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A systematic review of different type of tuberculosis

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Abstract. – Tuberculosis (TB) is still a leading cause of death worldwide. Almost a third of the world's population is infected with TB bacilli, and each year approximately 8 million people develop active tuberculosis and 2 million die as a result. However, there are few studies of long-term TB treatment outcomes from Directly Observed Therapy, Short-course (DOTS) programs in high-burden settings and particularly settings of high drug resistance. This study is a systematic review to evidence the incidence and prevalence of latent TB infection (LTBI) and disease and to evaluate the impact of various preventive strategies that have been attempted. To identify relevant studies, we searched electronic databases and journals, and contacted experts in the field. This review demonstrates that, various types of tuberculosis have different imaging findings, and typical computed tomography (CT) and magnetic resonance (MG) findings can suggest the diagnosis. Available evidence reinforces the need to design and implement simple, effective, and affordable tuberculosis infection-control programs in health-care facilities in our countries. With the revision of all the data's, we are able to conclude that the controlling of tuberculosis by human beings is yet not achieved. So, there is an urgency to develop awareness amongst the individuals and also a new drugs regimen for the proper treatment of tuberculosis.

Key Words:

Tuberculosis, DOTs therapy, Ocular tuberculosis, Spinal Tuberculosis.

Introduction

Tuberculosis (TB) has troubled human kind throughout the history. It has been a leading cause of death throughout the world, and still is in low-income and middle-income countries. The limitations of existing methods of prevention, diagnosis, and treatment of tuberculosis have been emphasized by the increased susceptibility of HIV-infected people to develop the disease, and by the emergence of drug-resistant strains[1]. Multidrug-resistant (MDR) tuberculosis – resistant to at least isoniazid and rifampicin – is an increasingly important public health and clinical issue, especially in countries with a high burden of HIV. Reports of MDR tuberculosis isolates resistant to second-line drugs have amplified these concerns. In March 2006, the first data were published on the world wide occurrence of tuberculosis with resistance to second-line drugs, termed extensively drug resistant (XDR) tuberculosis[1]. Outbreaks of nosocomial MDR tuberculosis have occurred in both poor and wealthy nations, typically in HIV-infected patients. Transmission has been reduced in industrialized countries through a combination of infection control strategies, including comprehensive treatment protocols and staff training programmes (administrative measures): ventilation, isolation, air filtration, and ultraviolet germicidal irradiation (environmental controls); and the use of respiratory masks (personal protection)[1].

Epidemiology

The World Health Organization (WHO)[2] estimates that each year there are 9 million new TB cases. Annually, TB kills approximately 1.8 million people, making it second only to HIV/AIDS as the leading cause of death from infectious disease. Approximately 2 billion people (1 in 3 individuals worldwide) are infected with *Mycobacterium tuberculosis* (*M. tuberculosis)*. Among those infected with *M. tuberculosis*, approximately 50 million are infected with drug-resistant

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strains. Worldwide, an estimated 5, 00,000 cases of MDR-TB emerges each year (5.3% of all new and previously treated TB cases), resulting in 110,000 deaths[3]. TB currently holds the seventh place in the global ranking of causes of death. Unless intensive efforts are made, it is likely to maintain that position through to 2020, despite a substantial projected decline in disease burden from other infectious diseases (Dye 1999, Smith 2004). Although effective drugs to treat and cure the disease have been available for more than 50 years, yet every 15 seconds someone in the world dies from TB. Even more alarming: a person is newly infected with *M. tuberculosis* every second of every day. Left untreated, a person with active TB will infect an average of 10 to 15 other people every year (Dye 2005). TB hinders socioeconomic development: 75% of people with TB are within the economically productive age group of 15-54 years. Ninety-five per cent of deaths occur in developing countries, with the greatest burden in sub- Saharan Africa and South East Asia. Household costs of TB are substantial (Dye 2006, World Health Organization 2006). In most countries, more cases of TB are reported among men than women. This difference is partly due to the fact that women have less access to diagnostic facilities in some settings, but the broader pattern also reflects real epidemiological differences between men and women, both in exposure to infection and in susceptibility to disease. In regions where the transmission of *M. tuberculosis* has been stable or increasing for many years, the incidence rate is highest among young adults, and most cases are caused by recent infection or reinfection[4]. According to WHO, global incidence of TB rising with co-infection of HIV patients, which has been shown in Figure 1. India has the largest number of infections, which has been shown in state wise detail of TB cases detected and put on treatment under the programme during the year 2006 and till date[6] (Table I). To control TB, with an objective to achieve cure rate of 85% of new sputum positive cases and to detect at least 70% of such cases, the Revised National TB control Programme (RNTCP) widely known as Directly Observed Therapy Short-course (DOTS) which is WHO recommended strategy, is being implemented in the entire country. Under RNTCP, diagnosis by sputum microscopy, instead of X-ray, helps in detecting and curing infectious cases on priority. Facilities for diagnosis by sputum microscopy have been decentralized and strengthened. Drugs are provided under observation and patients are monitored so that they complete their treatment. Drugs are provided free of cost in patient-wise boxes. Till date, the RNTCP has placed more than 78 lacs patients on DOTS treatment, averting more than 14 lacs cases on DOTS, more than any country in a single year in the world. Overall performance of RNTCP has been excellent with cure/treatment completion rate consistently above 85% and death rate reduced to less than 5%. To increase accessibility of the masses to the facilities provided under the programme, special emphasis is laid on the IEC activities, involvement of NGOs, private sector and medical colleges[6].

