STUDY ON PULMONARY TUBERCULOSIS IN THE ADULT POPULATION - SOCIAL, CLINICAL, RADIOLOGICAL PRESNTATION OF SMEAR-POSITIVE TUBERCULOSIS

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CERTIFICATE

This is to certify that this dissertation titled **"STUDY ON PULMONARY TUBERCULOSIS IN THE ADULT POPULATION - SOCIAL, CLINICAL, RADIOLOGICAL PRESENTATION OF SMEAR-POSITIVE TUBERCULOSIS** submitted by ***Dr .V.N.ALAGA VENKATESAN, (MD)*** to the faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I, **Dr. V.N.ALAGA VENKATESAN**, solemnly declare that the dissertation titled **"A *STUDY ON PULMONARY TUBERCULOSIS IN THE ADULT POPULATION-SOCIAL, CLINICAL, RADIOLOGICAL PRESENTATION OF SMEAR-POSITIVE TUBERCULOSIS*"** has been prepared by me.

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

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ABBREVIATIONS AND ACRONYMS

ATT	:	Anti Tuberculous Therapy
BMI	:	Body Mass Index
COPD	:	Chronic Obstructive Pulmonary Diseases
DOTS	:	Direct Observed Therapy Short-term
HIV	:	Human Immunodeficiency Virus
PPD	:	Purified Protein Derivative
PAO_2	:	Alveolar oxygen concentration
RFLP	:	Restrictive Fragment Length Polymorphism
TU	:	Tuberculin Units
WHO	:	World Health Organization
TB	:	tuberculosis

CONTENTS

Introduction

Mycobacterium tuberculosis is as old as mankind, ubiquitous and is believed one amongst the oldest bacteria in earth. TB is still a problem in the world. It is a major health problem through out the world.

TB is a leading killer of adults among the infectious diseases. One third of TB in the world population is from India. India has more cases of TB than any other country in the world and twice as many cases as China which has next highest cases. Studies show an incidence rate of more than 200 per lakh among the highest in the world. About 8 million new cases of TB in a year with two million deaths reported.

The age above >15 to 44 is 57.3% (Male-363,876,219 & Female-340,181,764).In India about 0.6 million people die of TB every year. Most cases between 15-44 age group. India accounts for one-fourth of the global burden. (Grazybowsky)Ind.J.Tub.199542-201)

1.prevalance rate of TB infections in India about 30%

2.Annual incidence of rate of infection of average is 1%

3.Prevalace rate of disease ranged from 333 to 406/ 100,000 population.

4. Annual incidence rate of disease ranged from 70 to 132/100,000 population.

5. Tuberculin test indurations of 20 mm or more had highest annual incidence of disease. The adult populations are increased risk for health care associated infections. The greater number of young people affected by TB today.

Tuberculosis in Adult

MacGregor Rr study (Am J Med 58:221) shows Tuberculosis affects greater numbers of adult people. According to Park, about 65% of people within the age of 55 in India are affected with tuberculosis. TB is a leading killer of adult. TB kills more adults than any other diseases. Because it affects adults, tuberculosis causes enormous social and economic disruption. TB burden is hidden by stigma and poor diagnostic quality. It was viewed as a dreadful disease. Although the cause of the illness was already understood, the cure remains elusive not to arrive for at least a decade. Tuberculosis, although predominant among the poor and underfed and rampant among those living in unsanitary surroundings, did not discriminate.

Tuberculosis attack the young and middle age, and took its toll among healthy. Their immune system succeeded in fighting the germs to a draw. But the invader remains, content to live quietly in his host, temporarily encapsulated by antibodies but awaiting the opportunistic moment for return. . The majority of pulmonary tuberculosis, in older people is due to inactivated diseases. In one study by Liaw et al (1995) about 26.2% of elderly tuberculosis patients suffer previous tuberculosis disease.

TB affect young adult are smear-positive TB. It may create more orphan than any other disease. Recent studies suggest that every year in India more than 300,000 children leave school on account of their parents have TB.

SMEAR POSTIVE – TB IN RELATION WITH AGE

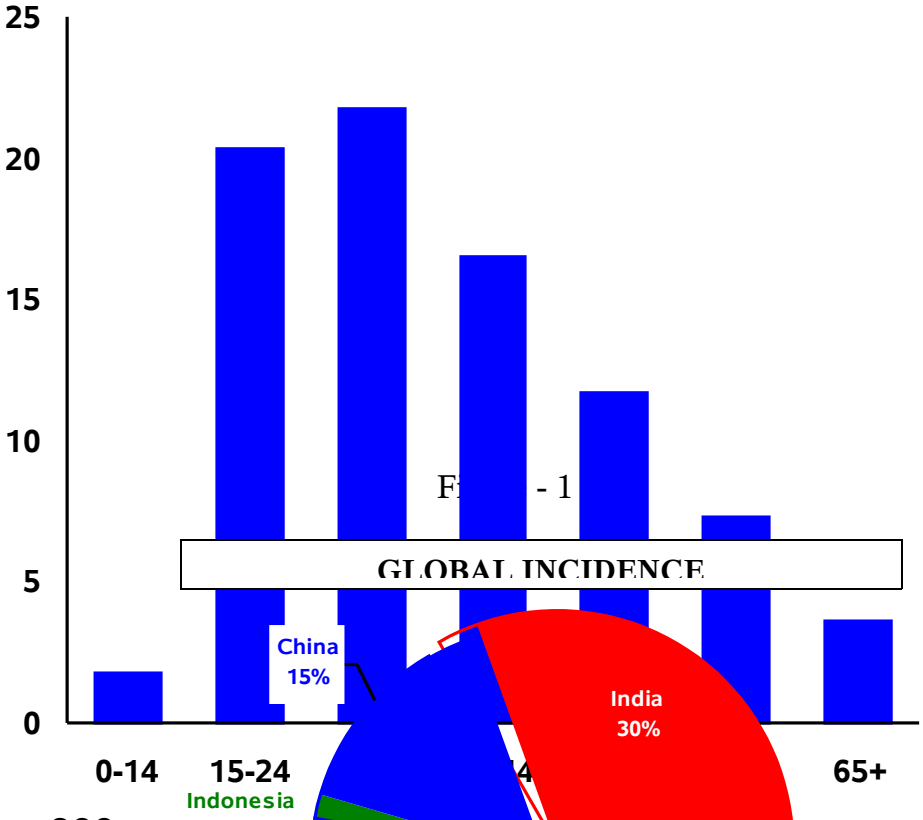

Figure - 1

GLOBAL INCIDENCE

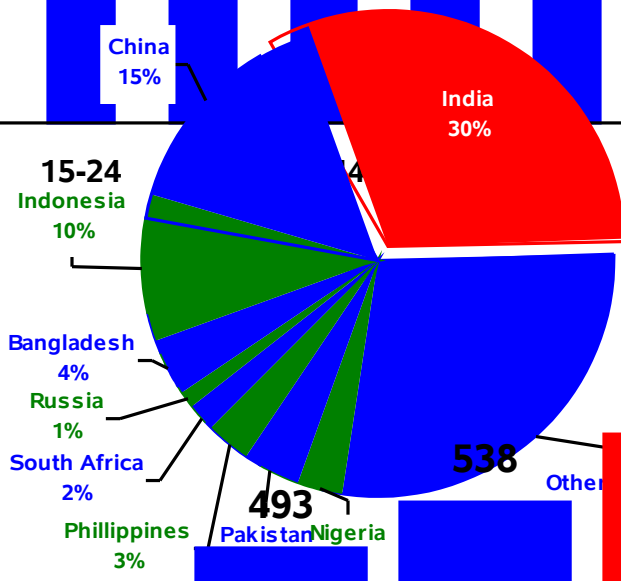

Figure - 2

TB & WOMEN

TB kills en n a fectious disease. TB kills more woma us l r nbined. Women with TB are often igr rec n India suggests that more than 100, ar om es each

year an account of TB.

Figure - 3

This present report deals with socioclinical dimension of adult tuberculosis.

.

