CLINICAL PROFILE OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS– A STUDY OF 210 CASES

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CERTIFICATE

This is to certify that the dissertation titled "**CLINICAL PROFILE OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS – A STUDY OF 210 CASES"** is the bonafide original work of **DR. M.C.DEIVASIGAMANI** in partial fulfillment of the requirements for **M.D. Branch-I (General Medicine)** Examination of the Tamilnadu DR. M.G.R Medical University to be held in March 2007. The Period of study was from November 2005 to June 2006.

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DECLARATION

I, **DR.M.C.DEIVASIGAMANI,** solemnly declare that dissertation titled **"CLINICAL PROFILE OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS – A STUDY OF 210 CASES"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during November 2005 to June 2006 under the guidance and supervision of my unit chief **Prof. R. DEENADAYALAN, M.D**, Professor of Medicine.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

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CONTENTS

INTRODUCTION

Tuberculosis is a disease of great antiquity. The infectious agent , tubercle bacilli was discovered by Robert Koch in 1882. The disease primarily affects lungs and causes pulmonary tuberculosis. It can also affect Lymph nodes, Meninges, Intestine, bone ,joints, skin and other tissues of the body. According to WHO estimates ,around 1722 million people (one third of word population) are infected with Tubercle bacilli and 16 – 20 million cases of tuberculosis were reported worldwide in 2001.[1] India accounts for nearly one third of global burden of tuberculosis.[2] Despite efforts at early detection and treatment , tuberculosis remains a major public health problem in India. A total of 1.82 million of new cases and 4.17lakhs of deaths were reported every year in India. Tuberculosis is a disease that affects various organs with variety of presentation and causes significant morbidity and mortality. This study is undertaken to analyse the various clinical presentations in patients with pulmonary tuberculosis and extra pulmonary tuberculosis attending TB clinic of Stanley Medical college Hospital.

AIM

To analyze the clinical profile of newly diagnosed pulmonary and extra pulmonary tuberculosis in patients started on DOTS chemotherapy.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

EPIDEMIOLOGY

Tuberculosis is the most common infectious disease in the world. As per WHO estimates, one third of world's population is infected with tubercle bacilli and about 16 – 20 million cases of tuberculosis are prevalent world wide. More than 3.8 million new cases of tuberculosis were reported to the WHO in 2001. 90 % of these cases were from developing countries. WHO estimates that this figure is a gross underestimate, as the system of detection and reporting of cases in developing countries are incomplete. It has been estimated 8.5 million new of tuberculosis occurred in 2001. It has also been estimated that 1.8 million deaths occurred in 2000, and 98% of them in developing countries.

In India 1.82 million new cases with 3.29 lakhs of death, were reported in 2004. One third of world's tuberculosis patients are in India. Currently India ranks first in incidence and prevalence of tuberculosis followed by China and Indonesia second and third position respectively. In India, the incidence and prevalence rates reported are 168 and 312 per 1 lakh population respectively. A total of 8.14 lakhs of smear positive tuberculosis cases with a smear positivity rate of 75 per 1 lakh population were reported every year. 4.17 lakhs of death due to tuberculosis with a death rate of 30 per 1 lakh population were reported

every year. Thus tuberculosis remains the most common infectious disease in India causing significant morbidity and mortality. 50% of Indian population above the age 20 years is infected and will remain at risk of developing tuberculous disease.

In males prevalence of tuberculous infection increases up to 45 - 54 years and in females the peak of prevalence is noted below 35 years. Infants and young children have weak defences and are prone for milliary tuberculosis and tuberculous meningitis. Most of the cases are reported from rural and semi urban areas among low socio economic population where malnutrition and overcrowding are rampant. In urban areas it is reported mainly in slum dwellers.

The major risk factors for development of tuberculosis are extremes of age, malnutrition, overcrowding and immune deficient states like AIDS, Diabetes mellitus, measles, whooping cough & leukemia. Chronic malaria and worm infestation are less important risk factors. Tobacco smoking, high alcohol consumption, corticosteroid therapy and immunosuppressive drug therapy reduce body defences there by increasing the susceptibility to tuberculous infection.

NATURAL HISTORY OF TUBERCULOSIS

Mycobacterium tuberculosis is the causative agent in most of the human tuberculous patients. Mycobacterium bovis is the cause of bovine tuberculosis, was once an important cause of intestinal tuberculosis due to consumption of unpasteurized milk in developing countries.

Mycobacterium tuberculosis bacilli are rod shaped long, and often beaded of 4 micro meter in length, 0.5 micro meter in diameter. They are non spore forming, thin aerobic gram positive organisms. Once stained with ziehl neelsen stain, they strongly resist decolorisation by acid and alcohol, hence they are classified as acid fast bacilli (AFB). The main source of infection is through the inhalation of tubercle bacilli in to the lungs from an infectious adult patient (inhalation of droplet nuclei). Tuberculous bacilli may be ingested in food and milk causing intestinal tuberculosis by mycobacterium bovis. The time from the receipt of infection to the development of positive tuberculin test ranges from 3 – 6 weeks. There after the development of disease depends up on various factors, so the incubation period may be weeks or months or years.

Patients are infective as long as they remain untreated. Effective anti tuberculous therapy reduces infectivity by 90% with in 48 hours. Once the infective material is coughed out in the air the smallest droplets (<10 micrometer in diameter) will remain in the air for several hours and gain access

to the terminal alveoli when inhaled. The probability of contact with a case of tuberculosis, the intimacy and the duration of contact, the degree of infectiousness of the case, and the shared environment of the contact are all important determinants of transmission. Patients with culture negative tuberculosis and extra pulmonary tuberculosis are essentially non infectious.

The risk of developing disease after being infected depends largely on endogenous factors such as individual's innate susceptibility and the level of cell mediated immunity. The first infection with tubercle bacilli is known as primary tuberculosis is common among children up to 4 years of age which essentially is non infectious. Majority of the infected individuals, if develop tuberculosis, they do so with in the first 2 years after acquiring infection.[3] Dormant bacilli may persist for years before reactivating to produce secondary or post primary tuberculosis which is usually infectious. Over all 10% of the infected will develop active tuberculosis.

A variety of diseases and conditions favor the development of active tuberculosis. The most important potent risk factor for tuberculosis among infected individuals is HIV co infection. Other conditions include silicosis, chronic renal failure, hemodialysis, diabetes, intravenous drug abuse and jejuno ileal bypass. The risk of developing active tuberculosis is directly proportional to the degree of immuno suppression.

TIME TABLE OF TUBERCULOSIS (WALLGREN'S TABLE) [3]

The pattern of disease behaviour , defined by Wallgren in 1948 in Sweden, describes the natural history of the disease before specific interventions were

WALLGRENS TIME TABLE OF TUBERCULOSIS

TYPE OF TUBERCULOSIS	**TIME OF OCCURRENCE AFTER PRIMARY INFECTION**
Miliary TB	< 6 Months
TB meningitis	< 6 Months
Pleural Effusion	6 – 12 months
Phlyctenular conjunctivitis	< 1 year
Infiltration & Cavitation	1 – 2 years or later
Skeletal TB	1 – 5 years
Cutaneous TB	5 – 15 years
Genitourinary TB	5 – 15 years

applied. He observed that 8.1% of infected individuals developed clinical tuberculosis in 10 years after primary infection. Of them who developed disease , 54% developed with in 1 year and 80% developed with in 2 years of primary infection. Among those with active disease 33% of the patients died with in 1 year and 50% died with in 5 years. Therefore the greatest risk of developing disease following primary infection is within the first two years.

Miliary tuberculosis and tuberculous meningitis (common in < 5 years of age) occurred within 6 months following primary infection. Pleural effusion developed within 6 to 12 months following primary infection. Infiltration and cavitation (progressive primary / post primary tuberculosis) developed 1 -2 years after primary infection. Skeletal tuberculosis occurred 1-5 years after primary infection. Genitourinary tuberculosis and cutaneous tuberculosis developed 5 – 15 years after primary infection.

PATHOGENESIS AND IMMUNOLOGY

Once the tubercle bacilli reaches the alveoli of the lungs , there is an influx of polymorphonuclear cells and macrophages into the area. After few weeks, macrophages predominate. The macrophage then undergo metamorphosis to form epitheloid cells, to form the multinucleated or langerhan's giant cells. Lymphocytes surround the outer margin of the tubercle and in the centre of lesion a zone of caseous necrosis may appear that may subsequently calcify.

