Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

REVIEW ARTICLE

EXTRAPULMONARY TUBERCULOSIS (EPTB) : AN OVERVIEW

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Abstract:

Despite extensive research, screening, education, and continuous efforts to try to eradicate and control the infection, tuberculosis is still one of the most prevalent infections throughout the world. Up to 25% of tuberculosis cases present extrapulmonary involvement. and affect mainly children and adults with compromised immune systems. The most common locations are the lymph nodes, pleura and the osteoarticular system. The problem with these types of tuberculosis is the difficulty in establishing a definitive diagnosis, since the clinical symptoms may be vague. It is often necessary to resort to invasive investigation to diagnosis. Treatment for EPTB is with same antitubercular drugs(ATD) regimens for 6 months used for pulmonary tuberculosis (PTB), and any extension of this period is advisable solely in tuberculosis affecting the central nervous system and in Pott's disease. Besides antibiotics, occasionally, adjuvant therapy with corticosteroid and surgical intervention is recommended. Recent epidemiological studies show a striking increase in DR-EPTB cases ranging from 10–15% across various reports. As a neglected disease, significant developments in rapid and accurate diagnosis and better therapeutic interventions are urgently needed to control the emerging EPTB situation globally. In this review, we discuss the clinical pictures, diagnosis, treatment, and challenges of EPTB.

Key words : *Extra pulmonary tuberculosis, Pleural Tuberculosis, Meningeal Tuberculosis, Miliary Tuberculosis, Lymph Node Tuberculosis,*

Received: 21-02-2022 *Accepted: 06-04-2022*
DOI: https://doi.org/10.3329/bjm.v33i2.59285

Citation: *Azad KAK, Chowdhury T. Extrapulmonary Tuberculosis (EPTB) : An Overview. Bangladesh J Medicine 2022; 33: 130-137.*

Introduction:

Pathogenic *Mycobacterium tuberculosis* complex organisms (MTBC) primarily cause pulmonary tuberculosis (PTB); are also capable of causing disease in extrapulmonary (EP) organs, which pose a significant threat to human health worldwide. TB is a communicable disease. About a quarter of world's population is infected with M Tuberculosis.[1] According to WHO classification criteria EPTB is defined as an infection by *M.tuberculosis* which affects tissues and organs outside the pulmonary parenchyma. It represents between 20 and 25% of all TB cases.[2] Although throughout recent years we have experienced a constant reduction of the overall number of TB cases, the reduction of extrapulmonary TB cases has not been as -relevant[3,4]. EPTB can occur through hematogenous, lymphatic, or localized bacillary dissemination from a primary source, such as PTB, and affects the brain, eye, mouth, tongue, lymph nodes , spine, bones, muscles, skin, pleura, pericardium, gastrointestinal, peritoneum, and the genitourinary system as primary and/or disseminated disease . EPTB has a very variable presentation that depends on the organ involved. and more than one organ could be involved at the same time, has nonspecific clinical findings developing insidiously[5] mimicking other noninfectious conditions [6]. Nevertheless, its presentation can be extremely acute causing a life threatening condition [5]. It requires a high clinical suspicion and carries a lengthy

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period from the initial symptoms to the final diagnosis. Delayed diagnosis of extrapulmonary forms is frequent and it entails an increased morbidity and mortality. In this chapter, a review of the most important clinical manifestations along with diagnosis and management of EPTB will be discussed.

Epidemiology:

Mycobacterium tuberculosis, as a single infectious agent, causes more deaths than any other infection[3]. Outside infectious diseases, it is the ninth leading cause of death worldwide[7].The mean age of EPTB patients is higher than for pulmonary TB. Among EPTB patients those who develop pleural or meningeal affectation are generally younger than those who present lymphatic, osteoarticular, genitourinary and gastrointestinal forms of the disease[7].Worldwide, the incidence of extra-pulmonary involvement of tuberculosis occurs in approximately 15%-20% of all cases reported[8]. In other publications, reported cases varies from 15% to 40%, with approximately 3–3.5 cases per 100,000 of the population from 2002 to 2011[9]. Man and women are almost equally affected[10] . Therefore, EPTB continues to be an important presentation within tuberculosis infectious spectrum.