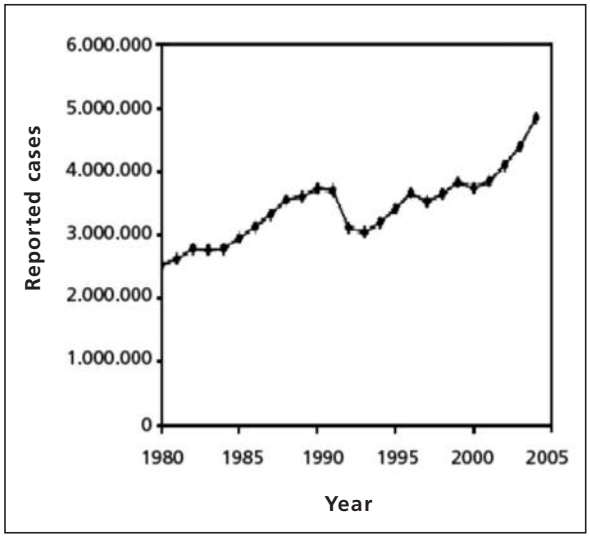

Figure 1. Global incidence of tuberculosis.

General Pathogenesis

Mycobacterium Tuberculosis is aerobic nonspore forming, nonmotile bacillus with a waxy coat that causes them to retain the red dye when treated with acid ("red snapper") in the acid – fast stains. Two species of Mycobacterium cause tuberculosis; it is transmitted by inhalation of infective droplets coughed or sneezed into the air by the patients with tuberculosis. *M. bovis* is transmitted by milk from diseased cows and roduces intestinal or tonsillar lesions (Figure 2). *M. Tuberculosis* pathogenicity is related to its ability to escape killing by macrophages and induce delayed type hypersensitivity. This has been attributed to several components of the *M. tuberculosis* cell wall.

Table I. India has the largest number of infections, which has been indicating state-wise detail of TB cases detected and put on treatment under the programme during the year 2006 and till date[5].

Sl.No	State	2006	2007 (up to Sep., 2007)
1	Andaman & Nicobar	920	590
2	Andhra Pradesh	107131	82954
3	Arunachal Pradesh	2607	2153
4	Assam	32311	27958
5	Bihar	61151	61476
6	Chandigarh	2322	1871
7	Chhattisgarh	28209	20779
8	D & N Haveli	391	300
9	Daman & Diu	280	256
10	Delhi	47606	39260
11	Goa	2036	1510
12	Gujarat	79821	61096
13	Haryana	34693	28097
14	Himachal Pradesh	13303	10913
15	Jammu & Kashmir	10268	9863
16	Jharkhand	33035	27505
17	Karnataka	64842	50737
18	Kerala	25248	18159
19	Lakshadweep	16	12
20	Madhya Pradesh	74435	60817
21	Maharashtra	138837	107827
22	Manipur	4603	3771
23	Meghalaya	3929	3649
24	Mizoram	1912	1657
25	Nagaland	2695	2339
26	Orissa	44790	37579
27	Pondicherry	1513	1042
28	Punjab	34537	28289
29	Rajasthan	107783	86845
30	Sikkim	1458	1225
31	Tamil Nadu	87065	65323
32	Tripura	2314	1972
33	Uttar Pradesh	224465	187188
34	Uttarakhand	11653	10567
35	West Bengal	109319	83157
	Grand Total	**1397498**	**1128736**

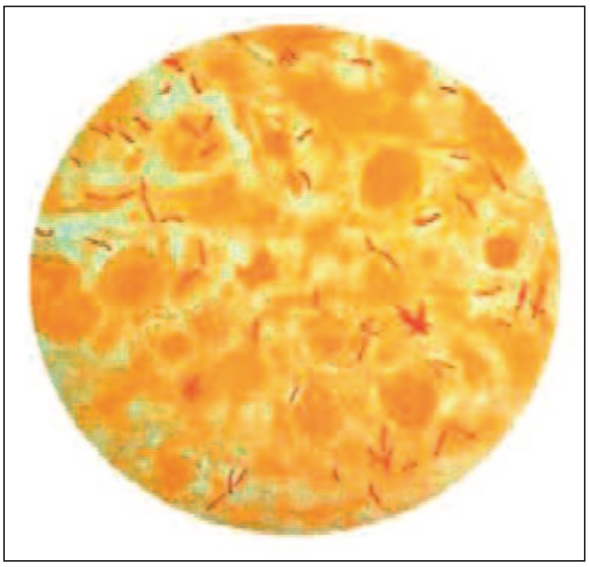

Figure 2. Mycobacterium Tuberculosis (Stained red) in sputum.

First is cord factor, a surface glycolipid that causes *M. tuberculosis* to grow in serpentine cords *in vitro*[7]. Virulent strains of *M. tuberculosis* have cord factor on their surface, whereas virulent strains do not, and injection of purified cord factor into mice induces characteristic granulomas.

Second lipoarabi nomannan (LAM), a major heteropolysaccharide similar in structure to the endotoxin of gram-negative bacteria, inhibits macrophage activation by interferon-γ. LAM also induces macrophages to secrete TNF-α, which causes fever, weight loss, and tissue damage, and IL-10, which suppresses mycobacteria-induced T-cell proliferation[8].

Third, complement activated on the surface of mycobacteria may opsonize the organism and facilitates its uptake by the macrophage complement receptor CR3 (Mac-1 integrin) without triggering the respiratory burst necessary to kill the organisms.