TB AND POVERTY

TB is more common in poor and malnourished people, but spreads without regard for socio-economic status. TB treatment is effective independent of nutritional or economic status. Adherence to treatment is irregular, regardless of age, sex, religion, education, or severity of disease — therefore, directly observed treatment is standard of care for all TB patients. Access to treatment is more difficult for the poor. Community-level treatment ensures cure of infectious patients and reduce spread of disease

Other names for tuberculosis disease

- TB (short for *tub*erculosis and also for Tubercle Bacillus)
- Consumption (TB seemed to consume people from within with its symptoms of bloody cough, fever, pallor, and long relentless wasting)
- Wasting disease
- White plague (TB sufferers appear markedly pale)
- Phthisis (Greek for consumption) and phthisis pulmonalis
- Scrofula (swollen neck glands)

- King's evil (so called because it was believed that a king's touch would heal scrofula)
- Pott's disease of the spine
- Miliary TB (x-ray lesions look like millet seeds)
- Tabes mesenterica (TB of the abdomen)
- Lupus vulgaris (the common wolf - TB of the skin)
- Prosector's wart, also a kind of TB of the skin, transmitted by contact with contaminated cadavers, to anatomists, surgeons, butchers, etc.
- Koch's Disease named after Robert Koch who discovered the tuberculosis bacilli.

DRUG RESISTANCE IN TUBERCULOSIS

a. **Primary resistance** It occurs when a patient develops tuberculosis after being infected by another patient who has resistant micro organisms
b. **Initial resitance** is seen in patients who deny history of previous treatment but might have taken anti tubercular drugs knowingly or unknowingly .It includes primary resistance and unknown amount of undisclosed acquired resistance
c. **Acquired resistance** is the one where the bacilli develop resitance to one or more antitubercular drugs during inadequate therapy
d. **Multi drug resistance** *Mycobacterium tuberculosis*resistant to isoniazid and Rifampicin with or without resistance to other drugs

Aim and Objectives

1) To study the socio-demographic pattern of adult tuberculosis.

2) To analyze their clinical presentation.

3) To analyze the diagnostic aspects.{Radiological, microbiological, immunological,)biochemical, hematological}

REVIEW OF LITERATURE

Global Epidemiology of Tuberculosis

In 1993, the World Health Organization declared tuberculosis as a global emergency because of the scale of the epidemic and the urgent need to improve global tuberculosis control.

According to Tuberculosis case notification and rates by WHO in 2002, three regions dominates the world wise distribution & notification i.e., South East region 36%, African region 24% & Western Pacific region 20%. (Maher & Raviglione 2005).

In Industrialized countries, case notification of Tuberculosis, which approximated the true incidence of tuberculosis more closely than in developing countries, steadily declines throughout most of twentieth century in industrialized countries. This is because of socio economic improvement and possibly because of the isolation of the infectious cases in sanitarium. The effective application of chemotherapy in the later half of twentieth century further accelerated the decline. From the mid 1980 onwards several countries saw an expected continuous decline, with case notification increasing for the first time in many years. Factors responsible for the

reversal of the previous trend include increased poverty among marginalized group in inner city areas, immigration from areas with high tuberculosis prevalence, the impact of HIV and the failure to maintain the necessary public health infrastructure under the mistaken belief, tuberculosis was the disease of the past.

TABLE 1 TUBERCULOSIS CASE NOTIFICATION AND RATES BY WHO REGION IN 2005 .

WHO region	No. of cases notified	Proportion of global total (%)
South East Asia	1,487,985	36
Africa	992,054	24
Western Pacific	806,112	20
Americas	233,648	9
Eastern Mediterranean	188,458	6
European	373,497	5

SOURCE: CLINICS IN CHEST MEDICINE 2005

In 2002, there was an estimated 8.8 million new cases of tuberculosis world wide, with an incidence rate of 141 per 100,000 population.

Epidemiology of Tuberculosis in India

Tuberculosis continues to be a major public health problem in India. Since the national reporting system is defective, the only reliable source of information on the magnitude of the tuberculosis problem has been the population sample surveys.

The only authentic survey on a country wide basis, is the national sample survey (1955 – 1958) conducted by ICMR. The National

Tuberculosis Institute, Bangalore undertook three longitudinal surveys at Delhi, Bangalore and Chengelpet. India ranks first in the estimated number of Tuberculosis cases i.e, 1,049,549 thousand cases. (Maher & Raviglione 2005).

The overall prevalence of infection (as judged by the standard tuberculin test) was about 30%, in males 35% and in females 25%. The prevalence was 4 cases per 1,000 population. The incidence of new cases was about 1.5 per 1000 population. According to experts it is safe to estimate that at least 50% of the population above the age of 20 years is infected and will remain at risk of disease throughout their lifetime (WHO 2002).

Gender difference in tuberculosis

Little has been written about gender differences in tuberculosis. In general, the notification rate is higher in men than women. Gender differences vary in different parts of the world. In their study, Chan-Yeung et al (2002) demonstrated that the tuberculosis rate was higher in men than in women in all age groups and the sex difference increases with age. In those aged 15-44, men are affected times more than women.

Martinez et al(2000) reported sex differences in the rate of tuberculosis in San Francisco(USA) from 1991 – 1996, higher men : women ratio was observed. They suggested that the observed sex difference was due to differences in transmission dynamics rather than diagnostic or reporting

bias. Sutherland et al (1979) studied the risk of tuberculosis infection in the Netherlands from 1967 to 1979 and found that there was no differences in the annual rate of infection between boys and girls aged 6 – 12 years. However for those between 12 – 18 years, an excess in the annual rate of infection was found among males.

Duration of illness

There is no delay in diagnosing TB in adult patients who attended to the hospitals with symptoms. They present with productive cough, non productive cough more than 15 days duration, anorexia, weight loss, fever(low grade), night sweats & fatigue. In elderly people diagnosis is difficult because they present more commonly with non-specific complaints. Therefore the tuberculosis may be suspected initially and there maybe considerable early diagnosis in adult patients before they may present with the advanced stage of the disease. Children and adult are more likely to experience reactivation of disease and often triad of symptoms fever, weight loss and night sweats.

In a study by Arora & .Bedi (1989) in Himachal Pradesh, it was found that only 40% of the tuberculosis patients were aware that these symptoms would be due to Tuberculosis. Another study carried out by Liaw et al (1995), in comparing clinical spectrum of tuberculosis in people less than 60 years of age, reported that diagnosis of TB in first visit was made out in

47.3% in patients less than 60 years of age against 38.6% in patients in elderly.

Pathogenesis & immunological aspects

The principal route of entry in tuberculosis is the lung. Inhaled tubercle bacilli are engulfed by alveolar macrophages and transported to regional lymph nodes. Infected macrophages and circulating monocytes secrete proteolytic enzymes, generating an exudative lesion and granuloma formation with activation of T cells. This leads to the onset of cell mediated immunity. The characteristic Ghon complex ultimately develops, tubercle bacilli ultimately restrain within caseous necrosis with eventual healing. A study by Zhmikrobiol et al (2002) reported that there is a decreased activity of natural killer cells in tuberculosis patients. The greatest decrease in the activity of natural killer cells was observed in patients with chronic fibro cavernous form of tuberculosis.

A study by showed that adult tuberculosis individuals are more likely to have concomitant illness that causes varying degrees of cellular immunodeficiency. It has long been known that patients with diseases such as HIV, diabetes, malignancies and renal diseases or who were receiving medications that suppress their cellular immunity were more likely to progress from TB infection to disease.

Interestingly, while these concomitant illnesses only produce a minor cellular deficiency, it is enough to make patients more susceptible to TB disease. Thus altered immune function might predispose the patients to potential reinfection with TB.

It is due to these defects in cellular immunity, patients who present with a chronic wasting or respiratory illness may not present in the classic form.

Clinical spectrum of Tuberculosis

Few adult patients may not present with the classic features of tuberculosis. Tuberculosis in the population may present clinically with cough, chronic fatigue, and anorexic or unexplained low grade fever.

According to Chan et al (1995), cough was the most common symptom in adult tuberculosis patients and old age patients. However non specific symptoms occur in 12% of the adult tuberculosis patients. Cough with expectoration is the commonest symptom in adult where as systemic symptoms dominates the picture in old age tuberculosis Chan et al(2002) &, that 'breathlessness' was the most common symptom in old age tuberculosis patients in Arora et al (1989) study.

Clinical features of pulmonary tuberculosis in the adult patients have are Symptoms of tuberculosis like fever, night sweats, weight loss, sputum production & hemoptysis were significantly in lower proportion in the old

age group as compared to the adult. Katz et al (1987) found no significant difference in the presentation with symptoms of fever and weight loss among the adult and elderly. They observed that the patients significantly present with hemoptysis, have cavitatory lesions on radiographs. Old age TB patients were more likely to present with dyspnoea as their main symptom common in people of Asian, African & Caribbean origin. Fever if present is usually low grade and is easily missed unless rectal temperature is measured in the late afternoon or evening (Brochlehurst et al 1992).

