Letter of Editor-in-Chief
The overview on current antimicrobial stewardship strategies in tuberculosis

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Tuberculosis (TB) is remains as one of the most public health concern that approximately 9.9 million individuals were fell ill with TB and 1.5 million people died from this disease (1-2). Routinely, local tuberculosis control programs follow the DOTS (directly-observed treatment, short-course) strategy that introduced by WHO since 2006 (3). Effective TB cases detection and appropriate treatment was considered as technical foundation of this Stop TB Strategy (4-5); However, the emergence and global expansion of Mycobacterium tuberculosis resistance to isoniazid and rifampicin or extensively drug-resistant (XDR) that characterized MDR-phenotype plus resistant fluoroquinolone and at least one of three injectable aminoglycosides were create a profound crack in current TB control approach (5-6). Mycobacterium tuberculosis is successful human pathogen that involved various signaling pathways to provide favorable condition to establish long-term infection adopted with the human lung micro-environment (7-8).

Antimicrobial resistance is critical issue that could be occurred due to previous history of exposure to antibiotics or misusage of antibiotics (9). It could be associated with high rate of mortality and morbidity or prolong hospitalization stay (10). Antibiotic stewardship is the ideal approach in antibiotic-resistance control program; Unfortunately, there is no specific antimicrobial stewardship strategy for anti-TB therapy (10-11). The antimicrobial stewardship for TB comprise two bases including 1) TB-case detection that ensure received adequate treatment regimen and 2) drug overuse, misuse, and abuse by attention to dosing and duration to reduce TB drug resistance burden (9).

Evaluation of current approach has been dedicated that following step can be considered for development of a successful plan for antimicrobial stewardship regarding TB-therapy:

1) Education of healthcare workers: education and sharing experience in a local level as well as supranational geographical region could favorite the suitable condition for management of TB patients to advise clinicians or healthcare worker staff clinical expert opinion regarding better management of tuberculosis; for example, Mussie et al., 2020 revealed that ongoing education of healthcare workers could be improved in management and control of drug-resistant tuberculosis in Addis Ababa, Ethiopia (12).

2) Laboratories modifications: Timeous detection and confirmation of tuberculosis can cause to prolong initiation of treatment course, early transmission, and emergence of Pre-XDR-TB patients (13). Conventional identification of pulmonary tuberculosis takes 2-6 weeks' time and molecular testing particularly Xpert MTB/RIF can be helpful in rapid case detection (14). Unfortunately, drug susceptibility testing was performed only for 6% of re-treatment cases or 4% of new TB-cases; In addition, only 55.6% of high burden TB countries have high quality condition with appropriate instruments (15). Mauch et al., 2010 showed that implementation of stewardship in the four fragile states i.e. Afghanistan, DR Congo, Haiti and Somalia could provide helpful results regarding TB control; they found that case notifications (from 39 to 62%) and treatment outcomes (from 81 to 90%) have improved in all four countries (16).

Moreover, Tuberculosis has non-specific symptoms such as fever, fatigue, chills, chest pain, weight-loss or hemoptysis that need to microbiologically confirmed (17). Previous Indian investigation discovered that there are 12-28.1% of tuberculosis suspected cases were

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inappropriately initiated anti-tuberculosis therapy due to lack of microbiological confirmation for the presence of Mycobacterium tuberculosis in sputum specimens (18-19).

3) Drug restriction: This competent of stewardship plan refer to appropriate drug selection that prevent allergies, adverse events, drug-drug interactions, previous treatment regimen or achieve to appropriate combination of drugs (20). For example, according to WHO reports, bedaquiline and delamanid are exclusively used for drug-resistant TB whereas linezolid can have recommended for MDR-TB as well as resistant gram-positive bacterial infection particularly methicillin resistant Staphylococcus aureus (21). Satyanarayana et al., 2016 showed that formulary restriction can successfully control antimicrobial misusage in pulmonary tuberculosis except in some urban Indian pharmacies (22). Indian population has the first ranks in total antibiotic use among the worldwide (23). According to previous studies; the range of wrong antibiotic usage in TB patients was 23%-28.1% in Indian population (18-19). We previously showed that antimicrobial restriction can significantly reduce meropenem-resistant rate nosocomial gram-negative bacterial infection (24).

4) Dose and treatment course optimization: overdosing of antibiotics lead to adverse side effects, In the other hand, suboptimal drug concentrations or inadequate therapy cause treatment failure and emergence of Pre-XDR-TB (25). Therefore, pharmacists have crucial role in TB-antimicrobial stewardship programs to curb TB drug-resistance. Unfortunately, selection incorrect dosage was common in high burden MDR-TB countries (26); For example, Prabhu et al., 2018 claimed that about 34% of inappropriately initiated tuberculosis antibiotic-therapy belongs to incorrected dosage (18). In another study conducted by Kunoor et l., 2019 revealed inappropriate drug dosage was common mistakes (about 22.7%) in tuberculosis control program (19).

In summary, tuberculosis is one of the top health challenge throughout the worldwide that HIV and emergence of drug-resistant TB confounds this problem. Implementation and evaluation of stewardship can helpful strategy to elimination of tuberculosis and curb drug-resistant TB. Development of new antimicrobial stewardship that guarantee treatment adherence and rapid case detection could be associated with decrease TB burden. According to previous literatures, antimicrobial stewardship plans containing ongoing healthcare workers' education, laboratories modification, formulary restriction as well as optimizing the drug dosage and treatment course could increase case detection and appropriate prescription that reduce drug-resistant TB burden in various geographical region.

Conflict of interest

authors declare that they have no conflicts of interest.

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