

A CLINICAL STUDY OF PULMONARY TUBERCULOSIS AMONG DIABETES MELLITUS PATIENTSMojjada Dhanunjaya Rao¹, K. Sunil Naik²**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Of all the non-tuberculosis complications associated with disease, Diabetes Mellitus exerts, the most adverse influence on the course of pulmonary tuberculosis. The combined diagnosis was invariably fatal before Specific anti tuberculous and anti-diabetic drugs were available. As per new diabetes guidelines, every diabetic patient should be under gone screening for Pulmonary Tuberculosis. We conducted a clinical study of 60 Patients with Diabetes and Pulmonary Tuberculosis. For establishment of Diagnosis Chest X-ray and Sputum for AFB were done for pulmonary tuberculosis and both blood & Urine Sugar were done for Diabetes Mellitus.

KEYWORDS: Diabetes Mellitus, Pulmonary Tuberculosis, Lower lung field tuberculosis.

INTRODUCTION: Tuberculosis is an infectious disease caused by mycobacterium. The disease is so called because of the formation of Tubercles in the affected part of body. Mycobacterium tuberculosis was identified in 1882 by Robert Koch. With control of smallpox, tuberculosis has become the world's most important communicable disease.

Of all Nontuberculosis complications and associated diseases diabetes mellitus exerts the most adverse influence on the course of pulmonary tuberculosis. The tuberculosis and diabetes mellitus are ancient scourges of man. Avicenna, the Persian Physician was reported to have noted the association between two diseases nearly 1000 years ago. Around 600 AD Shusrutha was reported to have described such an association in his Ayurvedic Text. Many workers have stressed the poor prognosis resulting from this association.

The classical radiological picture of diabetic tuberculosis supported by Sosman & Steidl mentions tuberculosis more often a lower zone disease with minimal lesion which is often clinically silent, present radiologically with a wedge shaped opacity spreading from the hilum with cavitation, over the age of 40 years.

Some others don't find any specific radiological features for Diabetic tuberculosis (Jain N.K. & Agarwal. K. 1985, Khanna 1968)

The present study aims mainly at:

1. To identify the radiological features of tuberculosis in Diabetes mellitus patients, if they are anyway distinctive.
2. To analyze the symptoms.
3. To assess the severity of Diabetes mellitus in Pulmonary tuberculosis and extent of tuberculosis lesion in Diabetes mellitus.
4. To assess the treatment response of both diseases.

EPIDEMIOLOGY OF PULMONARY TUBERCULOSIS: Tuberculosis remains the world public health problem despite the fact that the causative organism was discovered more than 100 years ago and

ORIGINAL ARTICLE

highly effective drugs and vaccine are available making tuberculosis a preventable and curable disease.

Technologically advanced countries have achieved spectacular results in control of tuberculosis. For example, from 1900 to 1980 tuberculosis death rate declined from 199 to 0.5 per 1,00,000 population in United states. This decline started long before the advent of BCG or Chemotherapy and has been attributed to improvement in the standard of living and the quality of life of the people coupled with the application of available technical knowledge and health resources. In 2008, there were an estimated 9.4 (Range, 8.9 – 9.9 millions) millions incident cases (Equivalent to 139 cases per 1,00,000 population) of Tuberculosis globally. Provisional analysis indicate that women account for estimated 3.6 million cases (Range 3.4- 3.8 million).¹

AETIOPATHOGENESIS OF PULMONARY TUBERCULOSIS: Tuberculosis, one of the major public health problems in the developing countries of the world of today, has made its impact felt throughout the ages. No others disease has so much sociological, economical and health significance as Tuberculosis has. Factors which Influence the susceptibility of an individual to disease² are Constitutional, hormonal, environmental and nutritional.

Natural resistance is genetic in character. To a certain extent, this resistance depends upon the length of time for which a race or community has been exposed to Tuberculosis. HLA BW₁₅ and HLA DR₂ are associated with increased susceptibility to Tuberculosis.

Diabetics are more prone to Tuberculosis because of increased levels of glycerol in the tissues. Low incidence of Tuberculosis in hyperthyroidism is believed to be due to destruction of bacilli is enhanced by increased physiological activity of phagocytes in hyperthyroidism, conversely increased susceptibility to hypothyroidism also occurs. Corticosteroids and adrenal hormones provoke activation of latent lesions and lead to multiplication of Tuberculosis bacilli in the lesions, thus favoring of the disease.

Tuberculosis is more common in low socioeconomic status people because of malnutrition, overcrowding and unhygienic living conditions. Protein deficiency is supposed to depress immunoglobulin production.

At onetime certain occupations were considered to increase chances of developing disease. Except those exposed to silica dust while at work, occupation does not seem to have any direct influence. Tuberculosis and malnutrition are interlinked. Recently, we know HIV patients develop malnutrition. Tuberculosis, HIV and malnutrition go hand in hand.

Hypersensitivity: Chances of developing disease are also influenced by the degree of hypersensitivity in an individual following infection. The higher the sensitivity, the greater is the risk. Prevalence of active disease is much higher among high reactors (induration >15mm) than low reactors (induration <15mm) in all age groups.

Pathogenesis of post primary tuberculosis: The most common portal of entry of the tuberculosis bacilli is the respiratory tract and lung is usually the first organ involved. If the immune response regulatory mechanisms are perfect, they will eliminate the bacilli very quickly. If the regulatory mechanisms are defective, excessive hyper sensitivity reaction results leading to attempt at localization of infection, by granuloma formation, caseation, cavitation and fibrosis.