Smoking and Tuberculosis

"Some patients commit suicide by drowning but many by smoking".

According to Arora et al (1989) about 68% of tuberculosis patients are smokers & chronic bronchitis occurs in about 64% of tuberculosis patients. This results in altered clinical presentation. The majority did not seek early medical relief as they attribute their complaints to smoking.

Cigarette smoking is responsible for 90% of chronic obstructive pulmonary diseases. Chronic mucous hyperplasia of the larger airway results in a chronic productive cough in as much as 80% of smokers over age advancing (Harrison16th edition).Since smoking is strongly related to these

elderly tuberculosis patients present late and they wrongly attribute these symptoms to chronic obstructive pulmonary disease.

In patients of both sexes over the age of 30 suffering from pulmonary tuberculosis, it has been shown by Lowe et al (1956) that there is a highly significant deficiency of non smokers and light smokers compared with controls of the same as suffering from other diseases. Kahn et al (1966) shown that mortality from pulmonary tuberculosis among doctors has been shown to increase significantly with the number of cigarette smoked and the similar effect has been also shown in investigations.

Co morbid Illness

Disease associated with impaired cellular immunity such as HIV, Diabetes, Hodgkins' disease, leukemia, and lymphoma may predispose to reactivation. Snider et al (1985) has shown gastrectomy probably predisposes to tuberculosis, particularly in patients with low weight / height ratios or malabsorption syndrome. Morrio et al (1992) has shown diabetes mellitus may predispose to tuberculosis and also lead to a significant increase in cavitations and smear positive disease. Chan et al (1998) He also showed about 9% of tuberculosis patients are diabetics. . Arora et al (1989) have found higher sputum conversion and cure rates in adult age group TB patients as compared to those of the old age group. One of the reason he proposed as the cause of decreased cure rate was that about 15 – 85% of old

age patients suffer from concomitant diseases like chronic bronchitis, emphysema, diabetes, etc and their presence would complicate both the diagnosis and treatment of TB.

Diabetes & tuberculosis

In most studies on this subject, persons with diabetes mellitus have two fold to four fold higher incidence of active tuberculosis than non-diabetic patients (Morse et al (1964). The predisposition of diabetes to infection that are normally controlled by cell mediated immunity may result from one or more defects of pulmonary host defense, including conditions that interfere with normal clearance mechanisms or that impair pulmonary function. The greatest difficulty in studying diabetes mellitus as an independent risk factor for the development of tuberculosis is the presence of potential confounding variables. These variables include other co-existent

medical conditions (eg. malnutrition, chronic renal disease) and personal behaviors, such as smoking & alcohol that may further weaken host defenses. Koziel et al (1998))

Henry & Stableforth (1983) described this finding from a group of diabetic TB patients living in the United Kingdom as diabetic tuberculosis patients presents with a higher incidence of cavitatory disease and sputum positive states than did a control group of Non Asian diabetic TB patients. This was presumably due to higher exposure risk of the Asians which appeared to be associated with their living in settings that replicate and concentrate the bacilli, the social behavior and condition of their birth communities.

TB & HIV

HIV infected persons are at great risk of TB. Without HIV the life time risk of developing TB in TB infected people is about 10%, compared with at least 50% in HIV infected TB infected people. The HIV pandemic could rapidly increase the incidence of TB. Diagnosis of TB in HIV infected person is more difficult due to more non TB- Respiratory diseases, more smear negative TB, extra pulmonary TB& X-Rays are even less specific .Even among HIV infected patients, TB can be cured in more than 90% of surviving HIV infected TB. Over all TB cure rate is slightly lower among HIV infected

patients, because of death from non-TB causes.

Miliary Tuberculosis

Miliary TB is common in immunocompramised adults. Miliary refers to diffuse tiny nodule; similar in size of millet seeds which are seen in x-rays. Skin test is often negative. This presentation occurs in 1 in 100 cases.(Pathy 1993). It is one of the common causes of pyrexia of unknown origin in the TB patients. Usually sputum will be negative for mycobacterium. According to Robert et al (1974), the classical acute or sub acute high intermittent fever and early onset of complicating meningitis or serositis is often present in adult and absent in the old. It presents as more chronic form of slowly progressing protracted, wasting illness with absent

or low grade fever without any localizing symptoms or signs. Examination may reveal only a hepatosplenomegaly. Abnormal chest x-ray is quite compatible with miliary tuberculosis (Kulpati).

Hematological abnormalities in tuberculosis.

Hematologic abnormalities, normocytic normochromic anemia, neutrophilia, high erythrocyte sedimentation rate & hypoalbuminia can observed in younger patients. However anemia and lower white cell counts are not common in the adult. A less incidence of drug induced neutropenia occurs in adult TB. Kaltenbach et al (2001) compared the biochemical parameters between young and old age TB patients. He observed that the commonly observed biochemical abnormality was increased erythrocytic sedimentation rate (49 vs 65 mm/h) & lymphocytopenia (1729 vs 1059 / μl, $p < 0.01$) which was also observed by Yokayama et al (2003). Hypoalbunimia and neutrophilia was lower in the adult group. In patients with military tuberculosis there is profound bone marrow suppression.

Investigations in Tuberculosis

Tuberculin Intradermal Test

The tuberculin was discovered by Von Pirquet in 1907. A positive reaction to the test is generally accepted as evidence of present or past infection by M. tuberculosis. The tuberculin test is the only means of estimating the prevalence of infection in a population.

Tuberculin – Now purified protein derivative is used. It contains 50,000 tuberculin units per milligram. One TU is equal to 0.01 ml of O.T. or 0.0002 mg PPD (Youman et al 1980).

Dosage

a) First strength or 1 TU

b) Intermediate strength or 5 TU

c) The second strength or 250 TU.

For routine testing, the vaccinating team in India use 1TU. (Comstoch et al 980.)

Mantoux test

The mantoux test is carried out by injecting intradermally on the flexor surface of the fore arm 1 TU of PPD in 0.1 ml. The WHO advocates a preparation known as PPD – RT – 23 with Tween-80. The result of the test is read after 72 hours.

In Tuberculin reaction induration is measured.

> 10 mm	Positive
< 6 mm	Negative
6 – 9 mm	Doubtful

(Source: Park's Preventive & social medicine, 18th edn.)

A positive reaction indicates that the person is infected with M.tuberculosis, it does not prove that the person is suffering from the disease. (The Tuberculosis Association of India, New Delhi, 1981).

An excellent but inadequately noticed paper by Zybowski & Allen in 1964 documents the phenomenon of reversal of tuberculin reaction to negative over time while the role of reversal varies with age. It was shown to continue for the life span at a rate of about 5% per year.

According to Yokayama et al (2003) antibody to tuberculin skin test with purified protein derivative was evident in 7% of patient under 60 and 14% of those over 60 years of age.

Now the American Geriatric Society routinely recommends two step tuberculin tests as per the base line information of all institutionalized. The two step test involves initial intradermal placement of 5 tuberculin units of PPD and the results are recorded at 48 – 72 hours. Patients are retested within 2 weeks after a negative response (induration of < 10 mm). The application of the second tuberculin skin test should be accompanied by dermal control

antigen (i.e. candida, mumps or tetanus toxoid) diluted to a 1.5 concentration with phenol buffered diluent to assess the presence of anergy. A positive booster effect and therefore a positive tuberculin skin test reaction is a skin test of 10 mm or more and an increase of 6 mm or more over the first skin test reaction. The booster effect occurs in a person previously infected with M.tuberculosis but who has a false negative skin test, repeat test elicits a truly positive test. It is important to distinguish the booster phenomenon from a true tuberculin conversion. Conversion occurs in persons previously uninfected with M.tuberculosis and who had a true negative tuberculin test but who becomes infected within 2 years as demonstrated by a repeat skin test that is positive during this period. 15 mm or more is considered positive for a conversion activity in persons 35 years and older and in persons with no risk factors for tuberculosis (Hazzaro et al).

Chest X-ray

The chest x-ray is mandatory in the diagnosis of Tuberculosis. The radiological features of tuberculosis are often similar in younger patients and old age patients, but there is a greater prevalence of mid and lower zone shadowing in old age (Umeki et al 1989). The criteria used for interpretation is described in Milka-Cabanne et al [12].

According to Guzman et al (2000) atypical radiological images of pulmonary tuberculosis are common in HIV & diabetic patients. The

proportion of patients with lower lung fields lesions progressively increases with age where as the frequency of cavitations steadily decreases with age.