Fourth, a highly immunogenic 65-kD *M. tuberculosis* heat shock protein may have a role in autoimmune reactions[9]. The development of cell-mediated or type IV hypersensitivity to the tubercle bacillus probably explains its destructiveness in tissues and also the emergency of its resistance. On the initial exposure to mycobacterium, the inflammatory response is nonspecific, resembling the reaction to any form of bacterial invasion[6]. Within 2 or 3 weeks, coincident with the appearance of a positive skin reaction, the reaction becomes granulomatous and the centers of granulomas become caseous, forming typical "Soft tubercles". The sequence of events that follows an initial lung infection is outlined in Figure 3.

Types of Tuberculosis

Tuberculous Lymphadenitis

Twenty-one percent of extra pulmonary TB may have typical or atypical presentations. Therefore, a high index of suspicion is warranted. HIV infected individuals are more likely to have disseminated (miliary), abdominal, or mediastinal tuberculosis. Diagnostic parameters such as an acid-fast smear and culture of specimens from extra pulmonary sites are often not sensitive as those from pulmonary tuberculosis. Histological examination of lymph node biopsies shows reactive hyperplasia and granulomata (with or without caseation). In 18% of TB adenitis, chest radiography revealed pulmonary change. Laboratory tests such as adenosine deaminase level or polymerase chain reaction (PRC) can be helpful in suspected cases or to establish a diagnosis of extra pulmonary tuberculosis[10]. In India, children under 14 years of age have prevalence rates of 4.4 cases per 1000. Tuberculous lymphadenitis in developed countries with low TB prevalence is more often seen in immigrants and in those who travel to countries of higher prevalence. In recent years, lymphadenitis is common between 20 and 40 years of age and exhibits female predominance. The infection of lymph nodes by mycobacterium occurs either through hematogenous dissemination following primary tuberculosis. Extra pulmonary tuberculosis in HIV infection is seen when CD4 counts are below 300/ml[11]. Often in those patients tuberculous lymphadenitis can also occur in association with pulmonary and/or miliary disease. Intrathoracic lymphadenitis may be the presenting feature of primary tuberculosis in HIV infection (Figure 4).

Clinical Features

It has non tender swelling without significant systemic symptoms in immunocompetent young adults. Cervical node involvement predominates in one two-thirds of TB adenitis. It is often unilateral involving one or more nodes of the anterior and posterior cervical chain. Over 90% of patients with non-HIV tuberculous adenitis will have positive tuberculin skin tests.

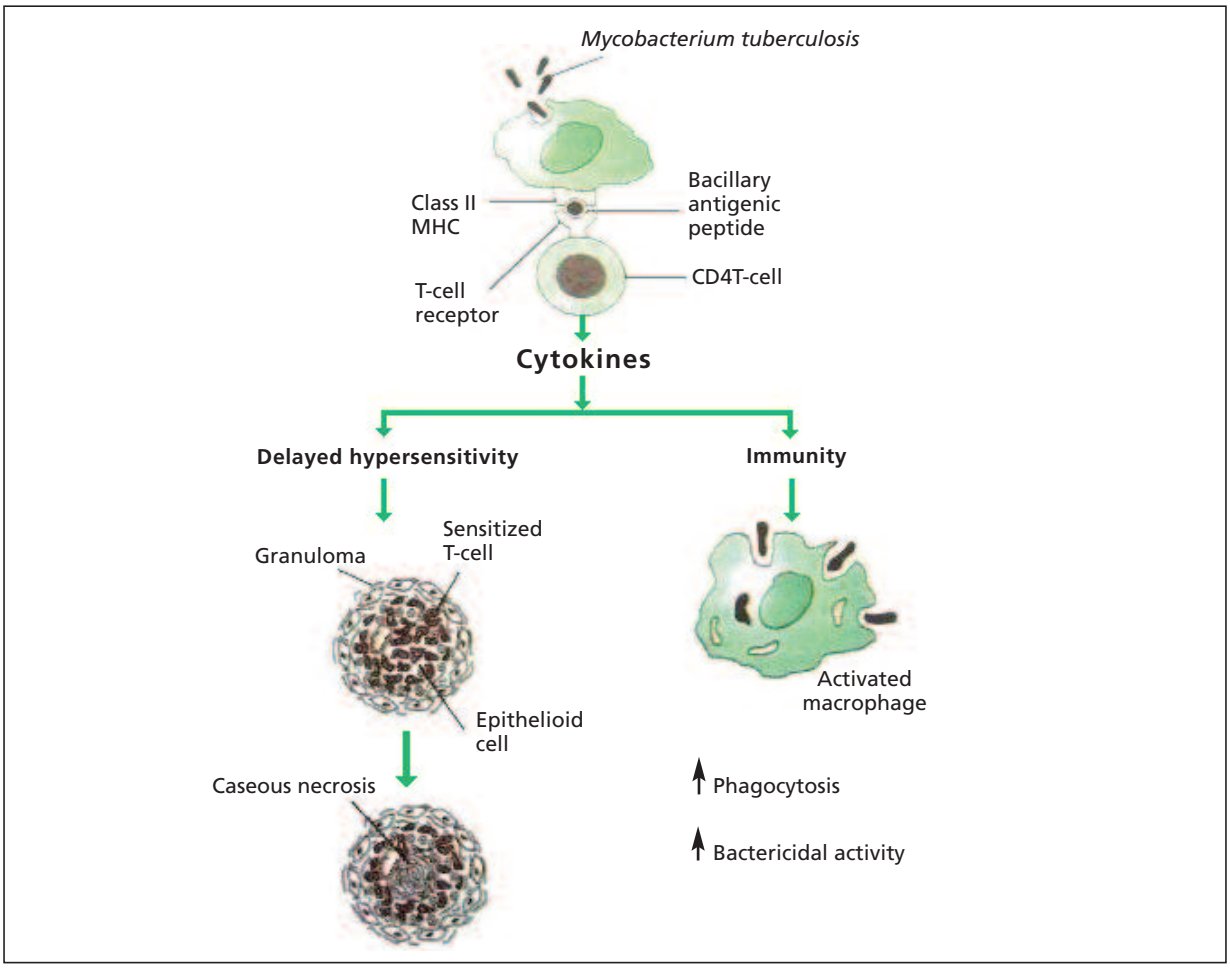

Figure 3. TB: dual consequences of macrophages activation and utilization.