ORIGINAL ARTICLE

In case of post primary tuberculosis, it is not possible to determine whether the disease is due to reactivation of dormant bacilli (endogenous) lurking in the body (or) due to fresh infection with bacilli from outside (exogenous). It is probable that both these form of reinfection may occur, the general opinion at the 22nd conference of the international union against tuberculosis regarding relative incidence of these two types was that exogenous reinfection occurred very rarely.

Reinfection occurs in persons who have had previous exposure to tuberculosis bacilli and had developed acquired cellular immune response to a greater (or) lesser extent. Regardless of source of infection (Exogenous (or) endogenous) the lesion in the post primary tuberculosis are granulomatous with necrosis. Such lesions frequently occur at the apices of upper lobes of lung. These lesions undergo enlargement and liquefaction of caseous centres resulting in cavitation. If the cavity opens into bronchus, dissemination to the parts is characteristic of post primary tuberculosis. The importance of cavity formation in tuberculosis lies in the communication, it provides the organism with the outside environment. This has two effects neither of which is beneficial to the host. First it results in a continuous supply of well oxygenated air to the interior of the cavity that stimulates rapid extracellular bacterial multiplication and second it provides a means for the spread of disease both to other parts of the lung and to other individuals. Lymphnode involvement and lymphatic spreads are also rare.

Post primary tuberculosis is tends to be localized initially to the apical and posterior segment of the upper lobes.

Caseous tissue is rich in lipids and tend to be float when such a person in upright, bits of caseous tissue (Leaving the heart) enter upper branches of the pulmonary arteries and are distributed to upper parts of lung.

EPIDEMIOLOGY OF DIABETES MELLITUS: Diabetes mellitus is a chronic disorder, characterized by impaired metabolism of glucose and other energy-yielding fuels as well as by late development of vascular and neuropathic complications. Diabetes comprises of a group of disorders involving distinct pathogenic mechanisms, for which hyperglycemia is the common denominator.

By 2025, it is predicted that more than 333 million persons will develop DM worldwide. In developed countries, it prevalence ranges from 6–11%, while in developing countries it may reach 30%. Its prevalence increases with age and has increased over recent decades. In India Diabetes People were 19.4 million in 1995 where as the predicted incremental diabetics are 57.2 millions by 2025.

PATHOGENESIS AND CLINICAL ASPECTS OF DIABETESMELLITUS: Clinically diabetes mellitus represents a syndrome with disordered metabolism and in appropriate hyperglycemia due to either absolute deficiency of Insulin secretion or reduction in its biological effectiveness or both. The true frequency in general population is difficult to ascertain because of differing standards of diagnosis. The disease is characterized by a series of hormone induced metabolic abnormalities by long term complications involving eyes, kidneys, nerves and blood vessels and by lesions of the basement membranes demonstrated by electron microscopy. The national diabetes data group of the national institute of health in 1979 provided revised criteria for diagnosis of diabetes following a challenge with oral glucose.³

ORIGINAL ARTICLE

1. Fasting (Overnight) Venous plasma glucose concentration more than or equal 126mg/dl at least two separate occasions.
2. Following ingestion of 75gm of glucose.

Venous plasma glucose concentration more than or equal to 200mg/dl at 2 hours and an at least one other occasion during the 2 hours test (i.e. two values equal or more than 200mg/dl must be obtain for diagnosis). If the two hour value is between 140-200mg/dl and one other value during the 2hour test period in equal to or greater than 200 mg/dl a diagnosis of impaired glucose tolerance is suggested.

Most often medical help is sought because of symptoms related to hyperglycemia.....i.e., polyuria, polydipsia and polyphagia, but the first event may be an acute metabolic decomposition resulting in diabetic coma. Metabolic derangements of diabetes are due to a relative or absolute deficiency of insulin and a relative or absolute excess of glucagons.

A REVIEW OF LITERATURE:

PULMONARY TUBERCULOSIS WITH DIABETES MELLITUS: Of all the nontuberculosis complications and associated diseases, Diabetes mellitus exerts the most adverse influence on the course of pulmonary tuberculosis. The combined diagnosis was invariably fatal before specific antituberculous and antidiabetic drugs were available. Early diagnosis of this combination is rare.

Epidemiology of pulmonary tuberculosis in diabetics: Tuberculosis and diabetes mellitus are ancient scourges of man. The seriousness of the association of pulmonary tuberculosis and diabetes mellitus was first noted by the Arab physician Avicenna nearly 1000 years ago. Around 600 A.D Shusrutha was reported to have described such an association in as Ayurvedic text. Liew Taud in 1779 and John Rollo in 1798 described clinical and postmortem records of cases of diabetes complicated by pulmonary tuberculosis. Prior to 1900, pulmonary Tuberculosis was found nearly 50% of autopsies in diabetic persons.

The danger of Tuberculosis for diabetic patients depend first upon the prevalence of Tuberculosis in the community in which the diabetics live and the second the diabetic susceptibility.

Blum and Atagun found that diabetes constituted 3.8% of 2342 patients admitted to the Tuberculosis division of Baltimore city hospital from January 1953 to December 1960, of the 90 diabetics, 45 were previously known to have this condition, 30 where newly diagnosed on routine workup at the time of admission to sanitarium and in the 15 the diagnosis was made subsequently when symptoms attributable to diabetes become manifest.

