Safe placement of tuberculosis treatment clinic – To prevent transmission of infection and drug resistance

Bhattarai MD, Thapa B, Pandit NRS

Bir Hospital, National Academy of Medical Sciences, Kathmandu, Nepal

Corresponding Author: Prof. Madhur Dev Bhattarai, 294, Kumari Marg 6, Dillibazar, Kathmandu, Nepal; E-mail: mdb@ntc.ntc.np

ABSTRACT

This paper aims at describing the high risk situation of a tuberculosis (TB) clinic in a central hospital and recommendations for its safe placement. Previously, the medical outdoor unit, along with the diabetes clinic was placed on the second floor and later on, the TB clinic was established near its entrance. Human Immunodeficiency Virus (HIV) clinics and the nephrology department with its transplant patients on immunosuppressive therapy were also nearby. With effort, the TB clinic was shifted separately outsidein an outdoor-building with well-ventilated waiting areas. However, TB patients, new treatment and under retreatment regimens still have to go inside the outdoor-building for sputum examination to the fourth floor laboratory. We reviewed the situation in six other hospitals in the capital. Their laboratories are inside the main hospital buildings. In almost all the hospitals, TB patients have to walk inside hospital-buildings, mixing with patients, staffs and even children to reach TB clinics, mostly without wearing face-masks. TB patients regularly visit the clinic for daily tablets and injections, which include a concentration of resistant cases. The number of undiagnosed drug-resistant TB patients, identified after a lag period of a few months, among new and retreatment TB patients should also be considered. High risk patients like children, people with diabetes, HIV positive patients and patients undergoing immunosuppressive therapy also gather in the hospitals. TB clinics have daily visits from all registered TB patients, and the associated sputum examination centers for them should be ideally placed safely in well-ventilated areas avoiding interactions with other patients. National and international TB agencies should take responsibility and identify financial support for the safe placement of TB clinics. Such TB centers should eventually be integrated with the Peripheral Health Service away from hospitals.

Keywords: Acid fast bacilli (AFB), multi-drug resistant tuberculosis, extensively-drug resistant tuberculosis, retreatment tuberculosis, sputum examination, tuberculosis transmission

INTRODUCTION

Control of tuberculosis (TB) epidemic is basically based on finding of TB cases, called case-finding, and treating them effectively. There are challenges of new drug discovery for treatment of TB, which were mostly developed in the central decades of the last century.[1,2] Such challenges to control TB epidemics by treatment of its sources indicate the need to consider all possible means that need to be undertaken so as to minimize the transmission of infection and drug resistance. Report of a dramatic tracing through different countries and subsequent detention and isolation of a patient with extensively drug-resistant tuberculosis by the US Center for Disease Control and Prevention has also highlighted the importance of taking all precautions for prevention of drug resistant TB.[3] In countries like ours facing a high burden of TB, particular attention may need to be given to TB clinics where patients regularly gather creating concentrated foci of both infection and resistance. Here, we report the situation of the TB clinic and recommendations hospital in Nepal, discussing its various implications and recommendations.

Safe placement of Tuberculosis Treatment Clinic

TB treatment clinic as TB sub-center for new (Category I) and retreatment (Category II or previously treated) TB patients under National TB Center was initially started in Bir Hospital in the medical out-door clinic perhaps considering TB clinic as a part of medical clinic. The medical clinic is on the second floor and the TB clinic was established near its entrance (Figure 1).

TB patients had to take the stairs from the ground floor and then cross the first floor to come to the second floor. These floors also have the Human Immunodeficiency Virus (HIV) clinic and nephrology department with its transplant patients on immunosuppressive therapy. TB patients coming to the clinics interacted with medical outdoor clinic patients waiting in the same area.The medical clinic consists of many patients on steroid therapy, and there also happens to be a diabetes clinic nearby. Soon after, the free multi-drug resistant (MDR) TB drug supply unit was also started in the TB clinic.

