td>48</td>
<td>0</td>
</tr>
</tbody>
</table>
In table 6, 12 cases (12%) showed clubbing 9 cases of which had severe TB shown by multilobe involvement and extensive TB.

**Table 6 : Clubbing incidence:**
<table>
<thead>
<tr>
<th>TOTAL NO. OF CASES</th>
<th>NO. OF CASES WITH CLUBBING</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

cervical lymphadenopathy is seen in 8% of the patients

As seen in table 7, 55% of the cases has duration of diabetes between six to ten years and 17% of the cases had a duration of diabetes between two to five years and in 6% of the cases less than one yr. 21% of the cases has duration greater than ten yrs.

Table 7 : DURATION OF DIABETES

<table>
<thead>
<tr>
<th>Diabetes -time period</th>
<th>No of individuals</th>
<th>% (Percentage)</th>
</tr>
</thead>
</table>
Table 8 shows a relation between FBS and PTB. 43% of cases have FBS between 200-299 mg/dl; 28% have values between 149-199 mg/dl; 24%
of cases have mean FBS of $>300$ mg/dl and 5% of cases have FBS between 126-149 mg/dl.

**Table 8 : FBS values in TB-DM patients**

<table>
<thead>
<tr>
<th>FBS (FASTING BLOOD SUGAR) mg/dl</th>
<th>NO.OF PATIENTS</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>126-149</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>149-199</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>200-299</td>
<td>43</td>
<td>43</td>
</tr>
<tr>
<td>$\geq 300$</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

Mean - 236.4

± SD ± 65.5

Range 120 – 380
Chart 6: Fasting blood sugar in tuberculous diabetes

- 126-149: 5 cases
- 150-199: 28 cases
- 200-300: 43 cases
- >300: 24 cases
Table 9 shows relation between PPBS values in TB patients. 15% of the cases have values between 201-249 mg/dl; 36% have values ranging from 250-349 mg/dl; 49% of the cases had values above 350 mg/dl.

**Table 9 : DMTB - PPBS**

<table>
<thead>
<tr>
<th>PPBS (POST PRANDIAL BLOOD SUGAR)</th>
<th>NO OF CASES</th>
<th>% (PERCENTAGE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>201-249</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>250-349</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>≥350</td>
<td>49</td>
<td>49</td>
</tr>
</tbody>
</table>

Mean - 351.5

± SD - ± 67.9

Range - 230 – 460

In table 7, 55% of cases showed anemia of which 23% had mild anemia (9-11 gm%); 25% of cases had HB between 6-9 gm% (moderate anemia); 7% of the cases had hemoglobin less than 6 gm% (severe anemia).
Table 10: Haemoglobin

<table>
<thead>
<tr>
<th>HEMOGLOBIN VALUE (gm%)</th>
<th>NO OF CASES</th>
<th>% (PERCENTAGE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;11</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>9-11</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>6-9</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>&lt;6</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Range 5 - 13
Table 11 shows leukocyte count of mean – 10760 with SD of 2401. The lymphocyte percentage mean – 43.5 with SD of 3.8.
Table 11: Leukocyte count and Lymphocyte%

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEUCOCYTE COUNT</td>
<td>10760 ± 2401</td>
<td>3600 -16000</td>
</tr>
<tr>
<td>LYMPHOCYTE%</td>
<td>43.5 ± 3.8</td>
<td>34 - 54%</td>
</tr>
</tbody>
</table>

Table 12 shows ESR values in TB patients. 9% of the cases showed an ESR value of >100 mm/hr; 48% of cases showed ESR between 50-99 mm/hr; 29% of cases were with ESR 21-49 mm/hr; remaining 14% had an ESR of <20 mm/hr. 86% of the total cases had a raised ESR.
**Table 12 : ESR**

<table>
<thead>
<tr>
<th>Erythrocyte sedimentation rate (mm/hr)</th>
<th>NUMBER OF PATIENTS</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; Twenty(20)</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>21-49</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>50-99</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>≥100</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean ± SD  
50.8 ± 26.5

Range  
13 – 114

Table 13 shows that out of 100 cases 86% of patients less than 40 years and 54% of patients more than 40 years showed sputum positivity.
### Table 13: Sputum AFB – results