Primary infection is usually a subpleural tubercle (primary ghon focus), which may be in any lung zone along with the involvement of draining hilar lymph nodes forms the primary complex. Most primary infections heals with or without calcification. Hematogenous spread probably occurs via lymphatics in the majority of infections, resulting in seeding of tubercle bacilli to other parts

of lungs as well as other organs. The infection is usually contained at extra pulmonary site, but the potential for reactivation of infection at all sites is always present.

The reactivation of tuberculosis is most often seen in upper lung zones, most frequently to the posterior segment of the upper lobe or the apex of the lower lobe. The high ventilation perfusion ratio with increased alveolar Po2 is believed to predispose to reactivation at these sites. Proliferation of tubercle bacilli in the caseous centres is followed by liquefaction of caseous material which may discharge into the bronchus with resultant cavity formation. 10^4 tubercle bacilli per gram are formed in caseous material and upto 10^9 organisms may be harboured within a single cavitary lesion. Fibrous tissue forms around the periphery of the lesion but is usually in capable of limiting extension of the tuberculous process.

Hemorrhage may result from extension of the caseous process into the vessels within the cavity walls. Spread of caseous and liquefied material through the bronchial tree may disseminate the infection into the other lung zones with or without the development of vigorous inflammatory exudates or tuberculous pneumonia.

The seeding of the bacilli into vessel walls may cause caseous vasculitis of the intima with subsequent discharge of bacilli into the vessel. Rupture of caseous material into the pulmonary venous circulation results in dissemination

to all other organs where as rupture into the thoracic duct results in miliary tuberculosis of lungs with formation of multiple 0.5 – 2 mm tubercles all over the lungs. [4]

Enlarged tuberculous lymph nodes (hilar / mediastinal) may cause pressure on the bronchus which causes collapse of a segment or a lobe. Collapse is also caused by the spread of tuberculous granulomatous tissue into the bronchus with resultant stenosis or by discharge of caseous material from the lymph node through the bronchial wall. The middle lobe is most often affected.

Distension of the bronchial wall beyond the point of bronchial stenosis due to destruction of the wall by caseous process along with secondary infection may result in bronchiectasis especially following lobar or segmental lesions. Occasionally a bronchus is compressed in such a way that a valve action results, with resultant development of obstructive emphysema. Calcified primary focus or more commonly a calcified lymph node may get extruded into the bronchus as a broncholith which may present with hemoptysis. Rupture of a subpleural focus into the pleural space results in the development of pleural effusion. Enlarged node may perforate into the pericardium to produce a pericardial effusion.

When the resistance is poor the primary lesion may progress to form a tuberculous pneumonia which may cavitate. Less commonly the primary lesion

may enlarge to produce a round coin shaped lesion which subsequently calcifies. The other sequelae of bronchial involvement are:

1. Stricture of bronchus
2. Cylindrical bronchiectasis of the area of old collapse
3. Wedge shadow with fibrosis and bronchiectasis following contracture of segmental lesion
4. Linear scar of fibrosis following segmental lesion

IMMUNOLOGY

Immunity and the hypersensitivity are mediated by a population of immunocompetent T lymphocytes originating from thymus dependant areas of spleen and lymph nodes. In the naturally infected host, both immunity and hypersensitivity are believed to develop simultaneously.

Acquired immunity is mediated by T cells, almost certainly by Th – 1 cells (T helper/ CD 4) which reach the tubercle from the spleen and lymph node. On contact with antigen processed by the macrophages in the tubercle, lymphokines such as interleukin -2 and interferon gamma are released and activate the macrophages entering the lesion. These activated macrophages show structural, enzymatic, and metabolic changes, and phagocytose and kills the bacilli at a markedly enhanced rate compared with unstimulated cells.

A positive tuberculin test is the earliest indicator of infection with TB. It is critical to note that a negative tuberculin test does not rule out tuberculosis. Occurrence of negative tuberculin test are noted in patients with miliary TB. Cryptic Miliary TB, extensive disease and in older patients. The presence of anergy may be due to the activation of suppressor T Lymphocytes or the presence of a population of adherent cells, presumably Macrophages with suppressor properties. As a rule tuberculin anergy disappears after successful treatment of the underlying cause.

Infected macrophages secrete IL – 12, which promotes a non specific immune response mediated primarily by NK cells. CD 4 cells co ordinate the specific immune response in two ways :

1. Secrtetion of IL – 2 supports cytotoxic T lymphocytes to kill the cells infected with the tubercle bacilli.
2. Secretion of Interferon gamma primes the uninfected macrophages, altering them to kill the intracellular bacilli.

The cytotoxic T lymphocyte response is only bacteriostatic against infection and does not confer immunity to tuberculous infection. IL -12 is important in development of cell mediated immunity, TNF alpha is responsible for granuloma formation and the production of reactive nitrogen intermediates to kill the bacilli. Interferon gamma stimulate the production of TNF alpha by macrophages.[5]

The immune response detailed above is able to control the primary infection in most of the situations. However in 5% of cases, primary infection is progressive, and in 5 -10 % immune system initially controls and later fails with resultant endogenous reactivation. The mechanism of endogenous reactivation is probably a gradual or acute decline in local cell mediated immunity, at sites of high oxygen tension that were hematogenously spread during primary infection. Thus endogenous reactivation mostly develops in posterior apical segment of upper lobe or upper segments of lower lobe, Renal cortex and end plates of vertebral bodies.

Variability in HLA – D gene locus and genetic polymorphism in the NRAMP – 1 (Natural Resistance Associated Macrophage Protein – 1) are genetic predispositions to the development of clinically apparent disease.

The non specifically activated alveolar macrophages ingest the tuberculous bacilli which reach the terminal alveoli. The balance between the bactericidal activity of the macrophage and the number and virulence of the bacilli determine the events following phagocytosis. In the initial stage of infection either the host's macrophages contain bacillary multiplication by releasing proteolytic enzymes or cytokines otherwise the bacilli begin to multiply. If the bacilli multiply, their growth kills the macrophages which subsequently gets destructed.

About 2 – 4 weeks later, two types of host responses develop to the bacilli. They are:

1. Tissue damaging response - Delayed type of Hypersensitivity.
2. Macrophage activating Response

Though both these responses inhibit mycobacterial growth, the balance between the two will determine the form of tuberculosis, that will develop subsequently. Initially the tissue damaging response destroys macrophages and produces solid necrosis in centre of the tubercle. At this point some lesions may heal by fibrosis and calcification. Cell mediated immunity is critical at this early stage. T cells activate macrophages when they are presented with bacillary antigens by macrophage. The activated macrophages aggregate around the lesion centre and effectively neutralize the tuberculous bacilli without further tissue damage causing central caseating necrosis. Later healing takes place and followed by calcification. In minority of cases the macrophage activating response is weak and mycobacterial growth can be inhibited only by delayed type hypersensitivity which leads to increasing tissue damage. This ultimately leads to erosion of bronchial walls, blood vessels and formation of cavities. In the early stages of infection bacilli are usually transported by macrophages to regional lymphnodes from which they disseminate to many organs and tissues. Cell mediated immunity confers partial protection against tuberculosis while humoral immunity has no defined role in protection.

CLINICAL MANIFESTATIONS

Primary Tuberculosis

This is often seen in children which is localized to middle and lower zones (upper part of lower lobe and lower part of upper lobe). The lesion is usually peripheral and accompanied by hilar or para tracheal lymphadenopathy. This lesion is called as ghon's focus and along with adenopathy ghon's complex (primary complex). Most of the primary complex heals spontaneously and may be evident as a small calcified nodule. In some children and in immuno compromised patients primary complex may progress rapidly to clinical illness. Acute cavitation with mediastinal / para tracheal lymphadenopathy are the end results of progression. Enlarged lymph nodes may compress the bronchi and cause bronchiectasis, active collapse and emphysema. Hematogenous dissemination of bacilli is common during the stage of primary complex where the bacilli reaches various organs and may lead on to formation of granulomatous lesions. This is usually asymptomatic in most of the individuals, but in immunocompromised individuals this hematogenous spread might result in miliary tuberculosis / tuberculous meningitis.