Fig. 1. The medical outdoor clinic hall in the second floor with the TB clinic situated previously just at the left side of entrance opposite to the Pulmonary Function Test (PFT) room with diabetes clinic further inside on the right side.

This raised concern regarding the increased risk of TB transmission to other patients and staff. We initiated the move to shift the TB clinic to a safe place, however, it was not an easy task. The TB clinic requires to be built separately, away from other activity areas, with well ventilated patient waiting area, with provision to allow a patient in the room designed for examination, tablet ingestion under Directly Observed Treatment Short Course (DOTS) and injection of aminoglycosides, as recommended.[4] The budget for the safe placement of TB clinics from various possible sources were explored. The debate "Whose responsibility was it to build the TB clinic, the hospital or TB agencies?" also delayed the process. It was ultimately possible by mobilizing the hospital resources to shift the TB treatment clinic separately outside the outdoor building (Figure 2).

Sputum examination for Acid Fast Bacilli (AFB) of patients under treatment

The sputum smear examination for AFB is done in the hospital. Though the TB treatment clinic was shifted outside, the new and retreatment patients visited the hospital laboratory on the fourth floor inside the outdoor-building for follow-up of their sputum AFB smear examination, intermixing with other patients. The outdoor-building is crowded with relatively inadequate ventilation. The TB treatment clinic in our hospital also supplies multiple drug resistant (MDR) TB drugs under the DOTS program. For follow-up, sputum smear and culture examination for AFB is done and the patients under MDR-TB treatment are sent to TB centers in other parts of the city outside the hospital.

TB clinic situation in other hospitals

We also looked into the situation of TB clinics in six other similar hospitals in the capital. The laboratories of the hospitals, where the new and retreatment TB patients under treatment went for sputum examination, were inside hospital buildings. Similarly, in almost all the hospitals, TB treatment clinics were inside the main buildings of hospitals and TB patients had to walk inside the complex, usually without wearing face-masks intermixing with other patients and stafffor regular, almost daily TB treatment. In two such hospitals dealing also with children, TB patients regularly came in contact with children.

DISCUSSION

The safe placement of TB clinic in a well ventilated area of the hospital away from other visitors and hospital activities as done here after realization of the risk by local professionals took time but could be an exceptional example. However, new and retreatment TB patients still have to visit the hospital laboratory on the fourth floor insidethe outdoor-building for sputum AFB examination intermixing

Fig. 2: The new TB clinic (on the left side of the picture with a person standing at its gate) now built separately outside the main outdoor building on one side away from the main entrance with well-ventilated open-air shelter in the waiting area with a roof, along with a separate open room (just behind the sitting person) designed for examination, tablet ingestion under Directly Observed Treatment,

with other patients and staff. The situation of TB treatment clinics and sputum examination laboratories for TB patients under follow-up in other hospitals are also risky. However, it would be fallacious to consider the high risk situation of TB clinic as a local problem of this place or country alone. Nepal is relatively a small country situated between China and India which, along with the Russian Federation, accounts for more than half of the estimated global MDR-TB cases.[5] It is well acknowledged that until quite recently, virtually no country with a high burdenof tuberculosis had implemented systematic measuresto reduce the risk of TB transmission in health facilities.[6,7] Regarding the systematic measuresto reduce the risk of TB transmision, particularly the drug resistant one, in health facilities in countries like ours with high burden of TB, five points need particular attention.

1. Selection and concentration of drug resistance in any TB clinic with regard to its risk of concentrated epidemic

TB treatment clinics generally manage new and retreatment TB patients. Now management of MDR and even further extensively-drug resistant (XDR) TB patients are increasingly done in the selectedTB treatment centers and sub-centers including in different hospitals.Treatment success documented in MDR-TB is 48% of overall patients, which requires prolonged therapy.[5] However, the diagnosed MDR- or XDR-TB patients under treatment are not the only source for transmission of drug resistance. There are new and particularly retreatment patients to be considered.