Holden and Hiltz reported in series of 106 Tuberculosis diabetics admitted to the Nova Scotia Sanitorium from 1931-1961. The Tuberculosis was initially far advanced in 65 patients, moderately advanced in 30 and minimum in 7. Among 102 patients with pulmonary Tuberculosis cavitation occurred in 37%. A high Proportion of far advanced cases were found among the patients who had severe diabetes then among the mild diabetes.

On the Philadelphia study conducted in 1946, the prevalence of Pulmonary Tuberculosis was 8.4% compared with 4.3% of healthy industrial workers. Age and duration of diabetes were significant factors. Under the age of 40, only 5% of the patients with diabetes of less than 10 years had active Tuberculosis in contrast to 17% those with diabetics of more than 10 years duration. A correlation between diabetes and presence of active Tuberculosis was suggested by the finding that 1.3% of those who received insulin and 1.7% of those who received less than 40 units of insulin had

received less than 40 units of insulin had Tuberculosis, while 5.3% of those who received more than 40 units daily has the disease.

Root (1952) reported that Tuberculosis was two or three times more frequent in diabetics than in general population. In Juvenile diabetics it was 10 times as frequent as in nondiabetic high school children. Prevalence of diabetes in Tuberculosis in 1952 was 2.8% (Joslin 1952)

Neogy and Roy (1952) found that of 3.3% among 1,862 diabetics in Jodhpur Hospital were suffering with Tuberculosis. Himsworth (1938), reviewing the association of the two diseases, showed that uncontrolled diabetics predisposed to the development of pulmonary Tuberculosis but effectively treated diabetic patients were little more liable to develop Tuberculosis than non-diabetics. Out of 230 new patients in his clinic, 6.5% were found to have Tuberculosis.

Deshmukh and others (1966) found radiological evidence of active pulmonary Tuberculosis in 20 out of 241 diabetics (8.3%)

Dingley (1969), states that Tuberculosis in diabetics is five times more common than that in general population. Bahulkar and Lokhandwala (1975) found that in the group of 400 diabetics 31 or 7.8% had pulmonary Tuberculosis approximately four times more than in general population.

In India, Tuberculosis Association of India noted prevalence of diabetes mellitus to be 9.7% in 935 patients of pulmonary Tuberculosis

Epidemiology of diabetes in pulmonary tuberculosis: Early records from sanatoria in the west showed that it varied from 0.17% to 0.33%, weiner and kavee (1935) found incidence as high as 14.2%

Deshmukh et al (1966).⁴ applied the screening test in 851 patients of pulmonary Tuberculosis and found diabetes to the extent of 14%, only 35% of them were previously known to be diabetics. Nicholas showed an incidence of 11% in 305 patients of pulmonary Tuberculosis

Nanda and Tripathy (1968).⁵ found 24 diabetics among 200 patients suffering from pulmonary Tuberculosis. Of those 24, only five were known diabetics.

Lahiri and Sen (1974) on the basis of a study of 875 Tuberculosis.

Patients at Jodhpur found.⁶

1. 8% of males and 5% of females suffered from diabetes.
2. Frequency of diabetes with age in percentage increased in males not in females.
3. 43.6% of cases of diabetes were above 40 years of age group.
4. Accepting the level of fasting blood sugar at 121mg % and above as proof of diabetes, they found the prevalence of diabetes 7.5% in Tuberculosis patients.

According to Bahulkar and Lokhandwala (1975) the prevalence of diabetes mellitus in pulmonary Tuberculosis was 4.5%.

Agarwal et al (1988) had screened 620 pulmonary Tuberculosis patients for diabetes mellitus.⁷ 5.3% were found to be diabetic. Prevalence in males was 5.8% and in females 4.4%. Lower lung Tuberculosis was more common in the diabetes. The Tuberculosis spectra in the diabetics included more advanced exudative and cavitatory types. The newly diagnosed diabetics tend to improve their glucose tolerance with adequate anti-Tuberculosis therapy.

There was statistical difference on the response rates (of the Tuberculosis) between those on oral agents and those receiving.

ORIGINAL ARTICLE

According to N.K. Jain et al (1984).⁸ the incidence of diabetes mellitus in pulmonary Tuberculosis was 6.9%. There was no specific radiological picture diagnostic of diabetic Tuberculosis except a predominance of exudative lesions in the upper and mid zones. Lower lung Tuberculosis typical of diabetes was not found and there was no appreciable difference among diabetics and non-diabetics in extent of lesions and presence of absence of cavitation. In another study in India Diabetes mellitus is reported to be in 4.1% to 5.6% pulmonary Tuberculosis patients.

A TYPICAL MANIFESTATIONS OF PULMONARY TUBERCULOSIS IN DIABETESMELLITUS:

Symptoms such as lassitude, loss of appetite, loss of weight are masked. The radiological picture shows confluent types of shadows, far advanced or moderately advanced diseases frequent cavitation. Cavitation is frequently seen in the lower lobe when pulmonary Tuberculosis is associated with diabetes mellitus.⁹ when compared with a control group there is significant increase in cavitory and sputum positive disease suggesting a more severe form of tuberculous infection.