Post Primary Tuberculosis

Post primary tuberculosis results from endogenous reactivation of latent infection. This is also called as Adult type, Reactivation or secondary

tuberculosis. This is usually localized to apical and posterior segments of upper lobe. This high predilection to the upper lobes is due to high ventilation perfusion ratio which maintains high partial pressure of oxygen which in turn favours the growth of aerophilic tuberculous bacilli. Because of same reason superior segments of lower lobes are also involved. The main presenting features are cough with sputum / cough only, fever, intermittent with night sweats with evening rise of temperature, loss of weight, and loss of appetite, hemoptysis, chest pain, breathlessness and unresolving pneumonia. Mild anemia and lecocytosis.

EXTRA PULMONARY TUBERCULOSIS

Tuberculous Lymphadenitis

Most common extra pulmonary site of tuberculosis is lymph node.[6] Tuberculous lymphadenitis commonly occurs in younger age group particularly in HIV positive patients. 90% of tuberculous lymphadenitis involves cervical lymph nodes and supra clavicular lymphnodes. Usually presents as painless enlargement of cervical lymph nodes which may become matted in later stages. Tuberculous lymph node may undergo caseation and lead to formation of cold abscess which may discharge and become a chronic non healing sinus. Primary lesion is very rarely identified in a case of tuberculous lymphadenitis and it may be due to hematagenous spread. Tuberculin test is usually positive and the diagnosis is mainly relied on fine needle aspiration cytology (FNAC) and excision biopsy. Excision biopsy is

more reliable as more tissue is available for study. 50% of the lymph nodes are AFB smear positive, 70% culture positive and 80 – 90 % shows granulomatous lesions.

Pleural tuberculosis

Pleural tuberculosis mainly results from penetration into the pleural space by tubercle bacilli, usually from rupture of a sub pleural focus. Other mechanisms by which tuberculosis involves the pleura are reactive, in which a immunological reaction to bacilli proteins leads on to pleural inflammation without bacilli entering the pleural cavity and rupture of a tuberculous cavity in to the pleural space which causes tuberculous empyema. Pleural effusion can occur along with primary lesion or as a post primary phenomena 6 – 12 months after primary infection. This commonly occurs in younger age group and tuberculous empyema occurs in elderly individuals. They commonly present as pleuritic type of chest pain which may later become dull aching. Sometimes they may have fever and mild irritative cough. If pleural effusion is massive , it can cause breathlessness.

Clinically pleural effusion pushes the trachea to opposite side with dull percussion note and diminished breath sounds on same side. Some times bronchial breathing can be heard above the level of massive pleural effusion. Pleural effusion is diagnosed by chest radiography and pleural fluid analysis. Pleural fluid is usually exudative with a protein more than 50% of serum,

normal or low glucose . WBC count of 500 – 2500/cu mm predominantly of lymphocytes is seen and PH is usually < 7.2. Usually pleural fluid is negative for AFB. Pleural fluid Adenosine Deaminase may also help in diagnosis . Pleural biopsy reveals granulomas and 70% of them may show positive cultures.

Genitourinary Tuberculosis

Genitourinary tuberculosis accounts for 15% of all extra pulmonary cases. Usually due to hematogenous spread following primary infection (5 – 15 years later). Renal tuberculosis presents as increased frequency, dysuria, haematuria, or Renal colic. Urine analysis is abnormal in 90% of cases. Sterile pyuria in acidic urine is the commonest abnormality. Renal tuberculosis can be diagnosed by intravenous pyelogram which reveals calcifications and urethral strictures. Urinary culture of morning sample may be positive for AFB in 90% of cases.

Genital tuberculosis is common in females. 85% of female genital tuberculosis affects fallopian tubes followed by endometrium. Commonest presentation being primary infertility and other presenting features are amenorrhea, menorrhagia and pelvic pain. Diagnosed by biopsy and culture of specimens obtained by dilatation and curettage. In males genital tuberculosis preferentially affects epididymis which usually presents as slightly tender mass

/ external fistula. Orchitis and prostatitis can also occur. 10% of male genital tuberculous patients present with primary sterility.

SKELETAL TUBERCULOSIS

Tuberculosis of bone commonly occurs in

- Spine – 50% (Potts disease)
- Hip – 15%
- Knee – 15%

In 70% of spinal tuberculosis 2 adjacent vertebral bodies get involved. The disease commences in the anterosuperior or inferior angle of the body and spreads to adjacent vertebral body. The disc gets involved and the disc space becomes narrowed, resulting in spinal cord compression which leads on to neurological deficit (paraparesis). Thoracic vertebra is the commonest site to be involved especially T 10 vertebral body. The presenting symptom is usually the spinal pain and patients finding difficulty in picking object from the floor by bending the spine. There may be a visible lump and angling of spine called gibbus. Other complications of spinal tuberculosis are paraspinal abscess and psoas abscess (cold abscess). CT scan and MRI scan are the main investigations to diagnose spinal tuberculosis. Aspiration of abscess and bone biopsy confirms tuberculous etiology. Tuberculin test is usually positive in skeletal tuberculosis.

TUBERCULOUS MENINGITIS

Tuberculous meningitis results from hematogenous spread of primary or post primary tuberculosis or from rupture of a sub ependymal tubercle in to the sub arachnoid space. This accounts for 5% of extra pulmonary tuberculosis. Most often children are affected but may occur in adults.

Tuberculous meningitis presents initially with low grade fever, malaise, intermittent headache which later become persistent with marked fever. Neck stiffness and oculomotor nerve palsies may occur. Later involuntary movements and focal neurological deficits can occur. In terminal stages intracranial tension progressively increases due to development of communicating hydrocephalus ultimately proceeding to decerebration and death.

CLINICAL STAGING OF TUBERCULOUS MENINGITIS [7]

STAGE	MANIFESTATIONS
I (Early – lasts upto 2 weeks)	Non specific signs and symptoms No clouding of consciousness or neurological deficits
II (Intermediate – lasts from days to weeks)	Lethargy or alteration in behaviour Meningeal irritation / cranial nerve palsies
III (Advanced)	Abnormal movements / convulsions / stupor/ coma Severe neurological deficits

Tuberculous meningitis is usually diagnosed by doing cerebrospinal fluid analysis which is exudative with elevated protein content (100 – 800mg/dl), Low glucose concentration and leucocytosis predominantly of lymphocytes (up to 400 cells / cu mm). CSF culture for AFB usually positive in 80% of cases. Tuberculin test is usually negative.

TUBERCULOMA

Tuberculoma presents as a space occupying lesion producing symptoms of raised intracranial tension , focal or generalized seizures , focal neurological deficit and headache. Cerebrospinal fluid shows a elevated protein level and CT scan / MRI scan reveals a contrast enhancing Ring lesions. Biopsy is necessary to establish the diagnosis.

GASTRO INTESTINAL TUBERCULOSIS

Commonly occurs in females. Intestinal tuberculosis usually results from swallowing of infective sputum with seeding of intestine. Sometimes it can also occur following hematogenous spread. In the era of consumption of unpasteurized milk, intestinal tuberculosis was commonly caused by ingestion of mycobacterium bovis. With wide spread pasteurization of milk this has become rare.

Terminal ileum ,caecum and jejunoileum are the commonest sites to be involved in intestinal tuberculosis. Usually presents with abdominal pain, alternating diarrhea and constipation and hematochezia. Some times intestinal tuberculosis may present with palpable abdominal mass. 20% of patients may go in for intestinal obstruction due to inflammatory thickening of the bowel , stricture formation , adhesion or extrinsic compression due to mesentric lymphadenitis. Perforation and fistula formation may also occur. Disease of the large bowel mimic inflammatory bowel disease with segmental ulcers, colitis, strictures and polyps. Abscesses particularly of psoas muscle and mesenteric lymph nodes occur frequently in abdominal tuberculosis and may lead to abdominal masses with or without sinus formation. Diagnosis is by plain X ray abdomen which may reveal psoas abscess and ultrasound abdomen shows thickened conglomerated loops of bowel, mesenteric adenopathy or hypoechoic lesions in liver and spleen. CT and MRI may be more informative. Ultimately diagnosis can be confirmed by intestinal biopsy or mesenteric lymphnode biopsy.

Tuberculous peritonitis follows either direct spread from ruptured mesenteric lymph nodes or seeding from intra abdominal organs. It also occurs due to hematogenous spread. Usually presents with abdominal pain, abdominal distension due to ascites and fever. Diagnosis of peritoneal tuberculosis is done by ascitic fluid analysis which shows exudative features with lymphocytosis. Laparoscopic Peritoneal biopsy is often needed to confirm the

diagnosis in 75% of cases. Adenosine Deaminase in peritoneal fluid is the most useful in diagnosis of peritoneal tuberculosis. Tuberculin test is usually positive.