The proportions of MDR-TB among new TB cases range from 0–28% with global average of 3.5%.[5-7] Failure rates ranged from 18% to 44% in those with isoniazid monoresistance.[8] The proportion of MDR-TB among previously treated cases under retreatment regimens range from 0%–61.6% with global average of 20.5%.[5-7] In a nearby South Asian country, among those that failed a retreatment regimen, 91% had MDR-TB.[6]The responding TB patients under different categories of treatment regimens may transmit the TB bacilli of their resistant patterns in the intervening period and even more resistant ones before they are declared treatment failure (Table 1), e.g. usually five months in new and retreatment regimens. As the number of patients on new or retreatment regimens is much more than that ofdiagnosed MDR-TB patients under treatment, thetotal number of MDR-TB patients receiving these regimens with first-line primary TB drugs would also be significant. For every diagnosed MDR-TB patient visiting MDR-TB clinic, there are three other undiagnosed MDR-TB patients under new and retreatment TB regimens visiting general TB clinics for months (Figure 3).

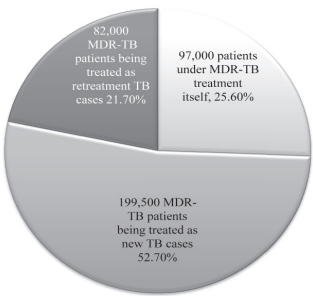

Fig.**3** Proportion of total 378,500 multi-drug resistant tuberculosis (MDR-TB) patients globally put under different categories of treatment in 2013and were likely to be regularly visiting TB clinics for months as new, retreatment, or MDR-TB cases – Apart from the 97,000 patients put under MDR-TB treatment itself, 199,500 (3.5% of reported 5.7 million) new TB patients and 82,000 (20.5% of reported 0.4 million) retreatment TB patients were estimated to have had MDR-TB.[5]

Moreover, apart from the MDR-TB, there could be resistance to any other first-line primary TB drugs among new and retreatment TB cases. In a recent report of primary drug resistance in Nepal, 8.1% of new cases of TB without previous history of any treatment had resistance to any single first-line primary TB drug and 4.8% had MDR-TB.[9] The global treatment success rate was 86% among all new TB cases in 2013.[5] Irregular or defaulting treatment could also be the other reason for unsuccessful responses. Known MDR-TB patients are treated in the selected TB centers with particular care. However, TB patients under new and retreatment regimens are treated in any TB clinic and hospital all over the country and do not draw much attention. The TB patients are generally assumed to be non-infectious after two weeks of appropriate therapy, but that applies for those receiving appropriate therapy and without having drug resistance.

Table–1: Usual time of designation as treatment failure without drug-susceptibility testing in various categories of tuberculosis (TB) treatment patients indicating the risk of transmission of drug-resistant infection during the intervening period.

Categories of treatment*	Treatment duration	Usual time of designation as treatment failure without drug-susceptibility testing
New or Category I TB patients	Total six months of therapy with four oral first-line primary TB drugs† in different phases and combinations	If sputum smear examination remains positive at the end of five months of treatment
Retreatment or Category II or Previously Treated TB patients	Total eight months of therapy with four oral first-line primary TB drugs† in different phases and combinations with injection streptomycin‡ for two months	If sputum smear examination remains positive at the end of five months of treatment
Multi-drug resistant (MDR) TB patients	Total 20 to 24 months with various second line TB drugs including injection kanamycin‡ for about 8 to 12 months, initially daily for four months and later thrice weekly	If sputum culture remains positive at the end of 12 months of treatment
Extensively-drug resistant (XDR) TB patients	Total 24 to 30 months with various second line TB drugs including injection capreomycin‡ for 12 to 16 months, initially daily for 8 months and later thrice weekly	If sputum culture remains positive at the end of 12 months of treatment

*Treatment followed in the country[11,12]

† Four oral first-line primary TB drugs: Isonizid, rifampicin, pyrazinamide and ethambutol

‡ Injection streptomycin, kanamycin, and capreomycin are aminoglycosides group of drug

For every diagnosed MDR-TB patient visiting MDR-TB clinic, there are three other undiagnosed MDR-TB patients under new and retreatment TB regimens visiting general TB clinics for months.