Upper lobe findings are common in adult tuberculosis. Juvekar et al(1998 IN J Tub 45,95) study observed that only 10% of urban and 21% rural patients were subjected to sputum examination. Majority of patients 78% urban, 56% rural reported have undergone x-ray before treating TB. Jagota (1995 IND J Tub 45 5) study showed even after National tuberculosis programme over diagnosis of TB patients which shows only 20% after sputum examination. Blind relay on x-rays need to be discouraged but if sputum facility is not available it is helpful. Aging leads to increased alveolar ventilation and reduced perfusion resulting in increased mismatch and increased PAO_2. These changes should affect the lower lobes more than the upper lobes because the latter have a higher ratio and higher PAO_2. Therefore age induced changes should favor multiplication of Mycobacterium tuberculosis in lower lung zones. Further more frequency of upper lung field lesion (with or without lower lung field lesion) was similar at all ages, suggesting that aging does not alter condition in upper lobes.

According to Rizvi et al (2003) radiograph in adult patients 14.9% had extensive bilateral infiltration and 32.4% ($P<0.05$) when compared with old age. A similar view was experienced by Umeki et al (1989).

According to Yamaguchi et al (2001) the frequency of cavitations was higher in the middle aged group (87.4%) than old age patients (56.67%)

According to Chang et al (1998), adult patients had less frequently extensive disease involving both lungs and old age patients more frequently had extensive disease involving both lungs, particularly in the advanced age group of 75 years and over. This may be caused by delay in presentation or poorer immunity in the elderly. Interestingly cavitations are common in adult patients and this may also explain why hemoptysis is common in adult subjects. Mlika-Cabanne et al. study defines hetrologous densities of varying size with irregular and ill-defined borders were recorded as patchy lesions. A virtually confluent and homogenous infiltration 2 cm in diameter was defined as an area of consolidation. Multiple discrete, rounded opacities were classified as nodules. A cavity was said to be was visible with in apatchy lesion or area of consolidation or an area of consolidation or an air-fluid level was present within the lucency. Bullae were defined as small lucencies, often present in clusters, with ill-defined walls. In addition, hilar lymphadenopathy, pleural effusion, pericardial effusion, retraction and the presence of a military pattern were seen in x-ray.

Sputum examination

Sputum examination for M.tuberculosis using smear and culture is indicated for all patients who have pulmonary symptoms and radiographic changes compatible with tuberculosis. Sputum examination is carried out by Ziehl Neelson & Kinyoun methods which utilize the carbolfuschin method. Otherwise auromine rhodamine dyes are used with uses flurochrome methods.

For suspected tuberculosis, it is recommended that 3 fresh consecutive sputum specimen obtained in the morning be used for routine mycobacteriological study (American thoracic society, Diagnostic standards of classification of TB, 2000).

For patients who are unable to expectorate, flexible fibroptic bronchoscopy to obtain bronchial washings & bronchial biopsy specimens is clearly feasible and is a valuable diagnostic option (Patel et al 1983). Patients who cannot produce sputum despite these measures may require gastric

aspiration. Smear test for M.tuberculosis may require a minimum of 10^{4-5} AFB per milliliter to be seen by light microscopy (Rajagopalan et al (2001)).

Arora et al (2003) compared sputum profile of tuberculosis between younger and geriatric patients. He demonstrated that the ratio smear positive to smear negative patients was almost similar in the two age groups. Further the treatment outcomes of new smear positive adult TB patients in comparison to old age patients showed better sputum conversion. This same view was endorsed by a study in Hong Kong where the bacteriologically confirmed pulmonary tuberculosis cases increases with age from 59.8% in those < 20 years to 76.2% in those ≥ 80 years. As against this Gaur et al (2004) showed that the percentage of old age tuberculosis patients found to be bacteriologically positive by direct smear was 59.6% as compared to 65.8% among the comparison group (35 – 50 years).

Culture

Routine mycobacterium culture methods which use Lowenstein – Jensen medium may require up to 6 weeks for growth of mycobacterium tuberculosis. A recent Bactec System which utilizes liquid broth media containing the 14 C labeled palmitic acid specific for mycobacterium allows culture in 2 weeks are an addition to our armamentarium for the diagnosis of tuberculosis. These are not yet available for routine clinical practice (Kulpati).

Immunoassay for mycobacterial antigen, serological tests for tuberculosis and detection of mycobacterial components or products by high performance liquid chromatography, gas chromatography and mass spectrometry are also important.

Henn et al (2001) evaluated the sensitivity and specificity of anti Lipoarabinomannan IgG antibodies for diagnosis of tuberculosis in cases of pulmonary, extra pulmonary or associated forms. She concluded that the test is easy and ideal for use in diagnosis of active tuberculosis in specific cases in conjugation with the other methods and permit to evaluate the humoral immunity. Rapid radiometric detection makes out mycobacterial growth (detection of 14 CO_2 released) in 10 – 12 days. A further advantage is that the DNA probe identification and antibiotic susceptibility tests can also be performed rapidly (Rajagopalan et al).

Other tests

Molecular techniques extend knowledge about TB. Genetic finger printing using restriction fragment length polymorphism patterns to identify isolates, have proved that HIV seropositive individuals and presumably other people as well can be re-

infected by TB. Molecular epidemiology again using RFLP pattern has helped identifying transmission network that the traditional epidemiology failed to identify. Early detection of drug resistance by rapid identification of genetic mutation and by chemiluminescent methods so called as "Fire fly".

Management of Adult Tuberculosis.

TABLE 2 Treatment categories in DOTS chemotherapy in India.

Diagnostic Category	Tuberculosis Patients	Tuberculosis Treatment Regimen*	
		Initial Phase	Continuation Phase
Category I	a) New sputum smear positive b) Seriously ill – smear negative c) Seriously ill – extra pulmonary	2 $(HRZE)_3$	4 $(HR)_3$
Category II	a) Sputum smear positive relapse** b) Sputum smear positive failure** c) Sputum smear positive after default.	2 $(HRZES)_3$ 1 $(HRZE)_3$	5 $(HRE)_3$
Category III	**a)Sputum smear negative not seriously ill b)Extra pulmonary**	2 $(HRZ)_3$	4 $(HR)_3$

	non seriously ill		

* The number before the letter refers to the number of months of treatment. The subscript after the letter refers to the number of doses per week.

** In rare and exceptional cases, patients who are sputum smear negative or who have extra pulmonary disease can have relapse or failure.

This diagnosis in all such cases should be made by a medical officer and should be supported by culture and histological evidence of current, active tuberculosis. In these cases the patient should be categorized as others and given category II treatment. (Source: Park's Preventive and social medicine 18th edition).

	Drug	***Adverse Reactions***
1.	INH	GIT irritation, peripheral neuropathy*, blood dyscarsias, hyperglycemia, giddiness, mild drowsiness & liver damage**
	2.Rifampicin	Hepatotoxicity, Gastritis, Influenza like illness, purpuric thrombocytopenia& nephrotoxicity

3.	Streptomycin	Vestibular damage, nephrotoxicity.
4.	Pyrazinamide	Hepatotoxicity, Hyper uricemia
5.	Ethambutol	Retro bulbar neuritis.

(Source: Park's Preventive & social medicine, 18th edition)

* Peripheral neuropathy can be prevented by pyridoxine 10 – 20 mg daily.

** A transient rise in serum enzymes to three times the normal may occur during INH therapy.

Therapeutic difficulties in adult patients

Whatever the age, the main cause of treatment failure is the lack of compliance especially among the patients. Adults due to their workload and stress, depression, fails them in taking particular drug at right time in right dosages. Their well feeling after starting the treatment for a month, symptoms improved they fail to take the drug. Adult patients are active and go to work outside they fail to take the drug in right time (Rita sood 2003). Adult people are less prone for drug reaction when compared with old people. Tealc et.al (1993) stated that the adult people are less likely to have reaction to antituberculous drugs as compared to old age patients. Pande et al 1996 reported that hepatotoxicity due to INH and rifampicin was very common in elderly tuberculosis patients. Rifampicin combined with 1NH has

additional hepatotoxic effects. As renal function, hearing acuity, vestibular function declines with aging, ototoxicity and nephrotoxicity due to streptomycin is less in adult patients when compared with old age patients. Since some visual impairment is common in the elderly, a careful examination that includes visual acuity and color discrimination should be performed before initiating ethambutol therapy. Drug interactions must also be considered. Patients may be taking other drugs for other illness which may interact with antituberculosis drugs.