Current global and bangladesh situation and impact of COVID 19

The COVID-19 pandemic has reversed years of progress in providing essential TB services and reducing TB disease burden. The most obvious impact upto June2021 is a large global drop in the number of people newly diagnosed with TB and reported. This fell from 7.1 million in 2019 to 5.8 million in 2020[11]. Reduced access to TB diagnosis and treatment has resulted in an increase in TB deaths. Best estimates for 2020 are 1.3 million TB deaths among HIV-negative people (up from 1.2 million in 2019) and an additional 2,14, 000 among HIV-positive people (up from 2,09, 000 in 2019), with the combined total back to the level of 2017[11].

With an estimated population of 164 million, Bangladesh is listed among the 30-high burden countries for TB and 27 for MDR-TB[12]. The incidence rate for all from of tuberculosis is 221 per 100,000 population per year. The TB mortality is 24 per 100,000 population per year with over 38,000 deaths annually[12]. Similarly, MDR-TB was 0.7% among new and 11% among retreatment cases with a large absolute number of patients (~3,300 MDR/RR cases) that need to be treated with the second line anti-TB drugs (SLDs). Although TB treatment coverage increased from 27% in 2002 to 81% in 2019, an estimated 68,000 (19%) TB patients remain undetected every year with a static TB incidence - between 225/100,000 and 221/100,000 from 2001 to 2019[12].

Risk Factors FOR EPTB:

Risk factors involved in the development of EPTB are mainly increasing age, concurrent HIV infection and alcoholism, co-morbidities such as chronic renal disease, diabetes mellitus or immune suppression . Among HIV patients admitted due to tuberculosis, almost 50% have extra pulmonary involvement[13].

Tuberculosis and organ system involvement:

Lymphnode tuberculosis

It is one of the most common forms of EPTB and it most frequently affects children and young adults. It accounts for between 30 and 40% of all EPTB cases [14]. It can be due to a primary form or the reactivation of a focus. The most common location is cervical lymphadenopathy (63-77%) although it can also affect other areas such as supraclavicular, axillary, thoracic and abdominal nodes[15]. It most frequently involves unilateral laterocervical and supraclavicular swelling . Typical TB symptoms, such as fever, night sweats, and weight loss, are observed in some patients . Initially lymph node swellings are firm and discrete, later become fluctuant and matted together followed by abscess formation .The skin may then breakdown leading to chronic sinus formation and ultimately heals with scarring. The specimens' paucibacillary nature makes TBL diagnosis challenging. Diagnosis requires FNAB of the affected lymphnode and microbiological cytological smear testing as well as culture and PCR studies (sensitivity 77%, specificity 80%). Open biopsy is only used when FNAB has not been diagnostic (sensitivity 80%). Viewing caseous granuloma is highly suggestive of tuberculosis[16]. treatment involves the use of ATDs in a regimen similar to PTB .The continuation phase of treatment may be extended upto10 months[17] based on clinical judgment of physician,. These cases should also be investigated for DR-TB at the end of 6 months of treatment . In selected TBL cases, incision and drainage may be required. After the standard treatment, residual lymph nodes' presence is not considered a sign of recurrence or treatment failure .

Pleural tuberculosis:

It is a common form of EPTB, accounting for almost 20% of all cases. It is caused by a set of hypersensitivity reactions against mycobacterial antigens in the pleural space. These organisms and/ or their antigens probably enter the pleural space due to leakage or rupture of a subpleural focus of

disease. It can occur in association with pulmonary TB. Effusions are typically unilateral , 0ccassionaly develop empyema. Its diagnosis begins with pleural fluid examination through thoracentesis. The pleural fluid is exudative, straw-colored, shows predominant lymphocytes, with low glucose concentrations. Microscopy of fluid have low diagnostic yield since only 10 to 25% of samples are positive. Pleural fluid cultures are positive in between 25 and 75% of patients. The Xpert MTB/RIF and Xpert Ultra sensitivities are 50% and 71% with 99% and 71% specificity, respectively, for adult pleural fluid[18]. In endemic countries, pleural ADA levels of >40 IU/L have a positive predictive value of 98%[19]. (sensitivity 92% and a specificity 90%). The determination of interferon gamma in pleural effusions has the highest yield with 89% sensitivity and 97% specificity rates[20]. Sensitivity and specificity values for PCR are heterogeneous depending on the specific test used. The diagnostic yield of closed pleural biopsy is about 75%[12] as the lesions are patchy. Multiple biopsies increase the diagnostic yield. PLTB treatment involves the use of ATDs in a regimen similar to PTB. The use of adjunct corticosteroid therapy is not recommended since the beneficial effects of such treatment are inconclusive. Thoracentesis could be performed in addition to chemotherapy to alleviate dyspnoea and reduce pleural thickening and associated functional impairment[21].

