EDITORIAL

ARE WE ADHERING TO NATIONAL GUIDELINES FOR DIAGNOSIS AND MANAGEMENT OF TUBERCULOSIS?

Tuberculosis (TB) is among the most serious infections causes of global morbidity and mortality. One third of world population is infected with tubercle bacilli. Approximately, 95% of new cases and 98% of deaths due to TB occur in the developing world [1]. According to World Health Organization (WHO), Pakistan ranked 7th among high burden countries in the world and it bears 44% burden of tuberculosis in Eastern Mediterranean Region (EMRO). There is dire need to fight this "monster of TB" in a scientific and unified manner; otherwise we are going to see further rise in resistant forms of TB. For quite sometime, WHO has been guiding and helping countries in Asia and Africa to develop and strengthen their National TB Control Programs and formulate guidelines on treatment of TB for local use. In Pakistan, first such guidelines were published by Directorate of TB Control (Ministry of Health) in 1995. These guidelines were revised and reissued in 2003 by National TB Control Program (NTP) and subsequently reviewed and endorsed by Pakistan Chest Society (PCS) [2]. Though these guidelines are available for more than a decade, but awareness about their existence and compliance to these guidelines is inadequate particularly in military hospitals. As a result, there are serious errors in the diagnosis and treatment of tuberculosis not only in general practice but also at specialist level. Various treatment regimens are being prescribed by various doctors for variable duration. The disease is being classified into severe and less-severe forms on the basis of x-ray findings. A term of expanded regimen consisting of six drugs has been coined and is being prescribed even in smear negative cases of pulmonary TB and that for an extended duration aiming at complete radiological resolution. In certain patients, high resolution computerized tomography (HRCT) scans are being advised for the diagnosis of pulmonary TB and response to treatment is being monitored by serial HRCT scans. Such practices so not only contrary to national and international guidelines but are increasing the cost of TB-treatment by many folds. Similarly, medical students are being taught Anti-TB treatment regimens written in medical text books published from Europe and North America. It is strongly urged that NTP and PCS should not confine these guidelines to chest physicians and to their TB centers only but should actively disseminate them to doctors at a large scale. Seminars may also be arranged for medical students in all the medical colleges on regular basis to increase the awareness about these guidelines. It is true that guidelines are just guidelines and experienced specialists can question and deviate from these guidelines, but there should be strong scientific evidences for such deviations. If such concerns and evidence are referred to NTP/PCS, these can form the basis for future revision of the guidelines. However, as responsible members of society, we should surrender our personal opinions to a scientific consensus. Though it is not in the scope of this editorial to reproduce these guidelines in detail, but an attempt is being made to give an overview. For the complete understanding of these guidelines and treatment strategies, there is need to understand various terms and definitions used in this document. Tuberculosis is mainly divided into two forms; Pulmonary and Extra-pulmonary TB. The term ***Pulmonary TB*** is applied when it involves lung parenchyma only, so pleural TB, hilar/mediastinal lymph nodes TB and even milliary TB are not considered to be pulmonary forms of TB. When TB involves any other part of the body, it is labeled as ***"Extra-pulmonary TB"***. If a person has pulmonary as well as extra-pulmonary TB simultaneously, it is labeled as a case of Pulmonary TB. According to WHO and National guidelines on TB, the most important diagnostic test in case of