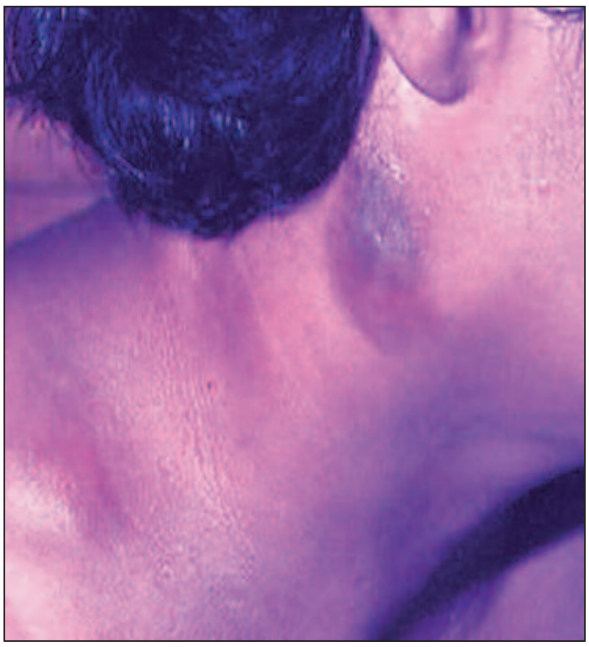

Figure 4. The subcutaneous nodules at the ricck of this adolescent patient are swollen lymph nodes. They are not ulcerated. This is a primary form of tuberculosis found mainly in adolescents, later accompanied by necrosis and formation of fistulae.

Diagnosis

A retrospective study reported specificity and positive-predictive value of 100% with fine needle aspiration of lymph nodes with sensitivity of 46% for tuberculous adenitis. The sensitivity increased to 53% if granulomatous inflammation was seen. In addition to smear and culture, polymerase chain reaction testing of the aspirate can establish a rapid diagnosis. Histological examinations of lymph node biopsies show reactive hyperplasia and granulomata (with or without caseation). In 18% of TB adenitis, chest radiography revealed pulmonary change[12].

Pleural Tuberculosis

TB is the most common cause of pleural effusion worldwide (30-60%). The pathogenesis of Tuberculosis pleurisy can occur with a primary infection, especially in young adults and adolescents. Merio et al[13,14] reported 22% of pediatric TB to be tuberculous pleural effusion. It is seen within weeks or months from rupture of a sub pleural tuberculous focus resulting in inflammation by mycobacterial antigens and T-cells previously sensitized of TB antigens with exudation of fluid due to a delayed hypersensitivity reaction of *M. tuberculosis*. The fluid has very few organisms and pleural tissue has granulomata.

Pleural Effusion with Reactivation Tuberculosis (TPE)

TPE can occur in the reactivation of the pulmonary TB and miliary TB with associated chest radiographic changes of active pulmonary TB. The clinical and laboratory presentations of TPE in primary and in reactivation of TB may differ. A longer duration of symptoms and a lower glucose level in the pleural fluid has been reported in the reactivation of TB compared to the primary TPE[14]. In addition, tuberculin skin test (TST) was positive in over 80% of the primary TPE and 61% in the reactivated TPE. The yield of acid-fast bacilli (AFB) in smear and culture of pleural fluid was statistically higher in reactivation of TB, while no such difference was noted in the pleural tissue. The presence of granulomata was 72% in the pleural tissue of the primary TPE and 25% in reactivated TPE, which is attributed in the last case to a less exuberant immune response to *M. tuberculosis*.

Tuberculous Emphysema

Tuberculous emphysema results from bronchopleural fistula following the rupture of cavitary pulmonary TB with frank pus in the pleural space. TB emphysema contains a large number of *M. tuberculosis*. Rarely a spinal abscess may drain into the pleural space. Tuberculous emphysema if untreated or inadequately treated can result in *emphysema necessitatis*, which often is a bronchopleurocutaneous fistula. The emphysema may also drain into retroperitoneal space. TB emphysema needs drainage with or without decortications in addition to chemotherapy.

Clinical Features

It includes cough, pleuritic chest pain, and dyspnea often constitutional symptoms such as fever, weight loss, and anorexia. On physical examination pleural friction rub and dullness to percussion with decreased breath sounds may be heard. On chest radiography small-to moderate-size pleural effusion, often unilateral, is seen.

Diagnosis

Pleural fluid is typically exudative with normal to low pH. The cell count range is usually 500 to 2500, with blood cells/mm^3 with lymphocyte predominance of 80% or higher in two-thirds of TPE cases. Rarely, initial polymorphonuclear cell predominance with subsequent change to lymphocyte predominance is seen. Interferon-γ and polymerase chain reaction are also useful diagnostic tools in TPE in combination with clinical findings. The sensitivity of polymerase chain reaction (PCR) testing of pleural biopsy for TB is similar to that of pleural tissue culture. While the testing of PCR, ADA, and interferon-γ in an appropriate clinical setting is helpful in rapid diagnosis of TPE, it does not replace the need for culture and sensitivity studies for *M. tuberculosis*[15] Smears of pleural fluid in TPE are positive for *M. tuberculosis* in 5 to 20% in immunocompenent hosts and are higher in AIDS (50%) with CD4 counts of less than 100. Positive PCR and presence of granulomata on histology of pleural tissue obtained via transcutaneous approach or video pleuroscopy are highly suggestive of TPE and confirmation of tuberculosis is made by culture of pleural fluid and/or tissue.