Central Nervous System (CNS) Tuberculosis:

CNS involvement is the most severe form, accounting for 5–10% of all EPTB cases, with TB meningitis (TBM) being the predominant condition. TBM is common in children (below four years of age) and immuno-suppressed individuals such as those HIV infection and can occur with or without an associated PTB. Besides TBM, intracranial tuberculoma, tuberculous brain abscesses, arachnoiditis, increased intracranial pressure, and hydrocephalus were noted in CNS disease [22,23] .The The onset of TBM manifests in neurological complications, such as headache, low-grade fever, malaise, vomiting, and confusion. When untreated, TBM can cause seizures, coma, and stupor. Prognosis is dependent on the stage of diagnosis and treatment [22,23]. Diagnosis of TBM usually depends on clinical symptoms, radiologic imaging such as computerized tomography (CT) scan, and the presence of extra-neural TB. Usually, the cerebrospinal fluid (CSF) of patients is analyzed for disease markers. In general, presence of predominant lymphocyte (60–400 cells/mL), elevated protein, a decrease in sugar levels, and an adenosine deaminase (ADA) level of 5–15 IU/L are indicators of suspected TBM [24]. the acid-fast bacilli (AFB) test's sensitivity is <25%, and culture is 25–70% with 100% specificity in the CSF of TBM cases [25,26]. Xpert MTB/RIF and Xpert Ultra, are reported to have a 70% and 87% sensitivity . MRI is the gold standard test since it detects early lesions more accurately. Hypercaptation of the meninges is highly suggestive of TB. Treatment of TBM includes chemotherapy using standard anti-TB drugs (ATDs) as prescribed for PTB in an extended form. The WHO recommends 2 months of initial treatment phase with isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (ETM), followed by 10 months of INH and RIF as a standard regimen for drug-sensitive TBM cases[27]. Besides the standard TB treatment, the WHO recommends using adjunctive corticosteroids, including prednisone and dexamethasone[27], The recommended dosage is 0.1 - 0.2 mg/kg/day (depending on severity of the disease) for 2-4 weeks followed by gradual tapering of the dose @ 0.1mg/kg/ week until it reaches a dosage of 0.1mg/kg/day (0.3 mg/kg/ day in 1st week of tapering, 0.2 mg/kg/ day in the 2nd week and 0.1 mg/kg / day in the 3rdweek). This is followed by weekly tapering of oral dexamethasone @ 1 mg/week (4 mg/day, 3 mg/day, 2 mg/day and 1 mg/day, each for a period of 1 week). The total duration is usually of 12 weeks[8].

Abdominal tuberculosis:

Tuberculous enteritis can involve any aspect of the gastrointestinal tract although the ileocecal region is the most common site of intestinal involvement. The pathogenesis can be attributed to ingestion of contaminated milk or food in the case of infection by *Mycobacterium bovis*, swallowing of infected sputum, hematogenous spread from active pulmonary or miliary TB or contiguous spread from adjacent organs. The organism penetrates the mucosa and localizes in the submucosal lymphoid tissue, where it initiates an inflammatory reaction with subsequent lymphangitis, endarteritis, granuloma formation, caseation necrosis, mucosal ulceration, and scarring. Nonspecific chronic abdominal pain is the most common symptom occurring in 80 to 90 percent of patients. A palpable abdominal mass, anorexia, fatigue, fever, night sweats, weight loss, diarrhea, constipation, or blood in the stool may be present. Fistula and intestinal stricture may occur,. Bowel obstruction is the most common complication and may be due to progressive stricture or adhesions [6,18]. Definitive diagnosis is based on a combination of CT imaging, histology and culture of biopsy material. Colonoscopy with biopsy is the most useful non operative diagnostic procedure to obtain material for histology and culture. Biopsy's sensitivity is up to 80%[28].

Tuberculous peritonitis usually occurs as a consequence of the reactivation of latent foci in the peritoneum following hematogenous spread of the infection or from the contiguous spread from adjacent foci such as genitourinary or intestinal TB. TB peritonitis is a common form of EPTB seen among patients with immunosuppressant therapy, HIV infection, renal failure, and cirrhosis. As a subacute disease, TB peritonitis progress with a slow onset of symptoms, including fever, night sweats, abdominal pain, and ascites.