THE PROBABLE REASONS FOR THE ASSOCIATION BETWEEN DIABETESMELLITUS AND PULMONARY TUBERCULOSIS:

1. The risk of Tuberculosis for the diabetic patients depends first upon the prevalence of Tuberculosis in the community in which a diabetic lives and second upon the diabetic susceptibility -Joslin's Diabetes mellitus.
2. Biochemical changes.
 - a) Hyperglycemia favours the growth, viability and propagation of Tuberculosis bacilli and impairs resistance to the infection and capacity for repair.
-Joslin (1952).
 - b) Disturbance of electrolyte balance and local tissue in diabetics favoured infection.
-Keeton (1944).
 - c) Low opsonic index in severe diabetes.
Decostal and Bearedsly (1908).
 - d) Over production of ACTH increases corticosteroids in blood interfering with normal defense mechanisms. As a result, exudative inflammatory response is enhanced while granulation tissue is regarded. - Banyal (1959).
 - e) Hypo vitaminosis due to hepatic dysfunction on plays a major role in the causation of pulmonary Tuberculosis in diabetics.
-Braser and Curtis (1944).
 - f) Over supply of Nitrogenous compounds supported the growth of Tuberculosis bacilli. In uncontrolled diabetes reticuloendothelial cells are distended with fat and their function is impaired.
-Root (1952).
 - g) Increased glycerol may account for multiplication of Tuberculosis bacilli in the diabetes in the tissues of diabetes.
-Long & Vorwald (1930).
 - h) Presence of excess of glucose in the tissue may promote the multiplication of Tuberculosis bacilli. But this is doubtful as concentration of glucose in the tissues is already sufficient to promote the optimum multiplication of Tuberculosis bacilli. Lactic acid, the product of metabolism extracellular fluid has been claimed to depress the resistance of the host and

ORIGINAL ARTICLE

this may produce suitable environment for the Tuberculosis bacilli to grow. Disturbance of fat metabolism lead to the production of ketone bodies and overloading of reticuloendothelial cells with fat products interfering with their defense mechanism. The disturbance of protein metabolism lead to poor bio availability of raw material for formation of antibodies. In the multi glandular stage, there is excessive secretion of adrenocortical hormones interfering with protective defence mechanism. This is further supplemented by the inhibition of formation of collagen tissues. These agents interfere with the syntheses of anti-bodies and tend to produce lymphocytosis. All this factors tend to spare the Tuberculosis bacilli completely from the protective mechanism of the host. The disturbance in the metabolism of vitamins especially vitamin A (which is concerned with integrity of respiratory epithelium) affect in general nutrition of the patients. These are bio-chemical aberrations which predispose a diabetic to Tuberculosis.

-Hoyer (1957) based on Miller stroms (1954) classification of bio chemical changes in diabetes.

- i) The presence of ketosis leads to diminution of opsonin content, depression of antibody titre of the blood and interference with the action of INH in Tuberculosis bacilli.
 - Lurie (1955)
3. Defects in migration and Chemotaxis result in inhibition of leucocyte infiltration and increased susceptibility to infection in diabetes mellitus.
 - Pathologic basis of disease Stanly L. Robbins.
4. Chemotaxis and phagocytosis are defective in hyperglycemic and ketoacidotic diabetics. PMNL microbicidal activity also be impaired these abnormalities are consistently found when fasting blood glucose levels exceed 10mmol/L There is a proven association between diabetes and Tuberculosis. This is due to the impaired metabolism of lymphocytes which is found in poorly controlled diabetics.
 - Oxford textbook of medicine.¹⁰
5. Defects in leucocyte function in diabetes
 - a) Defects in adherence.
 - b) Defects in migrations and Chemotaxis.
 - c) Defects in phagocytosis.

Phagocytosis is an energy dependent phenomenon that stimulates numerous intracellular events including e burst in oxygen consumption, glycogenolysis, increased glucose oxidation via HMP shunt and production of reactive oxygen metabolites including super oxide Hydrogen peroxide and HOCL / This is defective in diabetes. The basis for the susceptibility of the diabetes to Tuberculosis and pneumonia is multi factorial, impaired leucocyte function being one such factor.

-Robbin's pathological basis of disease¹¹

6. Phagocytes appear to be much less effective in uncontrolled Diabetes mellitus.
 - Joslin Diabetes manual

AIM OF STUDY: The present clinical study of Pulmonary tuberculosis in diabetes mellitus aims at to know the incidence of clinicoradiological manifestations of pulmonary tuberculosis in diabetes mellitus.

OBJECTIVES:

1. To know which symptoms are more common in diabetic tuberculosis than in tuberculosis.
2. To study the severity of diabetes in pulmonary tuberculosis patients and severity of tuberculosis in diabetics.
3. To study the incidence of lower lungfield tuberculosis and isolated mid zone lesions in diabetic tuberculosis.
4. To study the incidence of cavitory and non cavitory disease in combined diagnosis.
5. To study the radiological pattern which is distinctive in diabetic tuberculosis.
6. To study the response to treatment and complications.

METHODS AND MATERIAL:

Selection of the Patients: 60 cases of diabetes with pulmonary tuberculosis patients were taken from attending the Department of Pulmonary Medicine, Government General Hospital, Rajeev Gandhi Institute of Medical Sciences, Srikakulam (AP). During the period from June 2013 to May 2015.

As in our Medical College Hospital sputum for culture of the Mycobacterium tuberculosis, the golden standard test was not available, we took the basis for diagnosis of pulmonary tuberculosis were sputum for acid fast bacilli, chest symptoms with aid of chest X-ray PA View.

Status of diabetes was assessed by blood and Urine Sugar Levels.

CRITERIA FOR DIAGNOSIS OF DIABETES: According to the American Diabetes association, 2004

- a) Diabetes mellitus should be diagnosed if fasting blood sugar is more than 126mg/dl on more than one occasion.
- b) In oral glucose tolerance test, if two hour level of blood sugar is more than 200mg/dl, diabetes is to be diagnosed.
- c) If the two hour blood sugar level is more than 140mg/dl, but less than 200mg/dl, it is termed as impaired glucose tolerance test.
- d) If two hour level is less than 140mg/dl the case is to be termed as normal.