Treatment

Standard 6-months multidrug chemotherapy is recommended. An increase in pleural treatment relieves symptoms and prevents formation of fibrothorax and reactivation in the future. If required, decortications for pleural thickening is best considered after completion of at least 6 months of chemotherapy[16].

Miliary, Central Nervous System and Genitourinary Tuberculosis

Tuberculomas are uncommon and may present as one or more parenchymal granulomata and may cause seizures, focal neurologic deficits, or cognitive changes. Lesions are generally smaller than 2 cm and may not be visible on non contrast computed tomographic (CT) images. Cerebral spinal fluid (CSF) may demonstrate lymphocyte predominant pleocytosis with an elevated protein[17]. Meningitis may coexist in 10% of cases[18]. Miliary Tuberculosis (TBM) is not merely an extension of miliary disease, but instead represents the extension of a caseous focus of TB in the brain cortex or meninges from which bacilli are able to enter the subarachnoid space to cause diffuse meningitis. Hematogenous spread of bacilli, either during the primary infection or at some point later during the infection, results in the establishment of a focus within the cortex, meninges, choroid plexus or the walls of the ventricles[19]. This site of infection, also known as a Rich focus, may subsequently caseate and discharge its contents into the subarachnoid space. The CNS may also become involved through direct extension from the middle ear or vertebrae. The dense exudates that form around the spinal cord may obstruct cerebrospinal fluid at the tentorial opening, leading to hydrocephalus. Direct contact of the exudates with brain tissue may result in a hypersensitivity response. The most serious complication is development of CNS vasculitis and subsequent infarction leading to hemiplegia or quadriplegia. Patients may initially present with a prodromal period of fever, weight loss, headache, vomiting, or behavior changes. Delays in diagnosis and treatment may result in neurologic changes, loss of consciousness, or convulsions. Typical CSF changes include a low cell count <300 m^3, predominately lymphocytic, low glucose <2.2 mmol per liter, and elevated protein >0.8 g per liter. Nucleic acid amplification testing of CSF has high specificity (0.98) but low sensitivity (0.56) for TB, thus a negative test does not necessarily support discontinuation of treatment in a patient suspected of having CNS TB[19]. Identifying AFB-positive organisms may require repeated lumbar puncture. When TBM is suspected, anti-TB treatment should be considered early. Adjunctive treatment with corticosteroids while providing a mortality benefit to those 14 years of age has not been shown to prevent severe disability among survivors. Even with treatment, TBM is fatal in approximately 30% of cases. In a recent review of 545 patients with TBM[20], 64.6% of HIV-infected patients died by 9 months after start of treatment versus 28.2% of non-HIV infected patients. Patients with isolates resistant to both isoniazid and rifampicin had a significantly higher relative risk of death[21]. Paradoxical reactions have been reported in CNS TB where patients appear to have clinical deterioration several weeks into therapy demonstrating an increase in CSF pleocytosis, usually lymphocytic, but occasionally polymorphonuclear predominant[22]. Despite adequate medical and surgical treatment of tuberculomas or tuberculous brain abcesses, paradoxical enlargement and development of new lesions are well described. Adjunctive therapy with thalidomide, a tumor necrosis factor alpha-modulating drug, has been used successfully in four pediatric cases of intractable intracranial disease[23]. Further investigation of thalidomide in the treatment of intractable intracranial tuberculous infection may be warranted (Figure 5).

Genitourinary Tuberculosis

It has been reported in 4 to 8% of patients with pulmonary TB. The most common clinical presentations in one series was burning on micturition, increased frequency (29%) and renal colic (13%). Classically, renal TB is suspected when urinary symptoms do not respond to usual antibacterial agents, or when sterile pyuria is found. The kidney is usually infected hematogenously from a primary focus, such as the lung. Kidney infection may cause parenchymal necrosis and subsequent calcification; advanced disease may demonstrate calyceal distortion, ure-

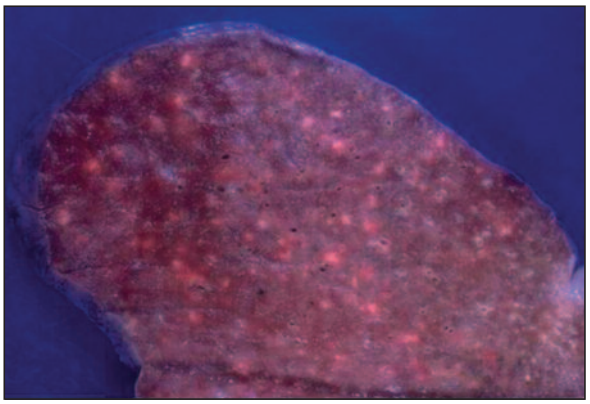

Figure 5. Miliary tuberculosis in lung can occur whe tuberculous lung lesions erode pulmonary veins or when when extrapulmonary tuberculous lesion erodes systemic veins.