<table>
<thead>
<tr>
<th>SMEAR-SPUTUM</th>
<th>LESS THAN 40YRS</th>
<th>MORE THAN 40YRS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITIVE</td>
<td>18 (86%)</td>
<td>43 (54%)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>NEGATIVE</td>
<td>3 (14%)</td>
<td>36 (46%)</td>
<td>Significant</td>
</tr>
</tbody>
</table>

**Chart-8 Sputum AFB-results**

- **Positive**: <40 yrs - 86, >40 yrs - 54
- **Negative**: <40 yrs - 14, >40 yrs - 46
Table 14 shows the predominantly involved side. In 39% of patients right side involvement was seen. In 30% of patients left side involvement was predominant and in 31% both sides were involved.

Table 14: Predominantly involved side (left/right/both sides):

<table>
<thead>
<tr>
<th>PREDOMINANTLY INVOLVED SIDE</th>
<th>AGE LESS THAN 40</th>
<th>AGE MORE THAN 40</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>RIGHT</td>
<td>5</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>LEFT</td>
<td>3</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>BOTH SIDES</td>
<td>4</td>
<td>5</td>
<td>13</td>
</tr>
</tbody>
</table>

In table 15, 34% of patients showed lower zone changes out of which 4 patients were below 40 years and 30 patients were in the age group more than 40 years.
Table 15: DM-TB-lower lobe involvement

<table>
<thead>
<tr>
<th>PATIENTS AGE</th>
<th>AGE LESS THAN 40</th>
<th>AGE MORE THAN 40</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO OF PATIENTS</td>
<td>4</td>
<td>30</td>
<td>P &lt; 0.05 - SIGNIFICANT</td>
</tr>
</tbody>
</table>

Chart -9 lower lung field tuberculosis
Table 16 shows radiographic features in DM-TB. 55% of cases showed cavity; 36% of the cases showed fibrotic lesions; 36% of cases had infiltration; pleural effusion was seen in 23%; 6% showed consolidatory changes; 5% had hydropneumothorax; aspergilloma was associated in 3% of cases; 2% showed bronchiectasis.
<table>
<thead>
<tr>
<th>PATTERN OF LUNG INVOLVMENT</th>
<th>M</th>
<th>F</th>
<th>AGE LESS THAN 40 n(%)</th>
<th>AGE MORE THAN 40 n(%)</th>
<th>TOT VAL</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIBROSIS</td>
<td>23</td>
<td>9</td>
<td>2(10)</td>
<td>29(36)</td>
<td>31</td>
<td>0.002</td>
</tr>
<tr>
<td>CAVITY</td>
<td>35</td>
<td>19</td>
<td>10(47)</td>
<td>44(55)</td>
<td>54</td>
<td>0.04</td>
</tr>
<tr>
<td>CONSOLIDATION</td>
<td>6</td>
<td>3</td>
<td>3(14)</td>
<td>6(6)</td>
<td>9</td>
<td>0.59</td>
</tr>
<tr>
<td>PLEURAL EFFUSION</td>
<td>6</td>
<td>4</td>
<td>4(23)</td>
<td>5(6)</td>
<td>10</td>
<td>0.29</td>
</tr>
<tr>
<td>HYDROPNEUMOTHORAX</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4(5)</td>
<td>4</td>
<td>0.23</td>
</tr>
<tr>
<td>BRONCHIECTASIS</td>
<td>3</td>
<td>1</td>
<td>1(4)</td>
<td>2(2)</td>
<td>4</td>
<td>0.69</td>
</tr>
<tr>
<td>INFECTION</td>
<td>20</td>
<td>16</td>
<td>7(33)</td>
<td>29(36)</td>
<td>31</td>
<td>0.89</td>
</tr>
<tr>
<td>ASPERGILLOMA</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3(3)</td>
<td>3</td>
<td>0.49</td>
</tr>
</tbody>
</table>
DISCUSSION

100 PTB-DM patients were clinically and radiographically evaluated. A significant relation between TB and DM is suggested by high occurrence of TB in diabetics.

In the study conducted by us, 70% are male population and 30% are females. The ratio between males and females is 2.3:1.

A higher prevalence as well as incidence of TB in male population is noted in several other studies also with male to female ratio between 3:1 to 5:1.