2. Risk due to the need for regular, almost daily visit for tablet ingestion under DOTS and aminoglycoside injections for retreatment and resistant TB

TB treatment is now increasingly provided under direct supervision of DOTS programme. The tablets may be supplied for a few days considering the holidays. Patients attend TB clinics for aminoglycoside injections. In the retreatment regimen designed for TB patients with a history of previous treatment, streptomycin injection is given for the initial two months therapy. Such aminoglycoside injections require them to regularly visit TB clinics and stay there for some time to get injection. Drug-susceptibility testing (DST) was reported to be performed in only 1% of new TB cases and in 3% of previously treated cases in many countries with high burden of MDR-TB.[6,7] Those who require such aminoglycosides injection have increased proportions of resistant TB and due to the lack of initial DST, the success or failure of their treatment is generally known only after months of regular visit for treatment. Such situations have further made TB clinics the concentrated foci of drug resistance.

3. The risk to patients with different immunocompromised states in the hospitals

The overall cost-effectiveness and social and psychological consequences of care for a patient receiving treatment for MDR-TB is considered toimprove with an ambulatory model.[13] In countries with high burden of TB, as such there may not be a choice. There is no doubt that any individual TB patient requiring admission needs to be admitted, as regularly practiced in hospitals. There should always be a provision for a back-up facility to manage drug resistant TB patients who need inpatient treatment.[13] However, potential exposure to people who are infectious has to be minimized by reducing or avoiding hospitalization where possible, reducing the number of outpatient visits, avoiding overcrowding in wards and waiting areas and prioritizing community-care approaches for TB management.[13,14] Hospital is the place of gathering of patients with different vulnerable states like children, old age, diabetes, HIV infection and steroid and immunosuppressive therapy. There is also an epidemic of diabetes affecting relatively young people in the countries, which also has a high burden of TB and significant proportions of patients and health

intolerance.[15] As discussed above, TB clinics are foci of selecting and concentrating drug resistance from among TB patients under new, retreatment or drug-resistant regiments and require almost daily visits from all registered TB patients. Mixing of the susceptible populations in hospital with potential sources of TBinfections and drug resistance in TB clinics should be minimized by the safe placement of TB clinics. With regular visits to the TB clinic in the hospital, the TB patients are also likely to become familiar with the hospital staff and situation. They could be inclined to visit different parts of the hospital, outdoor clinics or any acquaintances in the hospital, hence intermixing with other patients. Staff of TB clinics may also find it easier or safer to just refer TB patients to next door clinics for any expected minor symptoms of drug effects. Thus, wherever possible, and in the long run, TB clinics should be integrated in the Peripheral Health Services away from hospitals avoiding any potential mixing of susceptible people with infective source in one venue. TB treatment clinics in any place should be safely placed minimizing visits by other staff and patients for any examination or treatment.

4. Situation and quality control of sputum examination centers for TB

Though the TB treatment clinic is shifted outside the outdoor building in our hospital, the new and retreatment TB patients have to visit the hospital laboratory on the fourth floor inside the building for follow-up sputum AFB smear examination intermixing with other patients. As discussed above the numbers of MDR-TB emerging from treatment failure from the larger group of patients under new and retreatment regimens regularly visiting the TB clinics and laboratories usually for months was also quite significant. Thus apart from the TB treatment clinics, sputum examination centers for TB patients under treatment should also be safely placed. Either the sputum of the new and retreatment TB patients for follow-up examination may be collected in the TB treatment clinics or the patients themselves sent, (like the known MDR-TB patients), to the sputum examination centers situated in well-ventilated areas without them mixing with other staff, people or patients for any other examination or treatment. Moreover, quality controlof sputum AFB examination, for example by reexamination of all the positive and 10% of negative slides of the laboratory, is essential for decision regarding further treatment. The sputum AFB examination done with quality control in TB microscopy centers or even a healthpost may be more reliable than the sputum examination done in private laboratories or big hospitals in urban areas.[16]All sputum examinations of TB should be done in a quality controlled and safe manner.