TUBERCULOUS PERICARDITIS

Tuberculous pericarditis results from direct spread of primary focus in to the pericardium or reactivation of a latent focus or due to rupture of an adjacent mediastinal lymph node. It is a serious life threatening manifestation of tuberculosis. The commonest presentations are fever, retrosternal chest pain, cough and friction rub in initial stages. When effusion develops patient will have breathlessness, pulsus paradoxus , low blood pressure, raised JVPand enlarged liver. Ultimately leads to cardiac tamponade and constrictive pericarditis. Chest X ray shows cardiomegaly when pericardial effusions are present but the heart size may be normal when constriction predominates. ECG changes like low voltage complexes , T inversion or flattening occur in most of the cases. Echocardiography reveals pericardial effusion and pericardial thickening, with fibrinous or caseous debris. Pericardial fluid analysis is exudative with lymphocytosis and usually shows increased level of ADA (adenosine deaminase) and interferon gamma. Tuberculin test is usually positive.

DISSEMINATED TUBERCULOSIS

There are four types of disseminated tuberculosis :

1. Acute (Miliary TB)
2. Chronic Disseminated TB
3. Cryptic Miliary TB
4. Non reactive TB

ACUTE MILIARY TUBERCULOSIS

This is an acute progressively fatal illness occurring usually in children and elder people over 65 years of age. Miliary tuberculosis is due to hematogenous spread of tuberculous bacilli of recent infection or reactivation of old foci. Lesions are usually of granulomas of 1 -2 mm in diameter resembling millet seeds. The patients usually present with fever, loss of appetite and other constitutional symptoms. Patients may be having Hepatosplenomegaly , generalized lymphadenopathy, anemia, meningismus and choroidal tubercle. Granulomatous hepatitis occurring in disseminated tuberculosis may present with mild jaundice with elevation of serum alkaline phosphatase disproportionately than the transaminases. Chest X ray may be normal up to three weeks and later it may show miliary, reticulo nodular pattern. Sputum smear for AFB is negative in 80% of cases. Bronchoalveolar lavage and transbronchial biopsy may be needed for bacteriological confirmation. Biopsy of bone marrow and liver may reveal granulomas.

Mantoux test may be positive in early illness but become negative as the disease advances and again positivity is restored after treatment.

CRYPTIC MILIARY TUBERCULOSIS

Usually occurs in the elderly people which is characterized by intermittent fever and anemia ultimately there is meningeal involvement before death. Tuberculin test is usually negative . liver and bone marrow biopsy may reveal granulomatous lesions.

NON REACTIVE MILIARY TUBERCULOSIS

It occurs due to massive hematogenous dissemination of tuberculous bacilli. It is an acute malignant form of tuberculous septicaemia . The patient is extremely ill. Unusual blood dyscrasias like pancytopenia ,aplastic anaemia and polycythemia may be present. Histologically the lesions are necrotic but non granulomatous. Mantoux test is usually negative.

CHRONIC DISSEMINATED TUBERCULOSIS

This is a distinct form of tuberculosis in which involvement of individual organs for example wrist followed by lymph nodes, testis, and kidney occurs at intervals over a period of months or years.

CUTANEOUS TUBERCULOSIS

Cutaneous tuberculosis is very rare but may present in one of the following ways

1. Lesions caused by inoculation from exogenous source. In this primary skin lesions occur with regional lymphadenopathy and usually present with ulceration or a hyperkeratotic papule without adenopathy.
2. Lesions from endogenous source. In this type two forms of tuberculosis namely scrofuloderma and orificial TB occur. Scrofuloderma is a fistulous opening sinuses of necrosed lymph nodes, bones and epididymis. Orificial TB occurs in the mouth, rectum and vagina.
3. Lesions which occur as a result of hematogenous spread. In this type two forms of lesions occur . They are Lupus vulgaris and multiple abscess. Lupus vulgaris most commonly occurs over the face especially over the nose.
4. Tuberculides – These are due to hypersensitivity phenomena. In this category the lesions included are erythema nodosum and papulonecrotic tuberculides.

OCULAR TUBERCULOSIS

Ocular manifestations of tuberculosis are very rare occurring in 1.4% of patients. Phlyctenular conjunctivitis is characterized by single vesicular lesion near the limbus with erythema. Tuberculous keratitis and scleritis usually result from spread of infection and granulomatous reaction from with in the eye.

Granulomatous lesions are described commonly in posterior choroids also associated with pan uveitis.

OTHER LESS COMMON TYPES OF TB

Tuberculosis of the upper respiratory tract occurs in about 1.8% of TB patients. Larynx is the most common site involved which is highly infectious. Tuberculosis of the nasal mucus membrane is extremely rare and can mimic wegeners granulomatosis. Tuberculous otitis media usually presents with deafness facial palsy , multiple perforations of tympanic membrane and painless otorrhea. Adrenal tuberculosis is rare which may lead to addisons disease. Congenital tuberculosis is due to trans placental spread or hematogenous infection via the umbilical vein or fetal aspiration/ inhalation of infected amniotic fluid resulting in primary lesions in liver and lungs respectively.

DIAGNOSIS

SPUTUM EXAMINATION

Sputum smear examination by direct microscopy is now considered the method of choice for diagnosis of pulmonary tuberculosis. The reliability, cheapness and ease of direct microscopic examination has made it number one case finding method all over the world. Three specimens of sputum should be examined. The first spot specimen is collected when the patient first presents to

the TB clinic. The second specimen should be collected in the early morning of next day and a third specimen collected in the TB clinic on the second day.

Acid fast bacilli are stained red by Zeihl Neelsen method and then identified and counted using microscopy. In patients who are not able to produce sputum by coughing, the other methods like ultrasonic nebulisation with 3% hypertonic saline, fiberoptic bronchoscopy with bronchial brushings and broncho alveolar lavage may be performed to obtain sputum. Laryngeal swabs are useful in some cases. Resting gastric juice for AFB is useful in pediatric age group who often do not cough out sputum.

SPUTUM CULTURE

Culture of mycobacterium tuberculosis is difficult, time consuming and expensive procedure. This method is offered only to patients presenting with chest symptoms whose sputum smear is negative by direct microscopy and extra pulmonary tuberculosis like lymph node, bone marrow etc. Culture on Lowenstein jensen medium (egg or agar based medium) takes 3 – 6 weeks to give a result but rapid diagnosis is possible within 2 – 6 days by using a radiometric culture system (Bactec).

RADIOGRAPHY

Exceptionally pulmonary tuberculosis may present with a normal radiography. Although the classic picture is that of upper lobe disease with

infiltrates and cavities. Virtually any radiographic pattern ranging from a normal or a solitary pulmonary nodule or a diffuse alveolar infiltrates may be seen. In contrast immunocompromised patients including HIV may have atypical findings on chest radiography with lower zone infiltrates without cavity formation.

Pleural effiusion and hydropneumothorax can be diagnosed using chest radiography. Coin lesions , hilar or paratracheal adenopathy can also be diagnosed.

TUBERCULIN TEST

The test was discovered by Von pirquet in 1907. A positive reaction to the test is generally accepted as evidence of past or present infection by mycobacterium tuberculosis. The tuberculin test is the only means of estimating the prevalence of infection in a population. There are three types of tuberculin tests available.

1. Mantoux intradermal test
2. Heaf test
3. Tine multiple puncture test

The mantoux test is commonly used. The test material or antigen is known as tuberculin (PPD – Purified Protein Derivative). The PPD is standardized in terms of its biological activity as tuberculin units (TU). 1 TU is equal to

0.00002 microgram of PPD. The WHO advocates a PPD tuberculin known as " PPD – RT – 23 with tween 80'' .