Desmukh et al studied 2434 cases of PTB and reported that 62.9% of cases to be males and 37.1% of cases to be females. Of the 138 DM-TB patients, 72.4% of patients were males and 27.53% of them were females.

A similar M:F ratio was shown by Patel JC. Of the 179 patients studied by him males constituted 76% and females constituted 24%.
A study by Morris et al shows a higher incidence of DM-PTB in male population than female population.

Tripathy and Kar observed that males constituted 78% of the total patients.

It is made out that males are more susceptible than females for pulmonary tuberculosis associated with diabetes. ICMR [Anon 1958] conducted a national survey and presented its salient findings. Ibrahim Kareem Khalil

In a study conducted by Ibrahim kareem khalil ,”The relationship between tuberculosis and Diabetes Mellitus in patients” had shown higher incidence among males, with a male to female ratio of about 5:1

A similar observation of higher occurrence of DM-PTB is noted among males in all the above mentioned studies including ours.

Reason for increased occurrence of DM-TB in males :

1. Higher incidence of both diseases is seen among males.

2. Increased hospitalization of males.

In our study, the number of cases over the age of forty were 78% and peak incidence was in the age groups of 50 – 59 and 60 – 69 years. 57% of the total cases were in this age groups.
<table>
<thead>
<tr>
<th>STUDY</th>
<th>Age group showing peak incidence of PTB</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deshmukh</td>
<td>&gt;45</td>
<td>82.6%</td>
</tr>
<tr>
<td>Brijkishore</td>
<td>&gt;50</td>
<td>57.1%</td>
</tr>
<tr>
<td>Philips</td>
<td>&gt;50</td>
<td>52%</td>
</tr>
</tbody>
</table>

In the study conducted by us, greater occurrence of DM-PTB is noted among age group more than 50 years. 57% of total patients belong to this age group.

In a study conducted by Ibrahim kareem khalil, “The relationship between tuberculosis and Diabetes Mellitus in patients. Age of the patients ranged between 24 - 75 year-old (51.84 ± 10.71 year-old). 32 patients (64% of the sample) were 40-59 year-old. This study also shows the increased incidence after 40 years of age.

Major clinical features observed in study conducted by us are anorexia (82%), cough (77%), weight loss (44%), pyrexia (42%). Other clinical features are night sweats (31%), hemoptysis (11%), shortness of breath (20%), chest pain (16%).
In a DM-TB study done in Ethiopia, 3 most common clinical features are:

- Pyrexia (80.5%)
- Increased sweat (80.4%)
- Cough (70.5%)

- In the study done by us, there is a higher incidence of anorexia, cough, loss of weight.
- Past H/O TB was seen in 20% of patients
- 15% of the cases were hypertensives
- Family H/O TB was seen in 15% of cases.

48 among 70 males (68.5%) had history of smoking. There is increased incidence of pulmonary TB in smokers compared to non smokers in either sex of age more than 40 years.

As the majority of males (68.5%) are smokers, smoking is a major risk factor in development of TB.

12% of patients in the study done by us had finger clubbing of whom 75% had severe extensive TB as proven clinically and radiographically. Wide differences were noted in the prevalence of clubbing by different observers.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PREVALENCE OF CLUBBING</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEIRMAN</td>
<td>1%</td>
</tr>
<tr>
<td>NEUFELD</td>
<td>90%</td>
</tr>
</tbody>
</table>
Finger clubbing occurs in those with chronic TB and extensive lung damage and is thus a marker for extent of destruction.

Similar observation between clubbing and extensive TB was noted in the study done by us.

<table>
<thead>
<tr>
<th></th>
<th>Our study</th>
<th>Pavan Malhotra study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>55%</td>
<td>88.76%</td>
</tr>
<tr>
<td>Mild</td>
<td>23%</td>
<td>13.26%</td>
</tr>
<tr>
<td>Moderate</td>
<td>25%</td>
<td>17.34%</td>
</tr>
<tr>
<td>Severe</td>
<td>7%</td>
<td>58.16%</td>
</tr>
</tbody>
</table>

The difference in % of anemia may be due to

- Method of choosing the patients
- Geographical distribution
- Food habits

In the study done by us 9% of the cases showed an ESR value of >100 mm/hr; 48% of cases showed ESR between 50-99 mm/hr; 29% of cases were
with ESR 21-49 mm/hr; remaining 14% had an ESR of <20 mm/hr. 86% of the total cases had a raised ESR.