Along with GITB, the involvement of lymph nodes or abdominal lymphadenopathy is usually observed. The most commonly involved lymph nodes are the mesenteric nodes, omental nodes, porta hepatis, the celiac axis, and the peripancreatic area. TB of the visceral organs, including the liver, spleen, and pancreas, are rarely involved in isolation. Diagnosis of abdominal TB is exceptionally challenging as it mimics other chronic diseases, such as malignancy, Crohn's disease, and irritable bowel syndrome. The diagnosis usually requires paracentesis with the removal of peritoneal fluid for the determination of ADA, which has 100% sensitivity and 97% specificity[29] . Examination of an acid fast stained smear of ascitic fluid has a reported sensitivity of between 0 and 6% whereas culture is positive in 80% of all cases. If negative, CT guided or laparoscopic biopsy would be needed. Surgery is reserved for complicated cases where perforation, bleeding or obstruction occurs. Abdominal TB is generally responsive to standard ATDs used to treat PTB[30] . Surgery is recommended only when irreversible constrictions, strictures, abscesses, and fistula formation cause damage to the GI tract or other internal organs in the abdomen.

Adrenal gland TB occurs through hematogenous spread. In the developing world, however, tuberculosis continues to account for about 20–30% of cases of Addison's disease [31]. Symptoms of adrenal insufficiency may occur, such as fatigue and abdominal pain. When >90% of the cortex has been destroyed, patients may present with Addisonian crisis, which can be life-threatening[32].anterior pituitary hormonal assay with stimulation tests, MRI(usually shows bilateral adrenal enlargement) and histopathology remains the diagnostic tools.

Genito urinary tuberculosis:

Genitourinary tuberculosis has been estimated to account for 6.5% [33] of all EPTB cases. It is more common in men than in women. Hematogenous spread of primary pulmonary infection; late reactivation disease or miliary disease can lead to renal involvement. patients with miliary infection, 25 to 62% have been documented to have concomitant renal lesions [33]. The onset on genitourinary TB is often asymptomatic but eventually with the spread of the disease causes sterile pyuria and microscopic hematuria in up to 90% of cases. Ureteral stricture can occur and may cause obstructive uropathy with the development of hydronephrosis. By means of USG, or intravenous pyelogram, CT calcifications, papillary necrosis, calyx involvement, ureteral stricture and pelvic dilation can be demonstrated. As to improve Microbiological diagnostic yield, between 3 and 6 serial samples of urine should be collected every early morning (sensitivity 80-90% for several determinations). The use of polymerase chain reaction (PCR) for detection of *M. tuberculosis* in urine or renal tissue is improving diagnostic capabilities[34]

In men, the involvement of the prostate, epididymis and testicles is common with the development of subacute prostatism and epididymoorchitis. FNAB or open biopsy samples is necessary for the establishment of the diagnosis. In women, the Fallopian tubes are bilaterally involved in up to 80% of case . Diagnosis requires the realization of hysterosalpingography and culture of menstrual fluid, endometrial biopsy and sampling of other affected tissues by means of laparoscopy[35-36.]

Osteoarticular tuberculosis:

It accounts for 11% of EPTB forms according to published series[37]. Although it can affect any bone, **spondylitis or Pott disease**, represents 50% of all cases [38]. Infection generally begins with inflammation of the anterior aspect of vertebral bodies, typically, it spreads behind the anterior ligament to the disc and to adjacent bodies. Eventually the infection can spread to adjacent soft tissues with the formation of paravertebral or psoas abscesses and affecting the posterior aspect of vertebral bodies eventually involving the spinal cord which is then at risk of compression which is not uncommon in endemic region due to lack investigation access. of Pott's disease most commonly affects the lower thoracic region in younger patients and the upper lumbar region in elder patients. The most common symptom is local pain. Concomitant TB infection in other locations is present in between 20 and 40% of all cases. CT and x-rays are useful in the determination of the extension, the affectation of soft tissues and eventual neurological involvement. MRI is the most sensitive tool in the assessment of neurological commitment. Surgery can be sometimes necessary for patients with symptoms of spinal compression. Diagnosis of skeletal TB requires CT guided biopsy for subsequent culture and pathology study[39].

Tuberculous arthritis can occur in virtually any joint, but it tends to occur in the hip or in the knee. Clinical manifestations include swelling, pain and loss of joint function that progresses over weeks to months. The formation of fistula is common in advanced cases. Positive cultures of synovial fluid appear in up to 79% of cases, if negative synovial biopsy may be necessary . On the other hand, symmetrical polyarthritis involving large and small joints without local evidence of active TB(Poncet's disease), seems to be immune-mediated and related to HIV co-infection. **Osteomyelitis** may occur in any bone of the body, and it is more commonly insidious.