thral strictures, and bladder fibrosis and may lead to progressive renal failure when the disease is bilateral. It demonstrated calycaeal distortion and urethral strictures on CT or MR caused by renal TB. Chronic disease may be complicated by amyloidosis[24]. The male genital tract involvement is the epididymis, likely due to its rich blood supply. Patients may present with scrotal swelling, pain and discharge and may have lower urinary tract symptoms. An enlarged and hypoechoic epididymis may be seen on ultrasound and is usually unilateral[25]. Female genital TB is an important cause of female infertility and may present with nonspecific abdominal or pelvic pain, changes in menstrual patterns, and abnormal vaginal bleeding. Female genital TB is generally thought to be secondary to heamatogenous or lymphangitic spread. Sometimes with contiguous spread via the fallopian tubes from intrabdominal foci. CT or MR imaging may demonstrate tubo-ovarian abscesses[26]. Recently, polymerase chain reaction (PCR) for the presence of the mpt64 gene of *M. tuberculosis* has been used to accurately identify genitourinary TB in samples of endometrial aspirates, endometrial biopsies and fluid from the pouch of Douglas in women being evaluated for infertility[27] (Figure 6).

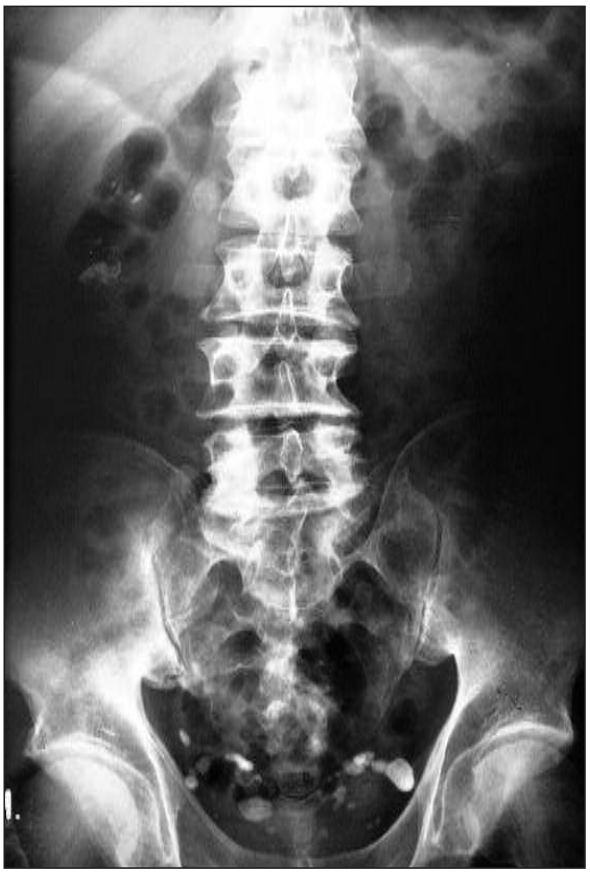

Figure 6. Plain abdominal radiograph in a male patient with genitourinary tuberculosis shows left renal, bladder, and seminal vesicle calcification.

Abdominal Tuberculosis

It has seen more commonly between 25 to 45 years of age. The modes of infection of the GI include hematogenous spread from a primary lung focus that reactivates later or miliary tuberculosis, spread via lymphatics from infected sources such as milk products of by direct spread from adjacent organs. Involvement of the abdominal lymph nodes and the peritoneum may occur without other organ involvement. The most common site for abdominal TB is the ileocecal area. Infection often results in granuloma formation, caseation, mucosal ulceration, fibrosis, and scarring[28].

Clinical features

TB may be acute or chronic, patients often have fever (40-70%), weight loss (40-90%), abdominal pain. TB may be acute or chronic. Patients often have fever (40-70%), weight loss (40-90%), abdominal pain (80-95%), abdominal distension, diarrhea (11-20%), and constipation. Fatigue, malaise and anorexia are also seen. Dysphagia and odinophagia is seen in oesophageal TB. Gastric TB may mimic peptic ulcer disease or gastric carcinoma[29,30]. Duodenal TB may present with dyspepsia or duodenal obstruction. Abdominal pain, nausea and vomiting, and symptoms of malabsorption may be seen in ileocecal TB. Colonic tuberculosis may be focal or multifocal with pain as the predominant symptom[31].

Diagnosis

Radiographic imaging such as plain abdominal series, barium enema, upper GI series with small intestinal follow-through, chest radiograph, computed tomography (CT), and/or ultrasonography (US) of the abdomen are often utilized. In the diagnostic evaluation of abdominal TB, CT of the abdomen is helpful in visualizing thickened peritoneum, ascites, mesenteric disease, lymph node enlargement, caseation within lymph nodes. Bowel wall thickening, omental thickening, and bowel obstruction. Patients with AIDS usually have a more severe form of involvement than those who did not have AIDS[32].

Ocular Tuberculosis

Tuberculosis affecting the eyelid is most often found in children[33]. The most common form of cutaneous tuberculosis, *lupus vulgaris*, is characterized by reddish-brown nodules that blanch to an "apple-jelly" color when pressure is applied and may appear on the skin of the eyelids[34,35]. Tuberculosis can also manifest as a "cold abscess," a soft, fluctuant mass without acute inflammation, or simulate a chalazion[36]. Primary infection of the conjunctiva is unusual and more commonly affects children. Tuberculous conjunctivitis is often a chronic disease that may lead to scarring of the involved tissue. Patients with tuberculous conjunctivitis have nonspecific complaints such as ocular redness and discomfort[37]. Examination may reveal mucopurulent discharge and lid edema, often with an accompanying marked lymphadenitis such as in Paranoid oculoglandular syndrome, which is absent in most other forms of bacterial and allergic conjunctivitis and less prominent in viral conjunctivitis[38]. In cases of primary conjunctival tuberculosis, *M. tuberculosis* can be detected via traditional acid-fast stains on either a conjunctival smear or a bioptical specimen[39] (Figure 7).