5. Taking responsibility and identification and even sharing of financial support by the national and international agencies to establish safe TB treatment clinics and sputum examination centers

Effective anti-TB drugs treatment currently available in the world are relatively limited and there are challenges of new drug discovery.[1,2] Supply of such precious drugs for new, retreatment, and MDR- and even XDR-TB regimens are supported by the national and international agencies in the countries with high burden of TB. However, if the TB clinics and sputum examination centers are established without considering the risk to the vulnerable populations, from the TB control point of view the gain by the successful treatment of new, retreatment, or MDR-TB patients may be offset by the transmission of sensitive or resistant TB to others.[17] There was delay in building and shifting the TB clinic in our example discussed above due to the confusion about the responsible agency and the financial resources to be mobilized for such safe placement. Thus responsibility needs to be acknowledged and financial sources be identified and even shared by the national and international agencies supporting the anti-TB drug supply to establish safe TB treatment clinics and sputum examination centers, minimizing the mixing of TB patients with other patients and staff. The need of Peripheral Health Service with Rural and Urban Health Centers and Sub-Centers and the support of various Vertical Public Health Services to establish such accessible network, emphasizes the major responsibility of any Government.[18] In the long run, supporting the establishment of easy accessible Peripheral Health Service in the rural and urban areas with appropriately designated separate areas for TB treatment and sputum examination centers away from hospitals need to be considered. Hostels for the MDR-TB patients are being provided in selected places in the country. Similar separate provision for patients under retreatment regimens, particularly in the intensive phase or till the response is assured, seems useful to consider especially in the areas with difficult terrain or transport. Mobilization of community with their involvement may also help to achieve the support of Local Government Authorities. The TB treatment clinics act as foci of selecting and concentrating the resistant TB cases. The resistant TB has the potential to spread as a concentrated epidemic through the TB treatment clinics providing new, retreatment or MDR-/XDR- TB regimens requiring regular visit of TB patients for months before they are identified as treatment failures. The TB epidemic continues in a slow inconspicuous manner over years

TB bacilli to cause infection and reactivation years or decades later as well as re-infection especially in the relatively immunosuppressive states indicates the need to consider all the possible aspects to prevent transmission of the infection and drug resistance. It is pertinent to note here that more than three quarters of the estimated cases of MDR tuberculosis occur in previously untreated patients.[7] Thus, as drug susceptibility testing is not routinely done before starting therapy with first-line TB drugs, among all the diagnosed and undiagnosed MDR-TB patients visiting TB clinics regularly for months, significant proportions of them are being treated as new or retreatment TB cases in the general TB clinics. Safe placement of TB treatment and sputum examination centers are urgent priority areas to consider by national and international TB agencies. Considering the situation we recommend the following below.

TB treatment clinics and sputum examination centers for following the treatment of new, retreatment and drug-resistant TB patients should placed safely in well-ventilated areas avoiding the mixingof other staff, people or patients for any examination or treatment. All TB sputum examination centers should be quality controlled.

For the safe placement of TB treatment clinics and sputum examination centers, responsibility needs to be acknowledged and financial sources be identified and even shared by the national and international agencies supporting the anti-TB drug supply or involved in the TB control programs. Such TB centers may eventually be integrated with Peripheral Health Service in the long run. In the Peripheral Health Service also, the mixing of TB patients under treatment with other patients should be minimized.

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