Sixty cases of pulmonary tuberculosis were diagnosed by sputum for acid fast bacilli and chest x-ray PA view without diabetes mellitus patients are of same age group as that of combined diagnosis (diabetic tuberculosis) were taken as controls.

According to national tuberculosis association of USA (1961):

Pulmonary tuberculosis lesions are classified based on chest x-ray into

1. Minimal
2. Moderately advanced
3. Far advanced

And

- a) Cavitory
- b) Non-cavitory

The above classifications based on presence or absence of cavity on chest x-ray.

Minimal: Minimal tuberculosis is present when non-cavitory infiltrates involves only a small portion of one or both lungs, but volume of involvement regardless of the distribution should not be more than the volume of a lung seen above the level of second costochondral junction and the spine of the 4th dorsal vertebra.

ORIGINAL ARTICLE

Moderately Advanced: When the volume of combined shadows of disease in both lungs is greater than the volume in minimal tuberculosis but does not exceed the volume of one entire lung. If the shadows are dense and confluent they should not exceed the volume of one-third of the one lung. If a cavity or cavities are present, the total sum of diameters of such cavities must not exceed 4 cms.

Far Advanced: When the extent of involvement, including dimensions of the cavities, is greater than that described for moderately advanced disease.

Lower lung field tuberculosis: Lower lung field tuberculosis is defined as an area of the lung below as imaginary horizontal line drawn through the hila in chest x-ray PA view. This includes parahilar region.¹² Anatomically superior segments of both lower lobes along with basal segments, the middle lobe on right and the lingual on left are included.

Upper zone: It is an area which lies above horizontal line drawn from the medial end of the second rib anteriorly.

Middle zone: It is an area lies below the horizontal line drawn from the medial end of the second rib anteriorly and inferiorly bordered by a line drawn similarly from the fourth rib.

Lower zone: It is an area which lies below the horizontal line drawn from the medial end of the fourth rib anteriorly.

Criteria for severity of diabetes:

- a) Mild Diabetes: Fasting blood sugar from 80 – 120 mg/dl but two hours after glucose, level above the 180 mg/dl, but less than 225 mg/dl.
- b) Moderately advanced: Fasting blood sugar from 120 – 180 mg/dl, and two hours after glucose, level from 225 – 300 mg/dl.
- c) Sever Diabetes: Fasting blood sugar above 180 mg/dl, and two hours after glucose, level above 300 mg/dl.

Sixty patients with combined diagnosis were studied in the chest hospital. Detailed history, clinical and laboratory examination as well as chest PA view were taken for each patient. Blood sugar was estimated by Folin and Wou method. The investigations performed were blood urea, serum protein, A/G ratio and fundus examination.

RESULTS:

ANALYSIS:

The data were pooled and analyzed according to

1. Age.
2. Sex.
3. Sputum smear AFB positivity.
4. Radiological extent of disease.
5. Cavitation.

[A] Number of controls, only pulmonary tuberculosis without diabetes are 60:

Number of male patients are 39(65%)

Number of female patients are 21(35%)

Number of cases, Diabetic pulmonary tuberculosis are 60

ORIGINAL ARTICLE

Number of male patients are 33(55%)

Number of female patients are 27(45%)

Sex	Controls	Percentage	Total number of patients	Cases	Percentage	Total number of patients
Male	39	65%	60	33	55%	60
Female	21	35%		27	45%	

[B] Controls: Out of sixty non-diabetic tuberculosis 39 cases were males (65%) and 21 cases were females (35%). Most of the patients belong to the less than 45 years (66%) and more than 45 years patients are (34%)

Cases: Out of sixty diabetic tuberculosis 33 cases were males (55%) and 27 cases were females (45%) most of the patients belong to the more than 45 years (58%) and less than 45 years patients are (42%).

Nondiabetic tuberculosis(controls)			Diabetic tuberculosis (cases)	
Sex	<45 years	>45 years	<45 years	>45 years
Male	24	15	12	21
Female	16	5	10	17
Total	40(66%)	20(34%)	22(37%)	38(63%)

[C] Symptomatic analysis of controls and cases: Frequency of symptoms in both control and cases were more or less equal except Haemoptysis and chest pain. Haemoptysis was seen in combined diagnosis was 42% and chest pain was 35% where as in control group was 26% and 30% respectively. Polydipsia and polyuria were seen in 70% of combined diagnosis.

Sl. no	Symptoms	Controls		Cases	
		No. of Patients	Percentage	No. of Cases	Percentage
1.	Cough	60	100%	60	100%
2.	Sputum	56	93%	57	95%
3.	Breathlessness	38	63%	39	65%
4.	Haemoptysis	16	26%	25	42%
5.	Chest pain	18	30%	21	35%
6.	Fever	50	83%	52	86%
7.	Loss of appetite And weight	48	81%	54	90%

[D] Duration of the time with onset of symptoms with pulmonary tuberculosis to attend the chest department: 80% of patients attended the chest hospital within the 3months of onset of the symptoms in controls.

87% of patients attended with combined diagnosis within the 3 months of onset of the symptoms.