Laryngeal Tuberculosis

Laryngeal tuberculosis is a complication of pulmonary tuberculosis in from 12 to 45 per cent of cases, depending on the severity of the pulmonary lesion. The tuberculous lesion is healed by the deposit of calcium salts in the necrotic areas and by an increase of fibrous tissue which develops from the fixed connective tissue cells, and probably by a changing of the epithelioid cells into fibroblasts. Such healing processes are encouraged by an increased blood supply. Rest is important in all cases of laryngeal tuberculosis. The electric cautery is used in all tuberculous ulcers, and infiltrations which do not despond to rest of the larynx. Heliotherapy has been used in many cases. The electric cautery heals, not by the destruction of all tuberculous tissue, but by the development of an inflammatory zone in which newly formed blood vessels and fibroblasts are produced, which hastens healing by cicatrization. Most early cases heal with the cautery, while the advanced cases are relieved of pain. Electric cauterization is a minor procedure, done best under cocaine anesthesia and by the indirect method[40].

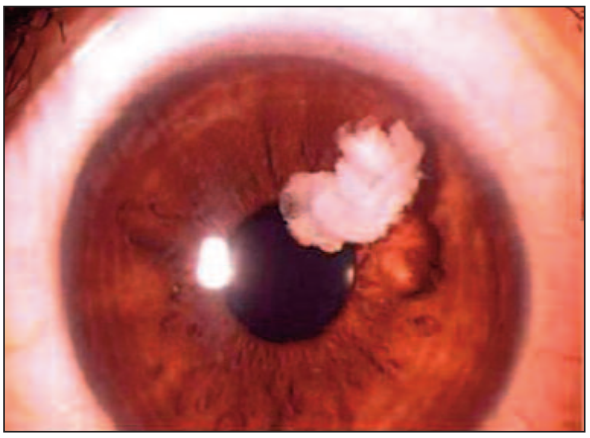

Figure 7. Ocular tuberculosis.

Musculoskeletal Tuberculosis

Musculoskeletal involvement with tuberculosis is relatively uncommon, representing approximately 1 to 3% of cases. Osteoarticular lesions result from hematogenous spread of a primary infection. Any bone, joint, or bursa can be infected, but the spine, hip and knee, in order of frequency, are the preferred sites of infection representing 70 to 80% of infections[39]. The diagnosis is often delayed due to the indolent nature of the disease and low clinical suspicion in areas with lower rates of tuberculosis.

Spinal Tuberculosis

Spinal tuberculosis, also referred to as Pott's disease, represents approximately half to all cases of musculoskeletal tuberculosis. In countries where tuberculosis is endemic, older children and young adults are affected[41]. While in developed countries it is often seen in older persons[41]. The thoracic spine is involved in 50% of spinal tuberculosis. Whereas the lumbar and cervical spine are each involved in 25% of cases. The typical presentation involves indolent and slowly progressive focal pain and muscle spasm. Tubercular disease involves the anterior vertebral endplates, resulting in herniation of the intervertebral disk into the vertebral bodies with loss of vertebral height and a "step-off" kyphosis. The most feared complication of spinal tuberculosis, occurring in 10 to 47% of patients, is neurologic compromise due to spinal deformity or epidural abscess formation[42]. Typical clinical presentations include disease that mimics a herniated intervertebral disc, tuberculous abscess without significant bony involvement[43]. Constitutional symptoms such as fevers, night sweats, and weight loss occur in many but not all patients. Radiographic imaging of spinal tuberculosis can be

suggestive but there are no pathognomic findings. Often early in the course of disease, plain radiographs can be normal. Later, they can show loss of vertebral height, indistinct vertebral endplates, erosions, angular kyphosis and paravertebral masses. Most patients have two or more contiguous vertebrae involved at presentation. Bone scanning, although sensitive is of limited value as it is nonspecific and has limited resolution. CT scanning provides more detailed delineation of bony destruction and extension of disease into the spinal canal and is the best test for guiding percutaneous biopsies. Contrast-enhanced MRI scanning is the optimal test for defining intraspinal extension, focal myelopathy, and spinal cord or nerve root compression[44,45]. Para vertebral abscesses are often seen at multiple levels and show peripheral enhancement with central necrosis on contrast enhanced images (Figure 8).

Extra Axial Musculoskeletal Tuberculosis

Tuberculous arthritis can involves any joint but has a predilection for weight-bearing joints such as the hips and knees. Usually a single joint is involved, but multiple lesions can occur. Tubercular osteomyelitis and bursitis have been reported at nearly every site[46]. The typical symptoms complex includes slowly progressive pain, swelling and loss of function. Muscle spasm can splint the joint and reduce pain. "Night cries" can occur with movement during sleep when the spasm relaxes[46]. As with spinal involvement, constitutional symptoms and active pulmonary disease occur in a significant minority of patients[47].