Treatment of osteoarticular TB and spinal TB for treatment is 12 months with 2 (HRZE)/10 (HR)[12]. Surgery should be considered for patients with neurological deficit or an unstable spine lesion.

Miliary tuberculosis:

Miliary tuberculosis (MiliTB) is a fatal form of disseminated TB developed by hematogenous spread from a primary locus. It can affect infants, young children, and older adults with predisposing co-morbidities, such as malnutrition, HIV infection, treatment with immunosuppressants, diabetes mellitus (DM), chronic kidney disease, and malignancy. The common symptoms are fever, malaise, anorexia, weight loss, and cough with septicemia. The most frequently affected organs are the liver, the spleen, the lung, the lymph nodes, the meninges, the bone marrow and the adrenal glands. Specific disease symptoms sometimes show cutaneous lesions (Tuberculosis cutis miliaris disseminate), choroidal tubercles, and commonly TBM. Atypical complications, including acute distress respiratory syndrome, pneumothorax, severe kidney injury, lymphadenopathy, cardiac, hepatic, and gastrointestinal manifestations, as well as immune reconstitution inflammatory syndrome (IRIS), are also observed . [40,41.]

Diagnosis is difficult due to its clinical course and sometimes delayed. Chest X-ray usually shows a miliary pattern, while high-resolution CT imaging specifically identifies miliary nodules, ground-glass opacities, and interlobular septal thickening. Depending on the organs involved, other diagnostic imaging, including ultrasound, MRI, Positron emission tomography-CT (PET-CT), or echocardiography, is recommended to assess the extent of organ damage. The blood profiling of MiliTB usually shows anemia, lymphopenia, pancytopenia, and elevated transaminase, bilirubin, ESR, and CRP. Collection of several samples in different locations, is required for culture and histological testing. Blood cultures are sometimes positive especially in patients with concurrent HIV infection. Necrotizing granuloma are most frequently obtained from liver samples (90-100%) rather than bone marrow (31-82%) or transbronchial biopsy (63-72%)[38] Treatment of MiliTB cases without meningeal involvement includes standard ATD therapy as recommended for PTB. In the case of MiliTB existing with TBM, treatment is continued for up to 12 months. Corticosteroids, such as prednisone, are beneficial as adjuvants for MiliTB,

Tuberculous pericarditis:

Pericardial infection may occur via extension of infection from the lung or tracheobronchial tree, adjacent lymph nodes, spine, sternum, or via miliary spread. It is usually associated to concomitant infection in other locations. Ecocardiography is useful in diagnosis as well as to assess potential complications such as constrictive pericarditis and cardiac tamponade. Tuberculous pericardial effusions. are typically exudative and characterized by increased leukocyte count, with a predominance of lymphocytes and monocytes. AFB are observed infrequently (6% sensitivity) and the yield is increased by culture (25-75% according to published series). The determination of interferon gamma is more sensible and specific (92% and 100% respectively) than the elevation of ADA levels (sensitivity of 87% and specificity of 89%). ·Standard chemotherapy with ATDs, similar to PTB treatment, is currently followed for tubercular pericarditis[42] Echocardiographic needle pericardiocente helps to alleviate cardiac tamponade[42]. Oral or intrapericardial corticosteroids are promising to immunocompetent individuals ·

Laryngeal tuberculosis:

Laryngeal tuberculosis usually entails the development of masses, ulcers or nodules in the larynx and vocal cords. The most common clinical manifestation is dysphonia but it can also produce coughing, stridor and hempoptysis. It is usually associated with concomitant pulmonary TB, and it is thus a highly bacilliferous and contagious form of the disease.

Cutaneous tuberculosis:

Cutaneous or skin tuberculosis (CTB) constitutes 1–1.5% of all EPTB. TB verrucosa cutis, manifests as a painful hyperkeratotic or verrucous papule with an inflammatory areola. CTB due to endogenous source (known as scrofuloderma) occurs on the skin as a contiguous extension of underlying TB, usually lymphadenitis or bone or joint or epididymis TB. Orificial TB is a less common manifestation of cutaneous TB that causes painful ulcerative disease

near orifices such as oral, perineal, and perirectal skin [42].Lupus vulgaris is the chronic form of CTB that produces lesions of individual plaques or nodules with some ulceration and scarring [42]. TSTs have shown 33–96% sensitivity and 62.5% specificity for CTB [43]. Skin biopsy is an ideal sample for CTB diagnosis by AFB staining and/or the bacilli culture. Treatment of CTB involves using ATDs similar to PTB therapy[26]. Surgical excision and debridement) are also recommended for scrofuloderma lesions, lupus vulgaris, or tuberculosis verrucosa cutis [44,45]