Erythrocyte sedimentation rate is an indicator of widespread illness or tissue damage and thus can be increased in various situations. Therefore ESR is not a specific test and does not possess much diagnostic significance. To be of value multiple readings are needed. It is also a marker of chronicity of disease in patients on treatment.

The mean total leukocyte count in the study conducted by us is 10760. Cases with extensive TB had normal leukocyte count and vice versa. Hence there is no significant relation between leukocyte count and extent of TB.

55% of the cases has duration of diabetes between six to ten years and 17% of the cases had a duration of diabetes between two to five years and in 6% of the cases less than one yr. 21% of the cases has duration greater than ten yrs. It has been shown that diagnosis of DM occurred before TB development in most cases.

Tripathy et al observed that the time gap between DM detection and PTB onset differed from several months to 16 yrs.

Duration of diabetes play an important role in the development of chronic diabetic complications that may alter the physiology of system. Diabetic
Autonomic neuropathy can lead to abnormal basal airway tone due to alteration in vagal pathways and thus cause a reduced bronchial reactivity and broncho dilation and thus can play an important role in creating this higher risk of respiratory tract infection including tuberculosis among diabetic patients.

In a study conducted by Ibrahim Kareem Khalil, “The relationship between tuberculosis and Diabetes Mellitus in patients” 56% of the sample included in this study was either newly diagnosed or had diabetes for less than 10 years.

Long standing DM is associated with higher risk of infections and hence time period of diabetes is important.

43% of cases have FBS between 200-299 mg/dl; 28% have values between 149-199 mg/dl; 24% of cases have mean FBS of >300 mg/dl and 5% of cases have FBS between 126-149 mg/dl.

15% of the cases have PPBS values between 201-249 mg/dl; 36% have values ranging from 250-349 mg/dl; 49% of the cases had values above 350 mg/dl.

In two different studies conducted by Sachdeva AK and Deshmukh PA, there was a higher occurrence of PTB in those with poor glycemic control.
In a study conducted by Ibrahim kareem khalil, “The relationship between tuberculosis and Diabetes Mellitus in patients” FBS in TB cases varies between 82-396 mg/dl and it had shown that tuberculosis associated with hyperglycemia.

Out of 100 cases 86% of patients less than 40 years and 54% of patients more than 40 years showed sputum positivity. P value is 0.01.

A study conducted by Ibrahim kareem khalil, “The relationship between tuberculosis and Diabetes Mellitus in patients” 38 patients (76% of the sample) had sputum smear positive and it had shown that higher incidence of sputum positive in diabetic patients.

Similar to other studies though smear positive cases were less among age group >40 years cavitation and fibrosis was more in this group. Inspite of increased bacterial count in cavitary lesions rate of smear positivity seems to be less in these cases due to fatiguability of muscles as a result of poor glycemic control and weak expectoration.

This is in similarity with the other studies like

1. Quazi et al study conducted during 2006, where “bilateral lesions were found in 27% of DM-TB”.

In 39% of patients right side involvement was seen. In 30% of patients left side involvement was predominant which combinedly accounts to 69%. 31% of cases had lesions bilaterally.

34% of patients showed lower zone changes out of which 4 patients were below 40 years and 30 patients were in the age group more than 40 years. This accounts to a P value less than 0.05 that is significant.

In two different studies conducted by Bacakoglu F et al and Ravindran P et al lower lobe involvement was higher among female sex and those aged more than 40 years which is the same in the study conducted by us.

The radiographic features in DM-TB showed that 55% of cases showed cavity; 36% of the cases showed fibrotic lesions; 36% of cases had infiltration; pleural effusion was seen in 23%; 6% showed consolidatory changes; 5% had hydropneumothorax; aspergilloma was associated in 3% of cases; 2% showed bronchiectasis.