MANTOUX TEST

It is carried out by injecting intradermaly on the volar surface of forearm usually left side, 1 TU of PPD in 0.1ml. The result of the test is read after 48 - 72 hours. Usually the induration is measured in the transverse diameter. Reactions of 10 mm or more are considered positive reactions, 6 – 9 mm are considered doubtful and less than 6 mm are considered negative. Doubtful reactions are due to mycobacterium tuberculosis or atypical mycobacterium. More than 20 mm reactions are considered as strongly positive. Tuberculin reaction is basically a type IV hypersensitivity which consists of erythema and induration. A positive reaction indicates a person is infected with TB. Positive reactions are significant in younger age groups especially below 2 -3 years. It is observed that strong reactors (> 20 mm) have greater chance of developing tuberculosis. Also those with less than 6 mm have more risk of developing tuberculosis. Mantoux test is limited by lack of specificity, sensitivity due to high coverage of BCG and cross reactions due to sensitization by other mycobacterium.

Factors with false negative tuberculin skin test are: [5]

1. Viral infections (measles, mumps, HIV)
2. Military TB, TBM
3. Chronic renal failure
4. Malnutrition [8]
5. Neoplastic diseases (Hodgkin's Lymphoma)
6. Corticosteroid / Immunosuppressive therapy
7. Very recent exposure (< 4-7 weeks)

DOTS CHEMOTHERAPY

DOTS – DIRECTLY OBSERVED TREATMENT – SHORT COURSE [2]

DOTS is a strategy to ensure cure by providing the most effective medicine and confirming that it is taken.

In DOTS during the intensive phase, health worker watches as the patient swallows the drug in his presence. During the continuation phase the patient is issued medicine for one week. Globally this strategy has been recognized as the best cost effective approach for TB control, to reduce disease burden and reduce the spread of infection. The target is successful treatment or cure rate of 85% of new sputum positive cases and detection of 70% of such cases. Since 1993, India has successfully implemented Revised National TB Control Programme (RNTCP) using DOTS strategy.

The cases are divided into three categories CATI, CATII, CATIII.

CATEGORY OF TREAMENT	**TYPE OF PATIENT**	**REGIMEN**
CAT - I	i) New sputum – smear positive ii) Seriously ill – smear negative iii) Seriously ill – extra pulmonary	$2(HREZ)_3$ + $4(HR)_3$
CAT - II	i) Sputum smear positive – Relapse ii) Sputum smear positive – Failure iii) Sputum smear positive – Treament after default	$2(HREZS)_3$ $1(HREZ)_3$ $5(HRE)_3$
CAT - III	i) Sputum smear negative – Not seriously ill ii) Extra pulmonary - Not seriously ill	$2(HRZ)_3$ $4(HR)_3$

- The number before the letters refers to the number of months of treatment
- The subscript after the letters refers to the number of doses per week
- H – Isoniazid (600mg) ; R – Rifampicin (450mg); Z – Pyrazinamide (1500mg)
- E – Ethambutol (1200mg); S – Streptomycin (750mg)

Examples of Seriously ill Extra pulmonary Tuberculosis are

1. TB Meningitis
2. Disseminated TB
3. TB Pericarditis
4. TB Peritonitis
5. Pleural TB
6. Spinal TB
7. Intestinal TB
8. Genito Urinary TB

PATIENTS AND METHODS

1. Patients attending RNTCP (Revised National TB Control Programme) clinic at Government Stanley Medical College Hospital for DOTS therapy who were newly diagnosed to have Pulmonary and Extra pulmonary Tuberculosis were taken up for the study.

2. Patients under study were analyzed for clinical features like productive cough, non productive cough, fever, loss of appetite/ weight and hemoptysis.

3. The following investigations were done:

- Sputum smear for AFB
- Chest X ray
- Mantoux Test
- Hemogram – TLC, DLC, ESR, Hb%
- Specific investigations for various types of Tuberculosis.

4. The following criteria were taken to select pulmonary and extrapulmonary tuberculosis:

a) **Pulmonary TB**

i) Sputum positive cases

ii) Chest X-Ray positive cases / Sputum negative

- Upper zone infiltrates
- Cavity
- Bilateral apical infiltrates

- Pulmonary fibrosis

b) **Extra Pulmonary TB:**

i. **Lymphnode** – Histopathological study by FNAC/Excision biopsy of Lymphnode showing tuberculous granuloma.

ii. Pleural effusion

- Patients with clinical and radiological evidence of pleural effusion
- Pleural effusion with concomitant parenchymal involvement were included in pulmonary category
- Pleural fluid analysis showing exudative pattern (increased protein and decreased sugar) with lymphocytosis
- Pleural fluid – AFB positive

iii**) TB Pericarditis**

- Radiological evidence of Pericardial Effusion
- Echocardiogram showing pericardial effusion with fibrotic strands
- Pericardial fluid – exudative (protein > 3 gms & low sugar) and Lymphocytosis

iv) **TB Ascites/Abdomen**

- Clinical features suggestive of abdominal pain, distention, loss of weight, loss of appetite

- Ultrasonogram of abdomen showing ascites or mesenteric LN
- Ascitic fluid analysis – exudative fluid and lymphocytosis

v) **TB Meningitis**

- Clinical features like fever / altered sensorium / neck rigidity with or without seizure / cranial nerve palsies / Headache
- CSF study showing exudative fluid and lymphocytosis.

vi) **Tuberculoma**

- Patient with focal neurological deficit / seizures with contrast CT – Scan showing ring enhancing lesion.

vii) **Intestinal TB (Ileocaecal)**

- Patients with abdominal pain / abdominal mass / diarrhea
- Colonoscopy and intestinal biopsy showing TB granuloma

viii) **Spinal TB**

- Clinical features – Gibbus / Back pain with or without neurological deficit.
- Radiological evidence (CT/MRI scan) showing destruction of intervertebral disc, collapse of vertebral bodies / paravertebral abscess (cold abscess)

ix) **Genital TB**

- Female – Patient with amenorrhea / infertility / lower abdominal pain with endometrial / adnexal biopsy showing TB granuloma
- Male – Swelling in the scrotum with thickening of epididymis / HPE of TB granuloma

x) **TB Arthritis**

- Patient presenting with joint pain and swelling with synovial aspirate showing exudate with Lymphocytosis
- Synovial biopsy – showing TB granuloma

xi) **Skin TB**

- Patient with non-healing ulcer / erythematous nodules with a biopsy showing TB granuloma

5. **Exclusion Criteria**

- Patients who were started on category II DOTS chemotherapy (Defaulters , Relapse , Failure cases).
- TB Patients with HIV co infection.

- Patients with other medical illnesses like Diabetes mellitus, Malignancy, Chronic Renal Failure and Renal transplant patients on immunosuppressive therapy.

RESULTS

RESULTS : 210 patients were analysed and the results are

TOTAL NUMBER OF PATIENTS - 210

NUMBER OF MALES - 143 (68.1%)

NUMBER OF FEMALES - 67 (31.9%)

MEAN AGE- 38.52 Yrs

RANGE - 13 TO 80 Yrs

TABLE – 1

AGE AND SEX DISTRIBUTION

AGE RANGE In YRS	MALE	FEMALE	TOTAL
13 – 20	19(13.3%)	16 (23.9%)	35 (16.7%)
21 - 30	30 (21%)	18 (26.9%)	48 (22.8%)
31- 40	31 (21.7)	13 (19.4%)	44 (21%)
41 - 50	22 (15.4%)	12 (17.9%)	34 (16.2%)
51 - 60	19 (13.3%)	05 (7.5%)	24 (11.4%)
61 - 70	18 (12.6%)	01 (1.5%)	19 (9%)
> 71	04 (2.8%)	02 (3%)	O6 (2.9%)
TOTAL	143 (68.1%)	67 (31.9%)	210

Around 50% of cases are within the range 13 to 40 years of age. Males were more commonly affected than females.