ORIGINAL ARTICLE

Duration of Symptoms	Controls		Cases	
	No. of Patients	Percentage	No. of Patients	Percentage
0-3 months	48	80%	52	87%
3-6 months	9	15%	6	10%
>6 months	3	5%	2	3%

[E] History of previous treatment: Only 25% of controls and 30% of cases were treated before joining the chest hospital with antituberculosis drugs. Because they are poor and could not buy drugs, they came to Govt. chest hospital after used ATT from few days to few weeks.

Treatment	Controls		Cases	
	No. of patients	Percentage	No. of patients	Percentage
Antituberculosis treatment	15	25%	18	30%
Non-specific Treatment	40	67%	40	67%
No treatment	5	8%	2	3%

[F] Sputum examination: Sputum positivity in controls is 62%, where as in cases it is about 70%

Category	Controls		Cases	
	No. of Patients	Percentage	No. of Patients	Percentage
Sputum positive	37	62%	42	70%
Sputum Negative	23	38%	18	30%

[G] Severity of the disease among the both controls and cases: Cavitory disease in controls was about 36% where as in cases was 44%. Extensive tuberculosis seen in controls was 13% where as in cases it was about 52%.

Sl. No.	Category	Controls		Cases	
		Number of Patients	Percentage	Number of Patients	Percentage
1.	Cavitory Lesion	21	36%	27	44%
2.	Non cavitory lesion	39	64%	33	56%
3.	Minimal lesion	15	25%	11	18%
4.	Moderate lesion	25	41%	18	30%
5.	Extensive lesion	20	33%	31	52%

[H] Analysis of side of the lesion: In controls, bilateral lung involvement was common, right lung was more commonly affected than left lung.

In cases, bilateral lung involvement was common, both right and left lung involvement separately were more or less equal.

ORIGINAL ARTICLE

Sl. No.	Side of lesion	Controls		Cases	
		Number of Patients	Percentage	Number of Patients	Percentage
1.	Right lung	21	35%	18	30%
2.	Left lung	14	23%	16	26%
3.	Bilateral	25	42%	26	44%

[I] Analysis of isolated zone involvement: Out of 60 controls 60 cases lower lung field tuberculosis was 5% in controls where as in cases it was 18%.

Isolated mid zone involvement in controls was 4%, where as in cases it was 10%.

Sl. No.	Zone Involved	Controls				Cases			
		Right	Left	Total	Percentage	Right	Left	Total	Percentage
1.	Isolated Upper zone	9	4	13	21%	6	3	9	15%
2.	Isolated mid zone	1	1	2	4%	3	3	6	10%
3.	Lower lung field	2	1	3	5%	6	5	11	18%

[J] Severity of diabetes among the patients of combined diagnosis: 70% had severe diabetes in combined diagnosed patients indicate that diabetes takes severe course among combined diagnosis.

Sl. No.	Severity of Diabetes	Number of Patients	Total No. of Patients	Percentage
1.	Moderate diabetes	14	60	23%
2.	Severe diabetes	42	60	70%

[K] Incidence of extensive tuberculosis among the patients of combined diagnosis with severe diabetes:

Total cases of severe diabetes = 42.

As the severity of the diabetes was increasing, incidence of severity of tuberculosis was also increasing with incidence of 53% of extensive tuberculosis. So, tuberculosis more commonly occurs in patients with uncontrolled blood sugar levels.

Sl. No	Category	No. of Cases	Percentage
1.	Minimal tuberculosis	6/42	15%
2.	Moderate tuberculosis	12/42	22%
3.	Extensive tuberculosis	22/42	53%

Results and detail investigation of 60 cases of pulmonary tuberculosis with diabetes.

ORIGINAL ARTICLE

I Associated disease:

Sl. No.	Disease	Number of cases	Percentage
1.	Hyper tension	10	16%
2.	CVS abnormality	4	6%
3.	Neurological	3	4%
4.	Renal disease	2	3%
5.	Fundus abnormality	2	3%
6.	Dermatological	3	4%

Results and detail investigation of 60 cases of pulmonary tuberculosis with diabetes.

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3.	Neurological	3	4%
4.	Renal disease	2	3%
5.	Fundus abnormality	2	3%
6.	Dermatological	3	4%

II. Serum protein analysis: Albumin/ Globulin ratio:

1.	Reversal	41	68%
2.	No reversal	19	32%

III. Blood urea, serum Creatinine levels were within the normal limits in all the patients studied except in two patients:

IV. Complications during treatment:

Sl. No.	Complication	No. of cases	Percentage
1.	Haemoptysis	25	42%
2.	Diabetic Ketoacidosis	5	10%
3.	Hypo glycemc attack	10	17%
4.	Hydropneumothorax	5	8%q
5.	Empyema	3	5%
6.	GIT intolerance	6	12%
7.	Peripheral neuropathy	2	4%
8.	Death	4	8%

ORIGINAL ARTICLE

IV. Response to treatment:

I. Response of Patients to antituberculosis drugs.

A. Periodic Sputum Examination of Category I Patients:

Month of Examination	No. of Sputum Negative Cases	No. of Sputum Positive Cases
II	30	8
IV	30	-
VI	30	-

After extension of one month of Intensive Phase, Three Cases were turned to sputum negative and rest of the 4 Months of maintenance phase was completed.

B. Periodic Sputum Examination of Category II Patients:

Month of Examination	No. of Sputum Negative Cases	No. of Sputum Positive Cases
III	1	6
V	1	6
VI	2	5

No. of patients with irregular treatment visited chest hospital were 4. They undergone subsequently category II treatment.

No. of patients were initially treated with Category I and Category III, subsequently undergone category II treatment were 7.