pulmonary TB is detection of acid fast bacilli (AFB) in sputum either by microscopy or on culture. A patient with pulmonary TB is labeled *as* ***"Smear Positive Case"*** , if AFB are detected on microscopy in at least two sputum specimens or if there are radiographic abnormalities consistent with TB, then such patient can be labeled as smear positive even if AFB are detected in one sputum smear. In contrast, if the patient has clinical features and radiographic abnormalities consistent with tuberculosis but AFB are not detected in three sputum specimens and there is no clinical response to a seven day course of broad spectrum antibiotics, then such patient should be labeled as ***"Smear Negative Case"***. The clinical features that are consistent with active TB are cough for more than 2-3 weeks, weight loss, fever, night sweats and fatigue. Cases which are sputum smear negative are 7-10 times less infectious than those who are positive on direct microscopy of sputum smear. To diagnose extra-pulmonary TB, one should have at least one bacterial culture positive specimen from an extra-pulmonary site or histological and/ or clinical evidence consistent with TB of these sites. As patients who have taken anti-tuberculosis treatment (ATT) in the past have increased chances of having drug resistant tuberculosis, so it is of paramount importance that patients suspected to have TB should be asked whether ATT had been taken in the past or not. A patient who has never had treatment for TB in the past or has taken ATT for less than four weeks is labeled as a ***"New Case"***, While those who have taken ATT for more than four weeks in the past are grouped in ***"Re-treatment Category"***. This re-treatment category contains cases of relapse, failure, chronicity and default. In case of pulmonary TB, a case is labeled as ***Relapse,*** if a sputum smear positive patient who was declared cured in the past after completing full course of ATT is found to have AFB in the sputum again. ***Failure Cases*** are those patients who remain, or become sputum smear positive 5 month or more after commencing treatment. In contrast, ***chronic case*** is the one who remains sputum smear positive even after completing a re-treatment regimen of ATT under supervision. "***Treatment after default***" means that patient had interrupted ATT for two or more months and is found to have AFB on return. The "***Tuberculin skin test***" has a limited value in clinical work especially in high prevalence countries like Pakistan. In adults, positive skin test is infrequently followed by disease and a negative tuberculin test does not exclude active disease. In our hospitals, Mantoux test is advised indiscriminately and diagnosis of tuberculosis is made or refuted on its bases. This practice is not in line with medical evidence. Similarly, erythrocyte sedimentation rate has no role in diagnosis or monitoring of response to treatment.

The basis of treatment of tuberculosis is chemotherapy, which not only cures an individual but also prevents transmission of TB in the community. To be effective, chemotherapy has to be taken in adequate dosage for appropriate duration without interruption. It is advisable to treat TB under Direct Observed Therapy (DOT) strategy, where it is ensured that patient has actually taken all the prescribed drugs. It has also been found that optimum duration of treatment of tuberculosis is eight months and no significant benefit can be achieved by extending this duration. According to above quoted guidelines, treatment strategy of tuberculosis depends upon the fact whether you are dealing with sensitive or resistant form of TB and whether it is a new case or a re-treatment category. A new case of TB, whether pulmonary or extra-pulmonary, whether sputum smear positive or negative should receive rifampicin (RIF), isoniazid (INH), ethambutol (EMB), and pyrazinamide (PZA) in adequate doses for first two months. This induction phase should be under DOT strategy. Following induction phase, patient should continue INH, EMB for further six months. The total duration of treatment is eight months. The reason for not recommending RIF and INH in continuation phase as applied in Europe and North America is that in South East Asia, there is high incidence of INH resistance and

practically RIF becomes mono-therapy that might lead to emergence of resistance to RIF in community. Loosing RIF as an effective drug will prove to be disastrous. Those who advocate using RIF in continuation phase recommend that three drugs (RIF, EMB and INH) should be used for four months. In re-treatment category, patient is prescribed five dugs; RIF, INH, EMB, PZA and streptomycin (SM) for first two months, then SM is dropped and remaining four drugs are continued for another one month. Following this, PZA is stopped and remaining three drugs are continued for another five months. Although there is no evidence indicating that fixed-dose combination medications are superior to individual drugs, but these formulations are strongly recommended by WHO as it reduces the risk of inadvertent mono-therapy, and there is an ease in administration [3]. It is to be remembered that one should never add a single drug to a failing regimen. So doing risks development of resistance to the new drug, further complicating management [3]. All physicians involved in the management of TB should know when to diagnose Multi-drug resistant tuberculosis (MDR-TB) that means resistance to RIF and INH. If AFBs are detected after five months of ATT that has been genuinely complied with, then one can clinically suspect MDR-TB that need to be treated with second-line drugs. Once there is an additional resistance to one of the fluoroquinolones and at least one of the three injectable second-line drugs (amikacin, kanamycin and capreomycin), then disease is to be labeled as extensively drug resistant TB (XDR-TB). As these resistant forms of TB are very difficult to treat, so it is advisable to seek guidance from specialists with reasonable experience of handling such cases.

REFERENCES

1. Camila C, Roa Jr. Prevalance and Genesis of Drug Resistant TB. Spiritus. 2008 Jan; Special Issue, 1-2
2. Guidelines for Diagnosis and Management of Tuberculosis.2003; National Tuberculosis Control Programme, Ministry of Health, Govt of Pakistan
3. Treatment of Tuberculosis, Morbidity and Mortality weekly Report; CDC Atlanta June 20, 2003: 52/No. RR-11

Brig Jawwad Khaliq Ansari
Associate Professor of Medicine
& Pulmonologist
Army Medical College, Rawalpindi