TABLE – 2

SEX DISTRIBUTION IN TYPE OF TUBERCULOSIS

TYPE OF TB	**MALE**	**FEMALE**	**TOTAL**(n- 210)
PULMONARY TUBERCULOSIS	94	29	123 (58.57%)
EXTRA PULMONARY TUBERCULOSIS	49	38	87 (41.42%)

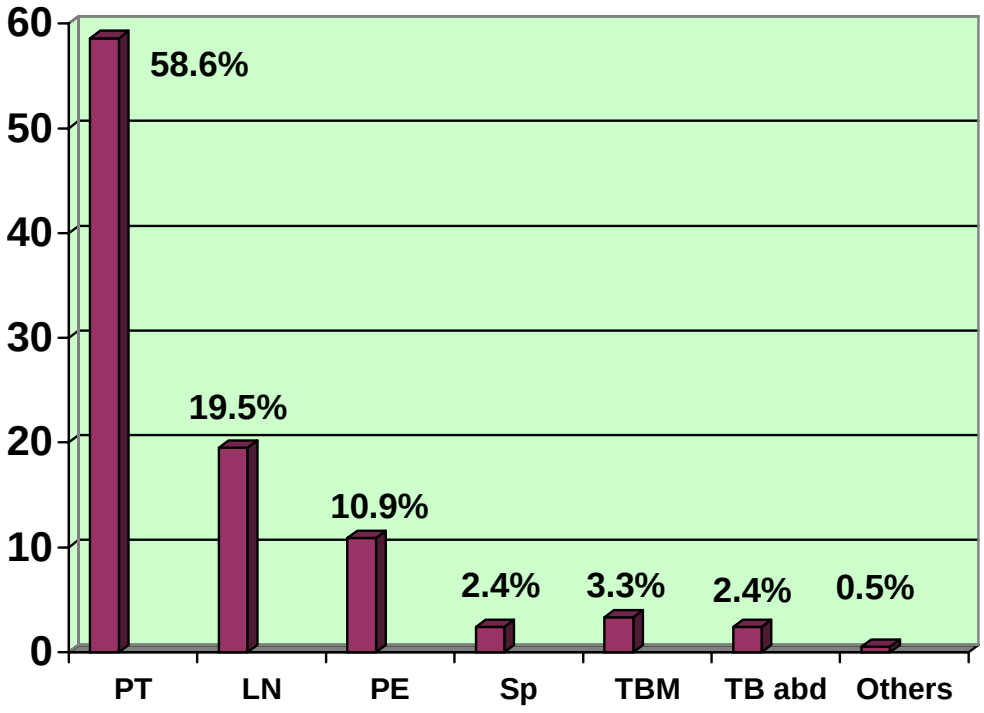
Pulmonary Tuberculosis is more common than extrapulmonary tuberculosis.

TABLE – 3

TYPES OF TUBERCULOSIS AND THEIR INCIDENCE

CATEGORY	**MALE**	**FEMALE**	**TOTAL** (n-210)
PULMONARY	94	29	123(58.6%)
LYMPH ADENITIS	19	22	41 (19.5%)
PLEURAL EFFUSION	17	06	23 (10.9%)
SPINE	04	01	05 (2.4%)
TB ARTHRITIS	01	-	01 (0.5%)
TB ABDOMEN	02	03	05 (2.4%)
PERICARDITIS	01	-	01 (0.5%)
TBM	03	04	07 (3.3%)
TUBERCULOMA	-	01	01 (0.5%)
GENITAL TB	01	-	01 (0.5%)
SKIN GRANULOMA	-	01	01 (0.5%)
ERYTHEMA NODOSUM	01	-	01 (0.5%)
TOTAL	143	67	210

BAR CHART SHOWING PROPORTION OF VARIOUS TYPES OF TUBERCULOSIS



LEGEND : PT – Pulmonary tuberculosis,

LN – Lymphadenitis

PE – Pleural Effusion

Sp – Spinal Tuberculosis

TBM – Tuberculous Meningitis

TB abd – Tuberculous Abdomen

Others – TB arthritis, TB pericarditis, Genital TB, Tuberculoma, cutaneous Tuberculosis each 0.5%.

TABLE – 4

VARIOUS PERCENTAGE OF EXTRA PULMONARY TUBERCULOSIS

TYPES OF EXTRAPULMONARY TUBERCULOSIS	MALE	FEMALE	TOTAL (n-87)
LYMPH ADENITIS	19	22	41 (47.1%)
PLEURAL EFFUSION	17	06	23 (26.4%)
SPINE	04	01	05 (5.7%)
TB ARTHRITIS	01	-	01 (1.1%)
TB ABDOMEN	02	03	05 (5.7%)
PERICARDITIS	01	-	01 (1.1%)
TBM	03	04	07 (8%)
TUBERCULOMA	-	01	01 (1.1%)
GENITAL TB	01	-	01 (1.1%)
SKIN GRANULOMA	-	01	01 (1.1%)
ERYTHEMA NODOSUM	01	-	01 (1.1%)
TOTAL	49	38	

Tuberculous lymphadenitis and pleural effusion were the common types of extrapulmonary tuberculosis.

TABLE - 5

TYPE OF TB IN VARIOUS AGE GROUP

TYPE	**13-20 yrs**	**21-30 yrs**	**31-40 yrs**	**41-50 yrs**	**51-60 yrs**	**61-70 yrs**	**71-80 yrs**
Pulmonary n-123	8 (6.5%)	20 (16.2%)	30 (24.4%)	26 (21.1%)	18 (14.6%)	17 (13.8%)	04 (3.2%)
LN n-41	14 (34.1%)	13 (31.7%)	06 (14.6%)	03 (7.3%)	02 (4.8%)	01 (2.4%)	02 (4.8%)
PL EFF n-23	06 (26.1%)	05 (21.7%)	06 (26.1%)	01 (4.3%)	03 (13%)	01 (4.3%)	01 (4.3%)
Spine	-	01	02	02	-	-	-
Arthritis	01	-	-	-	-	-	-
ABD	02	01	-	01	01	-	-
Pericardial	-	01	-	-	-	-	-
TBM	01	03	02	-	-	01	-
Tuberculoma	01	-	-	-	-	-	-
Genital	01	-	-	-	-	-	-
Skin	-	01	-	-	-	-	-
Erythema nodosum	-	01	-	-	-	-	-

The peak incidence of pulmonary tuberculosis is noted between 20 – 50 years. Most of the patients with tuberculous lymphadenitis and pleural effusion were noted in the age group of 13 – 40 years.

TABLE – 6

CLINICAL FEATURES : PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

CLINICAL FEATURES	**PULMONARY** TB (n – 123)	**EXTRA PULM** TB (n-87)
Cough & sputum	106(86.2%)	05(5.7%)
Dry Cough	11(8.9%)	15(17.2%)
Fever	76(61.8%)	32(36.8%)
LOA/LOW	70(57.8%)	48(55.2%)
Hemoptysis	28(22.8%)	-
Spinal pain	-	03
Gibbus	-	02
Joint pain/effusion	-	01
Abd pain/ distension	-	05
Chest pain	07(5.7%)	01
Neck stiffness	-	07
Seizures	-	01
Skin ulcer	-	01
Erythematous nodule	-	01
Epididymal nodule	-	01

Constitutional symptoms like fever , LOA/LOW were more common in pulmonary tuberculosis than extrapulmonary tuberculosis.

TABLE – 7

MANTOUX POSITIVE

MANTOUX IN mm	**PULMONARY** (n- 123)	**EXTRA- PULM** (n- 87)	**TOTAL** (n-210)
5 – 10	02	01	03
10 – 20	14	10	24
TOTAL	16 (13%)	11 (12.6%)	27(12.9%)

MEAN – 11.74mm

RANGE – 5 To 17 mm

TABLE - 8

MANTOUX POSITIVE IN TYPES OF TB

TYPE	**MALE**	**FEMALE**	**TOTAL** (n-27)
PULMONARY	08	07	15 (55.6%)
TB LN	05	05	10 (37%)
TB SPINE	01	-	01 (3.7%)
PL EFFUSION	01	-	01 (3.7%)

In extrapulmonary tuberculosis patients, Mantoux positivity is commonly noted in tuberculous lymphadenitis.

TABLE – 9

SPUTUM SMEAR AFB POSITIVE

PUL TB - 49 (39.83%)

EXTRA PUL - 0

GRADING SP +ve	**NUMBER OF PTS (n – 49)**
1+	25 (51%)
2+	04 (8.2%)
3+	20 (40.8%)

Sputum positivity occurred only in pulmonary tuberculous patients.