Cavitary lesions (53%) were the most common type of lesions noted followed by fibrosis (39%), infiltration (38%) in the age group of >40 yrs

Radiographically, cavity, opacification and pleural effusion are more common than reticulo-nodular pattern in TB-DM patients.
Perez Guzman et al observed that multiple cavities involving lower lobe is more common in TB-DM patients.

A study on Radiological Pattern of Pulmonary Tuberculosis in Diabetes Mellitus by Qazi M.A.1, Sharif N.2, Warraich M.M.3, Imran A.4 Haque I.U.5, Attique M.U.H.6, Gardezi M.A.7, Chaudhary G.M. had shown Out of 150 films, in 84 right lung was involved, in left lung about 39 and bilateral lesion found in 27 films.

In TB-DM patients there is increased incidence of caeseation and cavitation but with minimal involvement of pleura which the same in the study done by us.

Consolidation, bronchiectasis, aspergilloma and hydropneumothorax are the other radiographically detected lesions.

Our results show similar correlation with other mentioned studies with respect to side, site, extent of lung changes and radiographical features.
CONCLUSION

- Male population accounted to 70% and females to 30% with M:F ratio of 2.3:1 of which 78% of the individuals are in the age group of more than 40 years.
- The major clinical presentation is anorexia (82%), cough (77%) and loss of weight (44%).
- Past H/O TB is seen in 20% of cases and family H/O TB in 15%.
- Out of the total male patients, 68.5% are smokers. 12% of total cases had clubbing of which 85% was associated with advanced stage of TB proven radio graphically and clinically.
- Mean duration of diabetes in TB patients is 6.8 years.
- 55% of cases have anemia out of which 7% are severely anemic.
- ESR >50 mm/hr is noted in 57% of cases.
- The mean FBS value is 236.4 mg/dl and the mean PPBS value is 351.5 mg/dl.
- Sputum positivity in age less than 40 years is 86% and in age more than 40 years is 54%.
Lower lobe involvement is noted in 34% cases. 39% of cases have predominant right side involvement whereas 30% have left side involvement. Bilateral involvement is seen in 31% of cases.

The most common lung change noted in both less than and more 40 years age group is cavitation (55%). The second most common pattern in age more than 40 is fibrosis and infiltration whereas in age less than 40 fibrosis accounts for a lesser percentage.
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SCREENING OF TUBERCULOSIS IN DIABETES MELLITUS PATIENTS

PROFORMA

Sl. No. : O.P. / I.P. No.:  
Date : Hospital : BH/CGH  
Name : Religion :
Age :                Marital status :
Sex :                Socioeconomic :
Address :            Occupation :

**Presenting complaints :**
Cough :
Expectoration :
Fever :
Night sweats :
Hemoptysis :
Chest pain :
Breathlessness :
Anorexia :
Loss of weight :
Others :

**Past history :**
Tuberculosis :
Diabetes :
Hypertension :
Ischemic heart disease :

**Family history :**
H/o tuberculosis :
H/o diabetes :
Others :
Personal history:
Smoking:
Alcohol:
Appetite:
Sleep:

Diabetes history:
How diabetes mellitus was diagnosed:
Duration:
Treatment:

Treatment history:
Previous H/o anti TB drug treatment:
Duration:

PHYSICAL EXAMINATION:

General examination:
Pallor:
Cyanosis:
Icterus:
Clubbing:
Lymphnodes:
Pedal edema:
Respiratory rate: Pulse: B.P.:

SYSTEMIC EXAMINATION:
**Respiratory system:**

Upper respiratory system:

Lower respiratory system:

Inspection:

Shape of the chest:

Tracheal position:

Respiratory movements:

Drooping of shoulder:

Palpation:

Trachea:

Apical impulse:

Movements of the chest:

Tenderness of intercostal space:

Vocal fremitus:

Percussion: Right Left

Supra clavicular:

Clavicular:

Infra clavicular:

Mammary:

Axillary:

Infra axillary:

Supra scapular:

Inter scapular:
Infra scapular :

Auscultation :

Breath sounds :

Additional sounds :

Vocal resonance :

(in the above areas)

Cardiovascular system :

Abdomen :

Nervous system :

INVESTIGATIONS :

Blood examination :

Hb% :

T.C :

D.C :

ESR :

RBS :

FBS :

PPBS :

Sputum AFB :

Sputum culture :

Chest x-ray findings :