Ocular tuberculosis:

Primary progressive TB of the eye is rare, and most of the OTB cases involve exogenous infections of the eyelids, conjunctival, corneal, and scleral lesions, while the secondary disease is more common and affects the uveal tract, retina, and optic nerve. Uveitis is the most common EPTB due to the vascular supply and presents as anterior, intermediate, posterior uveitis, and pan-uveitis[46]. imaging techniques-including fluorescein and indocyanine angiography, fundus autofluorescence imaging, optical coherence tomography, fundus fluorescein angiography, ultrasonography, and microperimetry- are extensively used to assess the extent of damage to the eye as well as a therapeutic response[47]. Management of OTB involves the use of standard ATDs prescribed for PTB cases supplemented with adjuvant Systemic corticosteroid

Challenges of EPTB:

a. Diagnostic dilema

Diagnosis requires a very high index of suspicion due to its vague symptomatology that includes differentials like other chronic infections, and malignancies. Culture still remains gold standard for TB diagnosis, which is often negative due to paucbacilary nature of EPTB. Conventional diagnostic techniques provide different degrees of sensitivity and specificity according to location and bacterial load. Invasive methods are often needed to obtain samples for microbiological and histological testing. The yield of IGRA and the standardization of molecular techniques still remain to be established

b. Rising trend of drug-resistant EPTB:

An increased number of drug-resistant EPTB (DR-EPTB) cases have been reported in the last decade, which poses significant challenges to diagnose and treatment. Since EPTB is less contagious than pulmonary TB, it is often ignored during initial diagnosis; however, the rising trend in DR-EPTB cases redefines the focus and warrants immediate attention for intervention. Previous studies have reported 16–20% of EP-TB cases with collective drug resistance. Among the DR EP-TB cases, studies reported maximum resistance to isoniazid (8–14%), while the frequency of rifampicin monoresistance (2.4–3.9%) and MDR (2.0–10.0%) cases were comparatively low[48,49,50]. Lymph nodes, bone and pleura, are the most common organs involved in DR-EPTB reported worldwide. Rapid diagnosis of EPTB such as Xpert MTB/RIF Ultra and Xpert MTB/RIF, is recommended by the WHO [51].

c. Adverse drug reactions:

Adverse drug reactions to anti-TB drugs include gastrointestinal disturbance, hepatotoxicity, peripheral neuropathy, psychiatric disorders, optic neuritis, ototoxicity, renal toxicity, cardiac toxicity/ arrhythmias, arthralgia, and skin reactions that vary in intensity from one case to another. These add to the existing burden of poor treatment outcomes, non-compliance to treatment, and death.

Strategies for control of tuberculosis:

The "End TB Strategy", established by the WHO, aims to reduce TB deaths by 95% and new cases by 90% in 2035[8]. In 2016, Bangladesh adopted WHO's End TB Strategy[8]. After having successfully implemented the 'DOTS' or Directly Observed Treatment strategy in Bangladesh, the country embarked on ensuring high quality DOTS, better outreach so that more number of patients have access to quality TB care, management of multi-drug resistant TB (MDR-TB) and TB-HIV co-infection, strengthening of health systems, involving all healthcare providers in the public sector, private sector and Non-Governmental Organizations (NGOs), strengthening the advocacy campaign, promoting Medical College involvement and research.

Conclusion:

TB is preventable and curable disease. Achieving the goal of "End TB Strategy", involves applying improved diagnosis, treatment, ensuring patient compliance, and better vaccines to fight against TB. Close co-operation of all healthcare providers at all levels is essential for successful implementation of the control programme. In addition to PTB, it is imperative to address the impact of EPTB and its rising drug resistance on global health and the economy to control these diseases worldwide. An early and accurate diagnosis and drug susceptibility testing are essential to initiate the correct treatment regimen without delay. While the standard ATDs used in PTB is also approved to treat most of the EPTB cases, the duration and effectiveness of treatment vary strikingly, depending on the nature of disease manifestation and the organ involved. treatment with corticosteroids as adjuvant to antimicrobial drugs and surgery can be beneficial in special situations. The complexities associated with EPTB and DR-EPTB management highlight the urgent need to develop additional, advanced tools for early and rapid diagnosis, and more efficient treatment regimens.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study.

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