TABLE – 10

ERYTHROCYTE SEDIMENTATION RATE

ESR 1 hr reading	**PULMONARY** (n- 123)	**EXTRA- PULM** (n- 87)	**TOTAL** (n-210)
< 40 mm	65 (52.8%)	45 (51.7%)	110 (52.4%)
40 – 100 mm	47 (38.2%)	31 (35.6 %)	78 (37.1%)
> 100mm	11 (8.9%)	11 (12.6%)	22 (10.5%)

Around 50% of both pulmonary and extra pulmonary TB patients had ESR > 40mm in one hour

TABLE – 11

LYMPHOCYTE COUNT

TYPE	**< 40**	**40 – 60**	**> 60**
PULMONARY TB (n – 123)	105 (85.36%)	18 (14.6%)	NIL
EXTRA PULM TB (n-87)	76 (87.35%)	11 (12.64%)	NIL
TOTAL (n – 210)	181 (86.2%)	29 (13.8%)	NIL

Most of the patients had normal lymphocyte count

TABLE - 12

MANTOUX POSITIVITY IN SPUTUM POSITIVE CASES

Total sputum +ve	49
Mantoux +ve	05 (10.2%)

TABLE - 13

ESR AND SPUTUM POSITIVITY

ESR IN 1 hr	**SPUTUM +VE** (n – 49)
< 40	27 (55.1%)
40 – 100	18 (36.7%)
>100	04 (8.2%)

TABLE - 14

LYMPHOCYTE COUNT AND SPUTUM POSITIVITY

LYMPHOCYTE COUNT	**SPUTUM +VE** (n – 49)
< 40	40 (81.6%)
> = 40	09 (18 .4%)

TABLE – 15

RADIOLOGICAL PATTERNS OF PULMONARY TB

SL.No	RADIOLOGICAL PATTERN	No. (%)	SPUTUM +VE
1.	Upper zone / Apical Infiltrates		
	a) Unilateral	50(40.7%)	16(32%)
	b) Bilateral	44(35.8%)	17(38.6%)
2.	Lower zone Infiltrates	4(3.3%)	0(0%)
3.	Fibro cavity	23(18.7%)	14(61%)
4.	Miliary nodular pattern	2(1.7%)	2(100%)

Common radiological pattern observed in pulmonary TB was apical/ upper zone infiltrates.

DISCUSSION

DISCUSSION

Tuberculosis has been declared as global health emergency in the year of 1993 by WHO and it was emphasized to take adequate measures to control tuberculosis. In India, tuberculosis still remains to be a major infectious disease causing considerable morbidity and mortality in various age groups with variable presentations. This study is undertaken to analyze the various clinical presentations and laboratory parameters in the patients attending TB clinic, Govt. Stanley Medical college Hospital, Chennai.

A total of 210 patients newly diagnosed to have tuberculosis (pulmonary and extra pulmonary) who were started on DOTS chemotherapy, were analyzed. 143 (68.1%) were males and 67 (31.9 %) females. Mean age of presentation was 38.5 years and ranging between 13 to 80 years. In our study around 60% of patients were in the age group of 20 to 50 years.

Pulmonary Tuberculosis occurred in 123(58.6%) and Extrapulmonary tuberculosis in 87(41.4%) patients. Lowieke AM et al from Netherlands reported a similar incidence of Pulmonary Tuberculosis in 62% and Extrapulmonary tuberculosis in 38%, in their study of 13,000 patients. [9] There is a steady increase in occurrence of Tuberculosis from 20 years in females and 30 years in males.

Out of 123 Pulmonary tuberculosis patients 94(76.4%) were males and 29(23.6%) females. The male female ratio is 3.2 : 1. Mean age of occurrence of pulmonary tuberculosis was 42.96 years. Most of the patients were in the age group of 20 – 50 years with peak occurrence from 31 – 40 years (24.4%). This is consistent with the reported maximum incidence of Pulmonary tuberculosis in the age group of 15 – 59 years in developing countries as mentioned in Manson's text book of tropical diseases. [10] Lowieke AM et al from Holland reported a mean age of 39 years for occurrence of Pulmonary Tuberculosis. [9]

In our study, the common clinical presentation of Pulmonary Tuberculosis were cough with sputum(86.2%), fever (61.8%), loss of appetite/ loss of weight (57.8%), Hemoptysis(22.8%) and chest pain / breathlessness(5.7%). Manjula Datta et al from North Arcot district of Tamilnadu had reported a incidence of cough with sputum in 77% of pulmonary tuberculosis. [11] 39.83% of pulmonary tuberculosis patients showed sputum smear positivity for AFB and 12.2% of pulmonary tuberculous patients showed Mantoux positivity.

Out of 87 patients with Extrapulmonary tuberculosis 49 (56.3%) were males and 38 (43.7%) females. The male female ratio is 1.3:1. Mean age of occurrence was 32.28 years.Most of the patients (78.2%) were in the age group of 13 – 40 years. Lowieke AM et al from Netherlands reported a mean age of 40.3 years in Extrapulmonary tuberculosis. [9] Constitutional symptoms noted in

extrapulmonary tuberculosis were loss of appetite/ weight (55.2%), fever (36.8%) and Dry cough (17.2%).

In our study Tuberculous Lymphadenitis is the most common Extrapulmonary tuberculosis noted. Overall Lymphadenitis occurred in 41(19.5%) patients and accounted for 47.1% of Extrapulmonary tuberculosis. Most of these patients were in the age group of 13 – 30 years. 22(53.7%) were females and 19(46.3%) males. 37(90%) patients had isolated cervical node involvement, two patients had axillary node involvement along with cervical nodes and two had generalized Lymphadenopathy. B C Jha et al from Chandigarh reported highest incidence of tuberculous lymphadenitis between 11 – 30 years and 87.5% involvement of cervical lymphnodes in tuberculous lymphadenitis. [12] Lowieke AM et al from Netherlands reported a incidence of 15.1% of tuberculous lymph adenitis out of 13,000 tuberculous patients studied, which accounted for 38.9% of extrapulmonary tuberculosis. [9] The findings of both these authors were consistent with our study. Fever (9.8%), loss of appetite / loss of weight (53.7%) and non productive cough(9.8%) were other clinical features noted in Tuberculosis Lymphadenitis patients. 10 (24.4%) patients with tuberculous lymphadenitis showed positive mantoux reaction.

Pleural Tuberculosis is the second most common cause of Extrapulmonary Tuberculosis noted in our study, which occurred in 23(11%)

of tuberculous patients, which accounted for 26.4% of extrapulmonary tuberculosis. 17(73.9%) were males and 6(26.1%) females. . Male female ration is 2.8 :1. Peak incidence of pleural Tuberculosis is noted between 13 – 40 years of age. Common clinical features noted were fever (69.5%), non productive cough (30.4%), loss of appetite/loss of weight(56%), chest pain/ breathlessness(26%) and sputum production(13%). N R Rau reported a incidence of non productive cough (70%), Pleuritic pain (50 – 75%) and fever in most of the patients of pleural tuberculosis. [13]

Tuberculous Meningitis occurred in 7(3.8%) of tuberculous patients, which accounted for 8% of Extrapulmonary tuberculosis. 5(71.1%) presented in the age group of 20 – 40 years. Three were males and four females. 2(28.6%) patients had pulmonary tuberculosis in association with TBM and both were males. Prabakhar et al noted 20 -70% incidence of pulmonary tuberculosis in association with CNS tuberculosis.[14] Aparna agarwal and Rajasekar varma reported a 7-12 % incidence of CNS tuberculosis predominantly tuberculous meningitis.[15] Clinical presentations were fever 100%, headache 71.4%, altered sensorium and neck rigidity 85.7%, and cough sputum 28.6%. S Venkatraman et al reported fever (60 – 100%), neck rigidity (60 -70%) and Headache (50 – 60%) in tuberculous meningitis patients. [16]

Spinal Tuberculosis occurred in 5(2.4%) patients which contributes 5.7% to Extrapulmonary tuberculosis. Three patients reported with back pain

and two patients had gibbus. Two patients had loss of appetite / loss of weight and fever/ cough occurred in one patient each. All five patients were diagnosed by MRI finding of verteberal body and disc destruction with psoas abscess in one patient. Thoracic vertebra(T8 – T12) were affected in four patients(80%) and one patient (20%) had cervical tuberculosis (C6-C7). Neurological deficit occurred in two patients in the form of paraparesis.

Abdominal Tuberculosis occurred in 5(2.4%) patients which accounted for 5.7% of extrapulmonary. Three were females and two males. Two patients had (40%) ileocaecal tuberculosis and three had (60%) peritoneal tuberculosis. Abdominal pain occurred in three patients, mass abdomen in two patients and ascites in three patients. Constitutional symptoms like fever (3 patients), loss of appetite/ loss of weight (4 patients) and diarrhea (2 patients) were noted. A K Jain et al noted Abdominal Pain (86%), Abdominal distension (37%), Abdominal mass (33%) , Fever (61%), weight loss (63%) and diarrhea (22%) of patients with Abdominal tuberculosis and he had also reported a slight female preponderance in occurrence of abdominal tuberculosis.[17] Deepak Amarpurkar et al also reported a similar incidence of clinical features in abdominal tuberculosis. [18]

Other less common types of extrapulmonary tuberculosis noted were tuberculous pericarditis, tuberculoma, genital tuberculosis, tuberculous skin

ulcer, erythema nodosum and tuberculous arthritis which occurred in one patient each.