Other social factors, like lack of transport facility, inability of the service provider to visit regularly, lack of financial support, loneliness are also other reasons for increased default rate.

Materials and Methods

Study Design : Cross Sectional Study

Setting : Govt. Rajaji Hospital, Madurai

Period of study : Aril 2005 to March 2006

Ethical clearance : Ethical committee approved the methodology of the study

and copy enclosed in annexure I

Consent : Consent was obtained from all the patients considered for the

current study.

Financial support : Nil

Conflict of interest : Nil

Inclusion Criteria

Patients who satisfied the following were included in the study.

1) Adult patients (>15 to 44 years of age) who were sputum smear positive, were interviewed and examined with clinical and radiological profile suggestive of tuberculosis were included in the study.
2) Both sexes.
3) HIV negative status.
4) Willing & Co-operative individuals.

Exclusion Criteria

Patients who had any one of the following or a combination of them were excluded.

1) More seriously sick individuals.
2) HIV co-infection.
3) On immunosuppressive therapy.
4) Associated malignancy
5) Major abdominal / thoracic surgery.
6) Un-cooperative / unwilling patients
7) Major cardiac illness
8) Collagen vascular diseases
9) Occupational diseases
10) Extra pulmonary tuberculosis.

METHODS

Selected socio-demographic, clinical and laboratory data were elicited from the patients and recorded in a proforma (enclosed in annexure II).

I. Socio demographic data:

a) Age b) Sex c) Address d) Contacts e) Number of family members

II. Clinical data

a) Body weight b) Height c) Pulse rate d) Blood pressure e) Clinical examination

III. Laboratory data

a) Hemoglobin: measured using Sahli's hemoglobinometer.

b) Total count & Differential count using Leishmann stain.

c) Blood urea done manually by using Diacetyl monoxime technique.

d) Serum creatinine: estimation done using COBAS auto analyzer.

e) Blood glucose: estimation done using glucose oxidase method

f) sputum AFB: 3 early morning specimens collected and stained by Ziehl Neelson technique

g) X-ray Chest: PA view was taken in a radiation dosage of 0.02mSv.

The following definitions were used in this study.

***Ex-Smoker**: Patient who ceases smoking for 2 years.(Changes in the small airways of smokers will reverse after 1- 2 years of cessation) (Harrison 16th edition)*

Diabetes Mellitus:

a) Fasting plasma glucose ≥126 mg/dl

b) Two hour plasma glucose ≥200 mg/dl in oral glucose tolerance test.

c) Symptoms of diabetes plus random blood glucose concentration ≥ 200 mg/dl

Hypertension: Systolic ≥ 140

Diastolic ≥ 90

Based on the average of ≥ 3 reading, when any one of the value (systolic or diastolic BP) is less than the above given value but the other value is higher, the higher value is taken into consideration.

Anemia: *Anemia is defined as a decrease in the circulating RBC mass, the usual criteria are a hemoglobin of less than 12 g/dl in women and less than 14 g/dl in men.*

Body Mass Index: Weight in kilogram / Height in $m^{2.}$

X-ray zones: The chest x-ray was divided into three zones.

Upper zone: 1^{st} and 2^{nd} intercostal space.

Middle zone: 3^{rd} and 4^{th} intercostal spaces.

. *Lower zone: Rest of the intercostal spaces.*

Limitations of the study

1) Age and sex matched control was not attempted since only one disease was taken into consideration.
2) Over all outcomes is not measured since all subjects living outside Madurai were referred to concerned DOTS centre for drug treatment.

3) Pulmonary function test was not done.

4) Induced sputum was not attempted, as it was not approved by the institutional ethical committee.

5) Since single group of patients were analyzed, complex statistical analysis was not done.

6) Therapeutic aspects, drug toxicity and follow up of these aspects were not considered as they were beyond the scope of the objectives.

RESULTS

A total of 200 patients of TB were studied. The distribution of cases in relation to age and gender is furnished in table 3.

TABLE 3: DISTRIBUTION OF SUBJECTS ACCORDING TO AGE & GENDER

AGE (in years)	MALE		FEMALE		TOTAL
	No.	%	No.	%	
15-24	36	18	35	17.5	71
25-35	56	28	21	10.5	77
35-44	39	19.5	13	6.5	52
Total	131	65.5	69	34.5	200

The mean age is 29.5.

Using chi-square test, it was found the difference between age and sex was not significant. Thus, the distribution of age and sex are independent in this study. Almost 2/3 of patients are male.

The details are given in figure 4.

The distribution of subjects according to duration of illness and gender is provided in table 4.

TABLE – 4 DURATION OF ILLNESS AND GENDER.

DURATION OF ILLNESS	MALE		FEMALE		TOTAL	
	No.	%	No.	%	No.	%
< 3 Months	73	55.7	33	47.8	106	53
>3 Months	58	44.3	36	52.2	94	47

This table number 4 shows that majority of the male subjects (55.7%) presented with duration of illness for < 3 months, followed by 44.3% for > 3 months. In contrast, about 47.8% female subjects had the illness for < 3 months, 52.9% for >3 months before they sought treatment. The distribution of cases in those with symptoms less than 3 is slightly higher in male and more than 3 months was high in females irrespective of age.

The details are provided in pictorial manner in figure 5.

The distribution of subjects according to clinical symptoms and gender is furnished in table 5 given below.

TABLE – 5 CLINICAL SYMPTOMS AND GENDER

SYMPTOMS	MALE		FEMALE		TOTAL	
	No.★	%	No.★	%	No.★	%
Cough	131	100	69	100	200	100
Productive	121	92.4	67	97.1	188	94
Fever	104	79.4	59	85.5	163	81.5
Hemoptysis	59	45	32	46.4	91	45.5
Breathlessness	69	52.7	36	52.2	105	52.5
Chest Pain	101	77.2	52	75.3	153	76.5
Weight Loss	98	74.8	52	75.3	150	75
Anorexia	95	72.5	50	72.5	145	72.5
Other symptoms	19	14.5	10	14.4	29	14.5

★ Numbers does not tally with total due to more than one symptom.

In this study, cough was the most common symptom observed in males and females (100%) productive sputum is present in 94% of patients. Fever present in 76.5% (males 104 cases and females 59 cases). Loss of weight and anorexia is seen in 75% and 72.5% respectively took places almost third and fourth. Whereas breathlessness was the commonest symptom in elderly here it is 52.5%. In

males the next common symptom was cough with sputum (92.4%), followed by fever (79.4%). Almost more than 75% of the study subjects complained of weight loss.

The difference between the observed and expected values was not significant and hence clinical symptoms are independent of each other. Also the calculated probability value of chi-square was much less than the observed value of the chi-square at 5% level of significance with which it could be concluded that clinical symptoms among the subjects were independent of gender.

The details are provided in figure 6.

The smoking status of the study population is given in table 6.

TABLE – 6 SMOKING STATUS OF THE STUDY SUBJECTS

SMOKING STATUS	NO. OF CASES	PERCENTAGE
Current Smokers	86	43
Ex-Smokers	25	12.5
Non-Smokers	89*	44.5

In this study population all the female subjects were non-smokers as smoking tobacco is considered a taboo in this part of the country. Among the study population 43% were current smokers, 12.5% were Ex-smokers and 44.5% were non smokers. * Including female patients.

The details are shown in figure 7.

These adult patients have one or more co morbid illness. The distribution of cases in relation to co morbid illness is given below in table 7.

In this study of 200 population, diabetes was the most commonly observed co morbid illness affecting about 11% of the study population. Hypertension was found in 9% of patients followed by chronic obstructive pulmonary disease in 1% and ischemic heart disease in 2% of study subjects. Chronic renal failure noted in 1.5% of subject studies. No subject presented with malignancy.

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TABLE – 7 COMORBID ILLNESSESS AMONG THE STUDY SUBJECTS

COMORBID ILLNESS	NO. OF CASES	PERCENTAGE
Diabetes	22	11
Hypertension	18	9
Ischemic Heart Disease	4	2
Chronic obstructive pulmonary disease	2	1
Malignancy	0	0
Chronic renal failure	3	1.5

Details of wasting, anemia, clubbing and lymphadenopathy observed in the study population are provided in the table 8 given below. Wasting was the most common sign 68.5%, followed by anemia 39% in our subjects. clubbing 12.5% and lymphadenopathy 11% were infrequently noted and very few had hepatomegaly(2%), spleenomegaly (1%) and oedema in 1.5% of subjects study.