4 Cases were dead during treatment due to complications.

II. Cases with Bacteriological response to anti-tuberculosis treatment:

No. of Sputum Positive Cases Before Treatment with ATT	Response to Treatment with ATT	
	No. of Sputum Negative Cases	No. of Sputum Positive Cases
42	36	3

III. Cases with Clinical and radiological response to Antituberculosis Treatment:

Total No. of Cases	Response to Treatment with ATT	
	Improved	Not improved
42	36	3

4 Cases were dead during treatment due to complications.

Diabetic status was controlled in 79% of cases tuberculosis controlled in 86% of cases. Both were controlled satisfactorily in 76% of cases.

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Sl. No.	Category	No. of cases study	Controlled	Percentage
1.	Control of DM	60	47	79%
2.	Control of TB	60	51	86%
3.	Satisfactorily control of combined	60	46	76%

V. Mortality among cases of combined diagnosis: There were four deaths among sixty cases of combined diagnosis. One death was due to diabetic Ketoacidosis in a type I diabetic, one death was due to myocardial infarction in an uncontrolled adult type II diabetic, one death was due to hypoglycemic attack in an old aged type II diabetic, another death was due to massive Haemoptysis with aspiration asphyxia in a type II diabetic.

VI. Number of cases of type I and type II Diabetes mellitus:

Sl. No.	Type of DM	No. of cases	Percentage
1.	Type I IDDM	2	3%
2.	Type II NIDDM	58	97%

VII. Insulin requirement for control of diabetes in combined diagnosis:

Dose of insulin requirement was increased in combined diagnosis when compare with only diabetes.

Sl. No	Category	No. of cases	Total cases	Percentage
1.	Less than 30 u	11/52	52	21%
2.	More than 30u	41/52		79%

DISCUSSION: 60 Cases of pulmonary tuberculosis with diabetes mellitus were taken for the study. Another 60 cases having only pulmonary tuberculosis were taken as controls. In both the groups 15 years, and above were included.

Sex and Age: Out of 60 cases in combined diagnosis, 33 cases (55%) and 27 cases (45%) were males and females respectively. In control group male incidence of 65% and female incidence was 35%. Sex ratio was slightly more in females of combined diagnosis when compared with only females of pulmonary tuberculosis.

In combined diagnosis, patients about 37% were below 45 years age group and about 63% were above 45 years age group. In control group most cases belonged to less than 45 years age group (66%). The increased incidence in combined diagnosis above 45 years age group was due to more common occurrence of diabetes mellitus in elderly people. This finding was consistent with Deshmukh and Shaw, and also with Agarwal and Jain studies.

ORIGINAL ARTICLE

Symptomatic Analysis: 87 Percent of combined diagnosis patients presented themselves to the chest hospital with in three months of onset of symptoms where as in control group was 80%. This indicated that combined diagnosed patients were symptomatic slightly earlier.

Only 30% of people were taken specific antituberculosis treatment for a few days to weeks in combined diagnosis. In all known diabetic patients, the blood sugar was not under control when they were attending the chest hospital.

All symptoms were more or less equal occurrence in both combined diagnosis and control groups except Haemoptysis and chest pain. Increased Haemoptysis and chest pain may be due to increased incidence of Cavitory and extensive disease in diabetic tuberculosis patients. This finding was consistent with a study conducted by department of chest diseases EGE university medical school, Izmir, Turkey, 1998.

Sputum positivity in combined 70% where as in control group it was 62% this finding may be correlated with increased Cavitory disease in combined diagnosis.

Radiological Analysis: 44% of patients were having the Cavitory disease in combined diagnosed group. But in control group only 36% were having Cavitory disease this finding was nearer to finding of KS. Bhatia, Dept. of TB and Chest diseases, Amritsar, 2001

52% of the patients were having the extensive tuberculosis in combined diagnosed patients whereas 33% of patients were in control group. This finding was also nearer the finding of Agarwal and Gupta, 1988. This showed association of diabetes in tuberculosis patients produce far advanced type of tuberculosis commonly.

Moderate tuberculosis was seen in 30% and minimal tuberculosis was seen in 18% patients of combined diagnosis. In control group moderate tuberculosis was seen in 41% minimal tuberculosis was seen in 25%.

There was no significant difference in the side of lesions among the combined diagnosis, but in controls in which right lung was more commonly involved. In most of the cases of combined and control group were bilateral disease.

18% of cases were having lower lung tuberculosis and 10% of cases were having isolated mid zone lesions in combined diagnosis. In control group 5% cases were having lower lung field tuberculosis and 4% cases were having isolated mid zone lesions. So, lower lung field tuberculosis was more common in combined diagnosis when compared with controls. Isolated upper zone involvement in combined diagnosis was 15% and in controls it was 21%.

About 53% of the severe diabetics were associated with extensive tuberculosis. 22% of severe diabetes had moderately advanced tuberculosis and 15% of severe diabetes had minimal tuberculosis. This showed that moderately to extensive tuberculosis was common in severe uncontrolled diabetics.

Fundoscopy: Fundus examination was normal all cases of combined diagnosis except in two cases. Many patients had refractory errors and these refractive errors may be due to old age. Reversal of Albumin Globulin ratio was found in 68% of cases.

Associated Diseases: Hypertension was seen in 10 patients of the combined diagnosed people (16%). Hypertension was controlled with Enalapril 2.5 – 10mg OD very well. Diabetic nephropathy was seen in two cases.