Tuberculosis pericarditis occurred in a male patient aged 25 years, who presented with fever, chest pain and cough with sputum/ hemoptysis. Tuberculoma occurred in female patient aged 16 years, who presented with left focal seizures and headache. Tuberculosis arthritis occurred in a male patient aged 13 years who presented with right knee pain and swelling, fever and with restricted mobility. Genital tuberculosis occurred in a male patient aged 16 years in the form of epididymal nodule. Lupus vulgaris occurred in a female patient aged 23 years, who presented with the non- healing ulcer over the right leg with fever and loss of appetite/ loss of weight. Over all cutaneous tuberculosis occurred in two patients (0.95%), one lupus vulgaris and one erythema nodosum. Both were in the age group of 21 – 30 years. Patra A C et al reported peak incidence of cutaneous tuberculosis between 5 – 25 years.[19]

A total of 49(23.3%) patients showed sputum smear positivity for AFB. Sputum positivity was noted only in pulmonary tuberculosis and none of patients with extrapulmonary tuberculosis showed sputum AFB positivity. Hence 39.83% of pulmonary tuberculous patients were positive for sputum AFB. 40.8% of sputum positive cases were strongly positive, who showed a grading of 3+.

In our study a total of 27(12.9%) patients showed positive mantoux reaction, of which 55.5% had pulmonary tuberculosis and 44.4% extrapulmonary tuberculosis. 24 (88.9%) patients showed a induration of more than 10mm and 3 patients showed induration of 5 – 10 mm. The mean size of induration noted was 11.74mm and maximum size of induration noted was 17 mm. Among 12 patients of extra pulmonary tuberculosis patients who showed mantoux positivity, 10 were having tuberculous lymphadenitis. Thus in Extrapulmonary tuberculosis mantoux positivity is most common in lymphadenitis.

Only 13.8% of patients showed a lymphocyte count of more than 40% in peripheral smear. None of them showed a marked lymphocytosis of more than 50%. Thus there is no significant rise in lymphocyte count both in pulmonary and extra pulmonary tuberculosis.

100 (47.6%) patients had ESR of more than 40mm in 1 hour, of which 22(10.47%) patients had ESR more than 100. Around 50% of both pulmonary and extrapulmonary tuberculosis patients showed ESR of more than 40 mm in 1 hour. Charles D W Morris et al reported an incidence of elevated ESR in 52% of male and 80% of female pulmonary tuberculosis patients. [20]

Majority of sputum positive cases (81.6%) showed a lymphocyte count of less than 40% in peripheral smear. 22(44.9%) of sputum positive patients

had an ESR of more than 40 mm in one hour. Out of 49 sputum positive pulmonary tuberculosis patients, only 5 patients showed mantoux positivity which accounts for 10.2%.

94 (76.5%) of pulmonary tuberculous patients had upper zone/apical infiltrates. 50(40.7%) patients had unilateral and 44(35.8%) patients had bilateral infiltrates. Lower zone infiltrates were seen in 4 patients (3.3%). Fibrocavity was found in 23 (18.7%) and miliary pattern was seen in 2 (1.7%) patients.

This study highlights the varied presentations of pulmonary tuberculosis and extrapulmonary tuberculosis. This study also shows that tuberculosis presents in different forms in various age groups. In pulmonary tuberculosis sputum positivity alone can not be relied on for diagnosis, as 60% of cases were diagnosed only with chest X ray with negative sputum AFB. Extrapulmonary tuberculosis is mainly diagnosed by histopathological evidence of tuberculous granuloma. Most of these patients were followed up on DOTS chemotherapy and found to be improving. Response to treatment is not considered in this study as most of the patients have not completed the full course of chemotherapy.

SUMMARY

SUMMARY

- 210 patients of newly diagnosed tuberculosis (pulmonary and extra pulmonary) who were started on DOTS chemotherapy, were analyzed. Pulmonary Tuberculosis occurred in 123(58.6%) and Extrapulmonary tuberculosis in 87(41.4%) patients.

- There were 143 (68.1%) males and 67 (31.9 %) females. Mean age of presentation was 38.5 years and ranging between 13 to 80 years.

- Among 123 pulmonary tuberculosis patients, 76.4% were males and 23.6% females. The male female ratio is 3.2 : 1. Mean age of occurrence was 42.96 years.

- Clinical presentation of Pulmonary Tuberculosis were cough with sputum(86.2%), fever (61.8%), loss of appetite/ loss of weight (57.8%), Hemoptysis(22.8%) and chest pain / breathlessness(5.7%).

- Out of 87 patients with Extrapulmonary tuberculosis 49 (56.3%) were males and 38 (43.7%) females. The male female ratio is 1.3: 1. Mean age of occurrence was 32.28 years. Most of the patients (78.2%) were in the age group of 13 – 40 years.

- Tuberculous Lymphadenitis occurred in 41(19.5%) patients and accounted for 47.1% of Extrapulmonary tuberculosis. Most of these patients were in the age group of 13 – 30 years. 22(53.7%) were females and 19(46.3%) males. The male female ratio is 1: 1.2.

- 90% of tuberculous lymphadenitis patients had isolated cervical node involvement, two (5%) patients had axillary node involvement along with cervical nodes and two (5%) had generalized Lymphadenopathy.

- Pleural Tuberculosis occurred in 23(11%) patients, which accounted for 26.4% of extrapulmonary tuberculosis. 17(73.9%) were males and 6(26.1%) females. Male female ratio is 2.8:1. Peak incidence of pleural Tuberculosis is between 13 – 40 years of age.

- Tuberculous Meningitis occurred in 7(3.8%) of tuberculous patients, which accounted for 8% of Extrapulmonary tuberculosis.

- Spinal and Abdominal tuberculosis occurred in 5 (2.4%) patients.

- Tuberculous pericarditis, tuberculoma, genital tuberculosis, tuberculous skin ulcer, erythema nodosum and tuberculous arthritis which occurred in one patient (0.9%) each.

- 39.83% of pulmonary tuberculous patients were positive for sputum AFB and none of patients with extrapulmonary tuberculosis showed sputum/ specimen AFB positivity.

- Positive mantoux reaction occurred in 27(12.9%) patients, of which 55.5% had pulmonary tuberculosis and 44.4% extrapulmonary tuberculosis.

- Around 50% of pulmonary and extrapulmonary tuberculosis patients had ESR of more than 40 mm in 1 hour.

- 76.5% of pulmonary tuberculous patients had upper zone/apical infiltrates. Fibrocavity and miliary pattern occurred in 18.7% and 1.7% respectively.

CONCLUSIONS

CONCLUSIONS

- Age groups between 20 – 50 years are highly vulnerable for development of tuberculous disease.
- Males are more commonly affected in pulmonary tuberculosis than females.
- Extrapulmonary tuberculosis commonly occurs in younger age groups (10-30 years).
- Tuberculous Lymphadenitis and Pleural tuberculosis are the commonest forms of extrapulmonary tuberculosis.
- Sputum AFB and Chest X ray are equally important in diagnosis of pulmonary tuberculosis.
- Hitopathological evidence of tuberculous granuloma is the mainstay for diagnosing various types of Extrapulmonary tuiberculosis.
- ESR and Mantoux reaction has only additive role in diagnosis of tuberculosis.

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ANNEXURE

PROFORMA

Name : **Age:** **Sex:**

Chest Clinic No.

Clinical Features:

- Fever – Duration/ periodicity.
- Cough with sputum/ dry cough.
- Loss of appetite.
- Loss of weight.
- Hemoptysis.
- Other features like – Abd pain, Abd distention, Spinal pain and deformity, Neck stiffness, Cranial nerve palsies, Skin ulcerations, Neck Swelling, etc..

Laboratory profile

- Sputum smear for AFB
- Chest X ray
- Mantoux Test
- Hemogram – TLC, DLC, ESR, Hb%
- Specific investigations for various types of Tuberculosis.