TABLE – 8 GENERAL EXAMINATION FINDINGS IN STUDY SUBJECTS

GENERAL EXAMINATION FINDINGS	NO. OF CASES	PERCENTAGE
Wasting	137	68.5
Anemia	78	39
Clubbing	25	12.5
Lymphadenopathy	22	11
Hepatomegaly	4	2
Spleenomegaly	2	1
Oedema	3	1.5

Wasting is the commonest finding present in 68.5% followed by anemia is the next finding present in about 39% cases followed by clubbing in 12.5% of subjects. Only 11% of the study subjects presented with Lymphadenopathy. 2% present with hepatomegaly and 1% with spleenomegaly. Oedema present in 1.5% of study subjects.

Details are provided in figure 8.

AUSCULTATION.

On chest examination, crepitations were the most frequent auscultatory

finding, most commonly heard in the upper and lower zones. In Ethiopia and Gambian study lower zone crepitations are more. Bronchial breath sound heard more in upper zone most commonly in right side. Dullness, absence of breath sounds and wheeze were infrequently detected. In this study upper zone means supra clavicular, infra clavicular and supra scalpular. Middle Zone means mammary and axillary area. Lower zone means infra scapular, infra axillary and inter scapular area

TABLE-18 LUNG EXAMINATION FINDINGS

CREPITATION BY LUNG FEILD

LUNG	UPPER ZONE	MIDDLE ZONE	LOWER ZONE
RIGHT	54.5%	18.5%	42.5%
LEFT	34.5%	8%	48.5%

54.5% of right side upper zone crepitations were recorded among the lesions in the right upper zone lesion. In middle zone 18.5% and lower zone 42.5%. Left lung upper zone 34.5%, middle zone 8% and lower zone 48.5%. Bronchial breath sounds heard in upper zone frequently.

TABLE-19 LUNG EXAMINATION FINDINGS –BRONCHIAL BREATH SOUNDS BY LUNG FIELD—NUMBER OF SUBJECTS.

LUNG	UPPER ZONE	MIDDLE ZONE	LOWER ZONE
RIGHT	43	4	2
LEFT	18	7	2

Bronchial breath sounds are heard more in right upper zone (43), left upper zone it is 18 in number. Crepitations were common auscultatory finding recorded and auscultatory findings were not correlated with chest x-ray.

The biochemical and hematological profile in the study subjects is provided in table 9 given below.

TABLE – 9 BIOCHEMICAL & HEMATOLOGICAL PROFILE IN STUDY SUBJECTS

CATEGORY	RANGE	MEAN
Hemoglobin (gm %)	7 – 12.5	9.5 ± 0.50
Total count (cells / cu mm)	5500 – 11400	8450 ± 216
Polymorphs (%)	59 – 83	72 ± 0.95
Lymphocytes (%)	15 – 35	25 ± 2
Eosinophils (%)	0 – 6	2
Monocytes (%)	0 – 2	-
Blood Sugar (mg %)	55 – 252	106.5 ± 12.3
Blood Urea (mg %)	17 – 65	30.8 ± 2.7
Serum Creatinine	0.6 – 3.4	0.79 ± 0.58

The body mass index of the study subject vary from 12.7 to 29 and the mean ± SD was 17.4 ± 1.3.

RADIOLOGICAL PROFILE OF STUDY SUBJECTS

Majority of the subjects (58%) had involvement of both lungs followed by 23.5% with involvement of the right lung and only about 9.5% had involvement of the left lung. The details are furnished in 10provided below as well as in figure 9.

TABLE – 10 LUNG INVOLVEMENT AMONG STUDY SUBJECTS

X-RAY CHEST	**No. OF SUBJECTS AFFECTED**	**%**
Right Lung	57	23.5
Left Lung	19	9.5
Both Lungs	116	58

Infiltration was a common observation in the x-ray chest in 83.5% of the subjects while cavitations were found only in 21.5% of subjects. In 36.5% of subjects both cavitations and infiltration was found. Pleural effusion, pneumothorax was found in 2.5% and 3% respectively. 11% shows hilar lymphadenopathy. Miliary pattern seen in 2% of the study subjects. The details are furnished in table 11 A given below as well as in figure 10.

TABLE – 11A PATTERN OF LESIONS IN THE LUNG AMONG THE STUDY SUBJECTS

X-RAY CHEST	No. OF SUBJECTS AFFECTED	%
Cavitations	43	21.5
Infiltration	167	83.5
Both	73	36.5
Pleural Effusion	5	2.5
Pneumothorax	6	3
Miliary Tuberculosis	2	1
Hilar lymphnode	22	11

Involvement of upper and lower zone was found to be equally distributed in 46% of the study subjects where as middle zone involvement was seen in 39% of the subjects.34% of the subjects all the zones involved. The details are furnished in table 11 B.

The details furnished in figure-11

TABLE – 11B INVOLVEMENT OF ZONES OF LUNG IN STUDY SUBJECTS

X-RAY CHEST	**No. OF SUBJECTS AFFECTED**	**%**
Upper zone	*134*	*67*
Middle zone	*46*	*23*
Lower zone	*54*	*27*
All zones	*42*	*21*

The following table 12 gives the distribution of radiological findings according to gender in the study population.

TABLE – 12 RADIOLOGICAL FINDINGS ACCORDING TO GENDER IN THE STUDY POPULATION

SEX	**RADIOLOGICAL FINDINGS**			
	CAVITATIONS	**INFILTRATION**	**UPPER ZONE**	**LOWER ZONE**
Male	**37**	**112**	**82**	**37**
Female	**6**	**49**	**41**	**12**

In assessing the radiological findings in the x-ray chest of the study subjects, it was seen that in males 37 of them had cavitations, 112 had

infiltrations 82 had upper zone involvement and 37 had lower zone involvement. Similar observation was seen among females as 6 of them had cavitations, 54 had infiltration, 41 had upper zone involvement and 12 had lower zone involvement.

As the observed and expected values are almost equal, in both sexes, it is clear that cavitation (p = 0.99), infiltration(p = 0.6) and involvement of zones of the lung were independent of gender.

The table 13 gives the radiological presentation of tuberculosis in diabetic patients.

TABLE–13:THE RADIOLOGICAL PRESENTATION IN TUBERCULOSIS PATIENTS WITH DIABETIC STATUS.

STATUS OF DIABETES	*LUNG INVOLVEMENT*				
	Infiltration	**Cavitation**	**Upper Zone**	**Middle Zone**	**Lower Zone**
Diabetic	15	7	8	12	14
Non-Diabetic	152	36	124	29	38

Among the diabetic patients in the study population 15 presented with infiltration and 7 had cavitations in the lung which was evident from the x-ray chest. The middle zone involvement was found in 12 subjects, closely followed by lower zone involvement (14 subjects) while the upper zone is less affected among diabetics (8 subjects).Among the non-diabetic subjects infiltration was seen in 152 subjects, cavitations in 36 subjects, upper zone involvement in 124 subjects, middle zone involvement in 29 subjects and lower zone involvement in 38 subjects.

In the study population, it was observed that 22 diabetic patients had infiltration of the lung while 152 non diabetic subjects had infiltration.

The details are furnished in table 13A given below.

TABLE – 13A INFLUENCE OF DIABETES ON THE PRESENCE OF INFILTRATION IN THE LUNG.

STATUS OF DIABETES	INFILTRATION	NO INFILTRATON	TOTAL
Diabetic	15	7	22
Non Diabetic	152	36	188
Total	167	43	200

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Using Chi-Square test, we observed that the evaluated chi-square probability value is deviated far away from the chi-square table value. So, we conclude that diabetes significantly influences the presence of infiltration of the lung. (p = 0.0034)

Among the 43 subjects with cavitations in the lung 7 of them had diabetes while 36 subjects were non diabetic. The details are furnished below in table 13 B.

TABLE – 13B INFLUENCE OF DIABETES ON THE PRESENCE OF CAVITATION IN THE LUNG.

STATUS OF DIABETES	CAVITATION	NO CAVITATION	TOTAL
Diabetic	7	15	22
Non Diabetic	36	152	188
Total	43	167	200

The observed and expected values almost coincide with each other and hence the difference is not significant at 5% level of significance. Thus it can be concluded that cavitations in the lung was independent of diabetic status (p = 0.50).