ORIGINAL ARTICLE

Complications: Hemoptysis was the common complication during the hospital stay. Haemoptysis was controlled very well with conservative medical management.

One case of massive Haemoptysis was expired because of asphyxiation.

Five out of 60 cases (10%) developed diabetic Ketoacidosis. One was juvenile diabetic who was died due to severe dehydration. Other 4 cases are type II NIDDM and were well controlled by physician referral.

During will treatment with insulin, 8 patients developed hypoglycemic attacks. One death occurred due to self-administered high dose insulin by mistake. Other cases were managed by 100ml of 25% Dextrose and followed by 1 point of D₅ I.V. fluid.

Five cases in combined diagnosis developed Hydropneumothorax and all cases were recovered by intercostal tube drainage and O₂ inhalation. Three cases developed Empyema in combined diagnosed patients and manager with intercostal tube drainage.

Type of Diabetes: 97% of diabetics belonged to the type II NIDDM. 3% of diabetics belonged to the type I IDDM.

Response to Treatment: In 79% of combined diagnosis, diabetes was controlled. In 86% of combined diagnosis, tuberculosis was controlled. Both diabetes and tuberculosis were controlled satisfactorily in 76% of combined diagnosis.

The criteria for control of diabetes was the maintenance of urine sugar status and fasting blood sugar was normal (or) near normal with no ketone bodies in urine.

The criteria for control of tuberculosis was bacteriological, clinical and radiological improvement. Before initiation of antituberculosis treatment 70% of cases were sputum positive. About 86% of sputum positive cases were turned to sputum negative after the completion of the course of treatment. 86% of combined cases were improved clinically and radiologically after completion of treatment.

Fifty Two patients were required insulin for control diabetes (86%). Eight patients were controlled with oral hypoglycemic drugs. About 79% of Insulin treated cases were required more than 30 units of Insulin. Only 21% patients were required less than 30 units of insulin. The dose of insulin requirement was increased in diabetics after infected with tuberculosis. After control of tuberculosis, subsequent requirement of insulin and oral hypoglycemic drug dosage were decreased.

Mortality: Mortality among combined diagnosed patients was 7%. In combined diagnosed cases one death was due to DKA, one death was due to silent MI, one death was due to hypoglycemic attack and another death was due to massive Haemoptysis.

90% of people were underweight because most of them were coming from low shows economic status, malnutrition and under nutrition may be factor for underweight. This observation was similar to the finding of Tripathy and Kar, and Ramanet al.

The association of Diabetes mellitus and pulmonary tuberculosis can be explained by various hypotheses such as reduced general body immunity, lowered resistance of respiratory epithelium from hypovitaminosis, tissue hyperglycemia, and enhanced growth of acid fast bacilli due to increased blood glycerol level from disturbed fat metabolism in Diabetes mellitus. The same hypothesis can explain severity of tuberculosis among severe diabetics and vice versa.

ORIGINAL ARTICLE

SUMMARY AND CONCLUSIONS: Among sixty combined diagnosed patients are above 45 years. But in control group, peak age incidence is less than 45 years.

The majority of patients presented within 3 months of onset of symptoms (87%). They approach little earlier the Government Chest Hospital when compare with controls (80%).

All symptomatic manifestations are more or less equal in both combined and control groups except for Haemoptysis and chest pain. Haemoptysis and Chest pain are more common symptoms in combined diagnosis when compare with controls and may be due to association with increased incidence of cavitory and extensive disease.

There is an increased incidence of far advanced disease among uncontrolled diabetics and elder aged people in combined diagnosis when compare with controls. The advanced diseased in elder aged people is due to decreased generalized immunity with uncontrolled diabetes. Diabetes tends to be more severe among cases of combined diagnosis and severe uncontrolled diabetes in associated with far advanced tuberculosis and vice versa.

There is an increased incidence of lower lung field tuberculosis and also isolated mid zone lesions in combined diagnosed patients when compare with controls. 18% of combined diagnosis has lower lung filed tuberculosis and 10% have isolated mid zone lesions.

44% of patients with combined diagnosed patients have cavitory disease, 52% of the patients have far advanced tuberculous lesions. There is increased evidence of cavitory disease among the combined diagnosed cases when compare to the control group. Sputum positivity is increased in combined diagnosed patients due to increased incidence of cavitory disease.

Diabetes and tuberculosis are controlled satisfactorily. Response to antituberculosis drugs in combined diagnosed patients is similar to control group. Short course chemo therapy is as effective in combined group as in control group. Insulin and oral hypoglycemic drugs requirement are increased in combined diagnosed patients when compare with only diabetes mellitus patients.

Haemoptysis is the most common complication in both combined and control group. There is increased incidence of peripheral neuropathy with Antituberculosis treatment in combined diagnosed patients.

It is recommended that all diabetics should be examined regularly to exclude the association of tuberculosis and all the tuberculosis patients should be screened for the presence of diabetes mellitus.

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ORIGINAL ARTICLE

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AUTHORS:

1. Mojjada Dhanunjaya Rao
2. K. Sunil Naik

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pulmonary Medicine, Rajeev Gandhi Institute of Medical Sciences, Srikakulam.
2. Assistant Professor, Department of General Medicine, Rajeev Gandhi Institute of Medical Sciences, Srikakulam.

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NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Mojjada Dhanunjaya Rao,
C/o. Sri Chakra Medicals,
Besides Dharmana TVS Show Room,
Day & Night Junction,
Srikakulam-532001.
E-mail: drmdrao@gmail.com

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