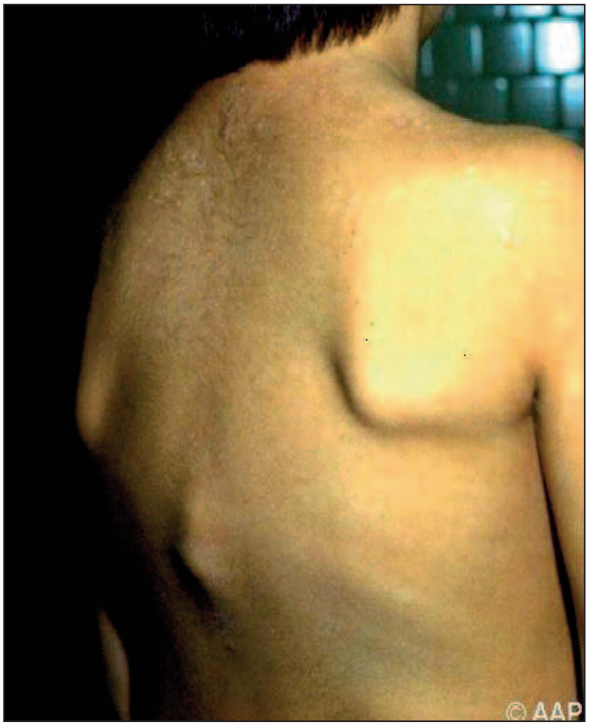

Figure 8. Spinal tuberculosis.

Both synovium and periarticular bone are usually involved at the time of diagnosis. Bony foci result in local demineralization and may destroy the epiphyseal plate, resulting in deformity to the affected limb[48]. Articular cartilage loss occurs as the infection spreads to subchondral bone and disrupts the nutritional supply of the cartilage. Synovitis develops with resultant joint effusion, growth of granulation tissue, and development of a *pannus* and erosions at the margins of the joint[49]. Necrotic cartilage and fibrinous material from the classic rice bodies found in synovial fluid. The weight-bearing articular surfaces are often preserved early in the course of disease, providing potential for good functional recovery if treatment is initiated early[47].

Plain radiographs will demonstrate soft-tissue swelling with loss of joint surface definition. With disease progression, marginal erosions may be seen. Cartilage loss and joint space destruction are late findings. Periarticular bone loss may be striking. Phemister's triad (juxtaarticular osteoporosis, peripheral osseous erosions, and gradual joint space narrowing) suggests tuberculous arthritis but is nonspecific. Other imaging modalities, including MRI, add little to the diagnosis of tuberculous arthritis.

Diagnosis and Treatment

In areas where tuberculosis is endemic, the diagnosis may be apparent with the appropriate clinical and radiographic scenario. In other areas, the diagnosis may be suspected with the appropriate clinical history including questions about country of origin, exposure to tuberculosis, and prior positive tuberculin skin test[50].

Pericardial Tuberculosis

TB-pericarditis occurs from haematogenous spread or as an extension of infected mediastinal lymph nodes or pulmonary tuberculosis. Rarely extension of infection from spine and tracheobronchial sources has been suggested. TB-pericarditis is often seen in association with active stages and these stages may or may not occur as a progression from one to the next[51,53]. These stages are as follows (1) dry stage: (2) effusive stage: (3) absorptive phase (4) constrictive phase.

The effusive stage may not be clinically recognized in nearly half of TB pericardial effusion may vary in amount and, on occasion, be sufficiently large enough to cause pericardial tamponade. The pericardium may be thickened with fibrosis and present with the physiological changes of constrictive pericarditis. Calcification of the pericardium may follow resolution and healing with or without treatment.

Clinical Manifestation

It includes dyspnea, orthopnea, chest pain, ankle edema, cough, night sweats, and weight loss, frequency of symptoms varies based on the clinical manifestation. Chest pain may be pleuritic in nature. Fever, tachycardia, pericardial rub, and increased jugular venous pressure may be present on physical examination. Pericardial rub, hepatomegaly, cardiomegaly, pleural effusion, ascites, and peripheral edema may also be seen. In cardiac tamponade *pulsus paradoxus* is noted. Other physical findings include lack of inspiratory reduction in jugular venous pressure (Kussmaul's sign) and a prominent Y-descent. Physical findings reflect the stage and type of tuberculous involvement of the pericardium.

Diagnosis

Echocardiogram is helpful in assessing the thickness of pericardium the amount of pericardial fluid, the physiologic impact of TB-pericarditis and in recognizing pericardial tamponade. Electrocardiogram may show changes suggestive of pericardial effusion and tamponade such as low voltages QRS complexes inverted T-waves, and electrical alternans. PCR testing is very helpful on endemic areas and caution should be used in interpretation of PCR in low prevalence areas[54,55]. Pericardial biopsy with smear and culture may further increase the yield of microbiological confirmation. The histology of pericardial biopsy with caesating or noncaseating granuloma is suggestive of tuberculous infection[56,57]. The histological changes in HIV often contain less granulomatous change. In countries with high incidence of TB, a diagnosis of definite TB-pericarditis is made when there is a positive smear or culture from pericardial fluid or presence of tubercle bacilli or granulomata on pericardial tissue. A diagnosis of probable TB-pericarditis is made when pericarditis is noted with active TB elsewhere in the body, lymphocyte-predominant pericardial effusion with high ADA activity is present, or positive response to tuberculosis therapy occurs[58].

Treatment

In adults initiate prednisone at 60 mg daily for 4 weeks followed by 30 mg daily for 4 weeks and 15 mg daily for 2 weeks and 5mg daily in the last week. In children use 1 mg/kg daily for first 4 weeks with gradual tapering over the next 7 weeks[59].

Conclusions

With the completion of revision of all the data's, we are able to conclude that the controlling of disease tuberculosis by human beings is yet not achieved. This is due to the fact that opportunist tuberculosis gets the optimum environment for invading human beings who are suffering from HIV (immune deficiency). These factors are well supported by the increase in multiple drug resistance in patients. So, there is an urgency to develop awareness amongst the individuals and also a new drug regimen for the proper treatment of tuberculosis.

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