TABLE – 14 SMOKING AND HEMOPTYSIS IN STUDY SUBJECTS

STATUS OF SMOKING	HEMOPTYSIS	NO HEMOPTYSIS	TOTAL
Smoker	59	42	101
Non Smoker	32	59	91
Total	91	101	200

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However, the difference between the expected and observed values was not significant at 2% level of significance using chi-square test. Thus it can be concluded that hemoptysis was independent of smoking status.

In this study about 96 subjects with the habit of smoking had infiltration of the lung while 40 subjects with no smoking habit had infiltration (p = 0.225).

TABLE – 15 : SMOKING AND INFILTRATION OF THE LUNG IN STUDY SUBJECTS

STATUS OF SMOKING	INFILTRATION	NO INFILTRATON	TOTAL
Smoker	96	15	111
Non Smoker	40	49	89
Total	136	64	200

In this study about 22 smokers had cavitations and 18 non smokers had cavitations in the lungs (p = 0.15). The details are furnished below in table 14 D.

TABLE – 16 : SMOKING AND CAVITATION OF THE LUNG IN STUDY SUBJECTS

STATUS OF SMOKING	CAVITATION	NO CAVITATION	TOTAL
Smoker	22	89	111
Non Smoker	18	71	89
Total	40	160	200

Using chi-square test, it was found that smoking has no influence on the presence of infiltrations and cavitations in the lung .

In this study about 99 subjects with the habit of smoking had upper zone involvement while 47 subjects with no smoking habit had upper zone involvement of the lung.

TABLE – 17 : SMOKING AND THE INVOLVEMENT OF THE UPPER ZONE OF THE LUNG

STATUS OF SMOKING	INVOLVEMENT OF UPPER ZONE	NON INVOLVEMENT OF UPPER ZONE	TOTAL
Smoker	99	12	111
Non Smoker	47	42	89
Total	146	54	200

It was observed that smoking influences the involvement of the upper zone of the lungs among

the study subjects in contrast to the involvement of the lower zone in diabetic patients in the study population.

DISCUSSION

In this report the clinical and radiological presentations of 200 adult patients with smear-positive tuberculosis discussed. These patients were predominantly males (131). They present to hospital with in 3 months of symptoms in 55.7%. Where as females present late to diagnostic health facility 52.9% > 3 months of symptoms .Patients usually present to diagnostic health facility with a productive cough, fever, and frequently, weight loss and wasting. In population India is currently the second largest in the World.

This study was intended to find out the Socio demographic patterns, signs, symptoms and diagnostic aspects of tuberculosis in the adults. 200 people who satisfied the inclusion criteria were subjected for study. After getting history, all the patients were clinically examined and relevant investigations were carried out.

The mean age of the study population was 29.5. It was 29.6 in males and 30.2 in females respectively. In the present study the male, to female ratio was 2:1. Analysis of sex ratio in WHO region for tuberculosis was found to be approximately 0.3 in South East Asia (SEARO), approximately 0.5 in the Western Pacific region (WPRO) and approximately 1 in Sub Sahara Africa. (Borgdorff et al 2000)

TABLE 15 Comparison of sex differences in the tuberculosis in WHO region

Study population	0.22
SEARO Region	0.3
WPRO Region	0.5
AFRO Region	1
Chan et al (2002)	0.25

According to Chan et al (2002) tuberculosis rate was higher in men than women of all age groups and the sex differences increase with age. The high rate of tuberculosis observed in women of reproductive age in the past had been attributed to the stress of pregnancy. However, studies by Snider et al (1984) and Hamedah et al (1992) failed to support such hypothesis. There was also high degree of unreporting by females in our set up.

Immunologically when compared with males, women were said to have high proportion of CD4 Lymphocytes (Prince et al 1985).Older men tended to have high rate of progression to disease. Alcohol abuse and smoking which depresses immune function have been blamed for disease progression or reactivation in men (Brown et al 1961). Chan et al also demonstrated that women were more adherent to treatment when compared with men. The over all rate of cure and treatment completion at 12 months

was 80.4% and it was higher in women than men especially for those with extra pulmonary disease, when treatment was usually more prolonged.

In this study greater than 50% of patients present within 3 months after the beginning of symptoms. Arora and Bedi et al showed only 40% of the adult tuberculosis patients were aware that their symptom could be due to tuberculosis. The adults are less likely to have chronic cardiac and/or pulmonary disease and malignancy. Immunosuppression is equal in all age patients. Therefore symptoms may be over looked, or attributed to some other ailment common among the adult. Although the classic symptoms of fever, weight loss, chronic cough and hemoptysis were present in the adult they were often attributed to chronic bronchitis or malignancy .Therefore, tuberculosis a treatable condition was less considered. Non specific symptoms of anorexia and weight loss were more common in the adult patients. The diagnosis was frequently missed in the adult because the patient also suffers from a more acute condition which preoccupied the attention of the doctor.

TABLE 16 Frequency of symptoms in adult Tuberculosis in various studies

Clinical symptoms	Present study	Miller-wt Amj et al	Teklu.B.Ethiopia et al
COUGH	100 %	85 %	100 %
PRODUCTIVE	94%	79.3 %	97 %
FEVER	81.5%	27.6 %	94.4 %
Chest pain	76.5 %	65.3%	78.8 %
Weight loss	75 %	73.5 %	97.4 %
Anorexia	72.5 %	69.5 %	82.1 %
Hemoptysis	45.5%	27.4%	35.9 %

In our present study, the most common presenting complaint was cough (100%) which was also the commonest symptom in the series of Ethiopia study and Chan et al (1994). According to Ritasood (1993) presentation of patients with fever and hemoptysis was significantly low. It was 64% and 23% respectively in our population. Brande et al (1990) stated that prevalence of cough, anorexia, weight loss and wasting was higher in tuberculosis the adult.

In our study population Diabetes was the commonest co morbid illness (11%). Next was hypertension which was present in 9% of cases. Comparative analysis of co morbid illness among the adult tuberculosis is furnished in table 17.

TABLE 17 Comorbid illness in various studies in Tuberculosis in the adult

Comorbid illness	Present study	Vats et al (2003)	TEKLU.B.ETHIOPIA et al
Diabetes	11 %	13 %	7.5%
Hypertension	9 %	11 %	11.5%
Ischaemic heart disease	2 %	0%	5%
COPD / Asthma	2 %	5.5%	3.5%
Malignancy	0%	0%	1%
Renal failure	1.5%	--	1%

TABLE 18 Prevalence of Diabetes in tuberculosis among the adult.

Present study	11%
Claw et al (1995)	14.3%
Vats et al (2003)	14%
Chan et al (1994)	7.5%
Villarino et al (2001)	22%
Yamaguchi et al (2001)	12.7%

TABLE 19 Incidence of Pulmonary tuberculosis in Diabetic population

Windke et al (1883)	50%
Root et al (1984)	2.8%
Philadelphia Survey (1952)	8.4%
Korean study	8.3%

TABLE 20 Prevalence of Diabetes in Pulmonary tuberculosis population

Nicholas et al (1957)	5%
Muticentric study in India (1957)	9.7%
TANZANIA study	9%
OG TT Surrey (1990)	4%
Japan study (1987)	13.2%

Diabetes mellitus is recognized as an independent risk factor for developing lower respiratory tact infections. Tuberculosis occurs with increase frequency in diabetes and causes a significant mortality (Konda et al 1996). Root (1994) postulated that the association between two diseases was one sided i.e. diabetic patients tended to contract tuberculosis but the reverse was rare.

The Philadelphia population survey revealed that 8.4% of 3,106 diabetics had pulmonary tuberculosis as compared to 4.3% of the 71,767 presumably healthy industrial workers. Tuberculosis was present in 17% of the diabetics who had the disease for more than 10 years compared to 5% in the diabetics with less than 10 years of the disease. Diabetes mellitus was present in 8.3% of the cases of reactivation tuberculosis in New York City. (Basach et al 1928). The prevalence of diabetes in pulmonary tuberculosis and pulmonary tuberculosis among diabetes are provided in table 18 & 19 and table 20 respectively.

A probable cause of increased incidence of pulmonary tuberculosis in diabetics could be defect in host defense mechanism and immune cell function. The immune derangements predominantly involve the cell mediator arm of the immune system (Mamahon et al.1995). The degree of hyperglycemia had been found to have a distinct influence on the microbiological function of macrophages, with even brief exposure to blood sugar level of 200 mg %. This was borne out by observation that in poorly

controlled diabetic, with high levels of glycosylated hemoglobin, tuberculosis follows a more destructive course and associated with higher mortality. (Noziet et al1995). Infection with tubercle bacilli leads to further alteration of cytokines, monocytes, macrophages and CD4 / CD8 T cell population. The balance of the T-lymphocyte subsets CD 4 & CD8 plays a central role in the modulation of host defenses against mycobacteria and has a profound influence on the rate of regression of active Pulmonary Tuberculosis (Wang et al 1995).

TABLE 21 Frequency of smokers in Tuberculosis in the adult patients

Present study (Madurai – Tamilnadu)	84.7%
Chennai survey (1995 – 97) (Urban)(Northern Tamilnadu)	72.2%
Villupuram survey (1997-98) (Rural)(Tamilnadu)	58.62%

From this table, it became clear there is a high prevalence of smokers in adult tuberculosis population. The mechanisms for the development of TB among smokers are furnished below.

The prevalence of tuberculosis increases with the number of cigarettes smoked. In smokers airway was compromised. Smoke induces oxidative damage along with recruitment of inflammatory cells resulting in damage to the respiratory passages. Alveoli and airway secretions are increased through goblet cell metaplasia. Peribronchial fibrosis leads to air flow obstruction causing irreversible anatomical changes in the lungs. Lung defence

mechanism is further affected by declining mucocilliary clearance. Now the lung becomes the fertile ground for Mycobacterium tuberculosis (Stephen et al 1998). Smokers usually suffer from chronic bronchitis with constant coughing which leads to increase chances of droplet infection. Besides smoke itself may act as a carrier. Smoking has become a risk factor for development of active disease in family contacts of pulmonary tuberculosis cases with a close relationship to the number of cigarettes smoked per day (Al Caide et al 1996).

The mean body mass index in our population was 17.4. Chan et al (1994) showed that the body weight of the adult patients was significantly lower than that of the old age patients (. 48.3 $\pm$ 8.84 Kg Vs 44.2 $\pm$ 14.6 Kg, $p < 0.05$). Teklu.B. STUDY also made out that weight loss was significantly higher in adult tuberculosis patients (97%).

The reasons for the weight loss in adult tuberculosis may be

a) Coexisting medical illness
b) Malnutrition
c) Cytokines (TNFα , IL-2, 1 IFN γ) Produced by Fibroblasts, macrophages also contributes to cachexia. (Ashrun et al 1999) and
d) Smoking and alcohol abuse

Anemia was diagnosed in about 39% of study population. The mean Hemoglobin observed in our study was 8.1 mg .Chan et. al (1994) observed that 52% of elderly tuberculosis patients were anemic.

The causes for anemia in tuberculosis in the elderly are

a) Appetite loss
b) Hemoptysis
c) Anemia of chronic disease
d) Disseminated tuberculosis which have depressive effect on bone marrow
e) Co morbid medical illness and
f) Malnutrition

In this study 1% of patients had military tuberculosis. According to MacGreor R R (2000) 1% of adult tuberculosis had miliary pattern whereas it was 0.7 % in the younger patients.

In this study infiltrative pattern was observed in 83.5% whereas cavitation was made out in 21.5% of the chest x-rays. Rizvi et al (2003) also made out extensive infiltrative lesions in their study of "Clinical presentation of pulmonary tuberculosis in association with age" with younger patients. Perez-

Guzman et al (2000) also noted declining frequency of cavitations with age. Chan et al (1995) stated that tuberculosis patients had extensive infiltrative lesions involving both the lungs.

Lower and upper zone involvement was found to be 67% and 27% distributed among the study subjects. This result was similar to the study by Perez- Guzman et al (2000).As age advances there will be reduced perfusion and increased alveolar ventilation. This results in ventilation perfusion mismatch. These changes were more observed in the lower lung fields. They have higher alveolar oxygen concentration and ventilation perfusion ratio. In contrast to the above Brande et al (1989) concluded that the radiological manifestations of pulmonary tuberculosis in adult patients do not differ in

frequency or distribution from those seen in the elderly adults.

When the radiological manifestations of adult tuberculosis in diabetic population were studied it was found that there was a significant involvement of lower zone and more infiltrative pattern when compared with non diabetic population. Perez – Guzman et al (2000) also demonstrated similar type of findings. Marias (1980) observed lower lung field tuberculosis in 29% patient with diabetes as compared to 4.5% in non diabetic population.Cavitation was less common because diabetes mellitus itself is an immunodeficiency state which decreases cell mediated immunity and it results in less tissue destruction.

In this study, infiltration and cavitation was observed in 43 and 23 patients respectively among smokers. Upper zone and lower zone was almost equally involved. Cavitation and infiltration was noted in 35% and 70% in males where as it was 35% and 80% in females respectively. It was found statistically that smoking and gender has no influence on the radiological patterns in tuberculosis in the elderly.

In the study sputum was positive in all tuberculosis patients in our study. Gaur et al (2004) had shown previously bacteriologically positive cases were more in adult people when compared with old age people (59.6% Vs 63.8%). Cavitation was more commonly found with a high grade sputum positivity. (Ethiopia R R study).

AREAS OF RESEARCH IN PULMONARY TUBERCULOSIS

1. Response to DOTS schedule.
2. Drug toxicity.
3. Pharmacodynamics status.
4. Compliance pattern.
5. Microbiological and genetic studies of isolate of pulmonary tuberculosis.

CONCLUSIONS

1. Adult men more likely to suffer from tuberculosis when compared with women (M: F = 2:1).
2. Irrespective of gender patients were diagnosed to have tuberculosis only 3 months after the onset of symptoms.
3. The commonest presenting symptoms were cough and sputum production, anorexia, weight loss and fever are next common symptoms.
4. About 83.2% of adult male tuberculosis patients were smokers. (All females were non smokers).
5. Body Mass Index was lower than the Indian standards.
6. Wasting observed in 75% in patients and anemia was observed in about 39% of the study population.
7. Involvement of both lungs (58%) was more common than the isolated involvement of the right (23.5%) or left lung (9.5%).
8. Infiltrative pattern was observed more than the cavitatory pattern on the chest x-ray of the study population. 1% of the study population has miliary tuberculosis.
9. Radiological findings were not influenced by smoking or gender. Auscultatory findings poorly correlate with radiological abnormality.

Cavitation associated with increasing bacterial load in the sputum, and is therefore a strong indicator for early treatment. X ray findings matched only one-third of auscultatory findings.

10. Diabetes mellitus was observed in about 11% of the study population. These patients had significantly lower lobe and infiltrative pattern of involvement.

11. If the Sputum smear are unavailable or cannot be processed, the presence of cavitations on chest X-ray in an appropriate clinical setting should be considered a strong indication for the commencement of anti-tuberculosis treatment, in symptomatic patients.

SUMMARY

Studies on pulmonary tuberculosis in adults are gaining importance globally, in view of future the increase in TB orphans (Loss of parents due to TB) and their immunological susceptibility to tuberculosis. The present reports deals with pulmonary tuberculosis in adult with special emphasis on the socio-demographic, clinical and laboratory aspects. A total of 200 adults (Males = 131 & Females =69, mean age 29.5years) subjects who satisfied a rigid set of inclusion and exclusion criteria were analyzed with respect to the objectives after obtaining institutional ethical clearance and informed consent. Data were analyzed statistically.

It was observed from this study that adult men suffered from tuberculosis more than the adult women and about 83.2% of them were smokers. Most of the subjects were diagnosed to have tuberculosis only three

months after the onset of illness with the commonest symptoms, being cough and breathlessness. About 75% of the study population had wasting and 39% had anemia with body mass index lower than the Indian standards.

Involvement of both lungs was common with infiltrative pattern more frequently observed than cavitatory pattern in the X-ray chest. 1% of the study population had military tuberculosis. 11% of the study population had diabetes mellitus where these patients had significantly involvement of lower lobe of lung and infiltrative pattern. Radiological findings were not influenced by gender and smoking.

In view of the increased prevalence of pulmonary tuberculosis in the adult and multiple reasons for the susceptibility, clinicians should suspect pulmonary tuberculosis in the adult with cough and productive and treat them accordingly after identifying associated co morbid status. Wasting is seen in 75% of adult tuberculosis. Cavitation on X-ray is associated with increasing smear grade and it should be considered a strong

indication for the commencement of anti-tuberculosis treatment if non availability of sputum smears in symptoms with appropriate clinical settings.

TB IS A GLOBAL EMERGENCY.

BUT

TB CAN BE CURED AND THE SPREAD OF DISEASE STOPPED.

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