Chapter

Introductory Chapter: Plan to Prevent and Combat against the Drug-Resistant Tuberculosis/ Zoonotic Tuberculosis

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1. Molecular Epidemiology of MTB drug resistant

Tuberculosis (TB) is a primary cause of death from a single infectious agent by *Mycobacterium tuberculosis* complex (MTBC) remains a major global public health problem which infects one thirds of world's population. Despite being largely TB is a curable and preventable disease, WHO estimates that 10 million new cases and 1.2 million deaths occurred in 2019 [1]. Majority of deaths were in developing countries with more than half occurring in Asia and Africa. TB is spread when people who are sick with TB expel bacteria into the air; for example, by coughing. TB usually affects the lungs (pulmonary TB), although other organs are involved in 15–30% of other sites (extra pulmonary TB) [2]. *Mycobacterium tuberculosis* (MTC or MTBC) is a genetically related group of *Mycobacterium* species that can cause tuberculosis in human or other animals i.e. *M. tuberculosis*, *M. africanum*, *M. orygis*, *M. bovis*, *M. microti*, *M. canetti*, *M. caprae*, *M. pinnipedii*, *M. suricattae*, *M. mungi* [3].

The emergence of drug resistant including multi-drug resistant (MDR-TB: It means that the TB bacteria that a person is infected with are resistant to two of the most important TB drugs, isoniazid (INH) and rifampicin (RMP) [4] and Extensively drug-resistant TB (XDR-TB) is a rare type of multidrug-resistant tuberculosis (MDR TB) that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) [5] are also poses a serious public health threat to the success of TB treatment and control programs across worldwide. Globally in 2019, close to half a million people developed rifampicin-resistant TB (RR-TB), of which 78% had multidrug-resistant TB (MDR-TB). Molecular genotyping of MTB has been well developed over the years. WHO has developed the End TB strategy, which was endorsed by the sixty-seventh world health assembly in 2014. According to WHO, strategy ambitiously proposes to "end the global TB epidemic" by 2035. The strategy targets a 90% reduction in patients suffering from TB, and a 95% reduction in deaths from TB by 2035-all while protecting families from catastrophic costs that push them further into poverty [6].

The main genotyping typing methods mainly IS6110 restriction fragment length polymorphism (RFLP), spoligotyping and mycobacterial interspersed repeat unit variable-number tandem repeat (MIRU-VNTR) analysis, are commonly used for fingerprinting MTB strains to detect recent transmission [7]. However, the discriminatory power of these genotyping methods is not sufficient in countries such as South East Asia, South Africa and Russia including Nepal where MTB of Beijing

family has been reported in high prevalence [8]. These factors might be the driving force for the spreading and emergence of MDR-TB as well as extensively drug resistant TB (XDR-TB) involved in clonal expansion of strains [9]. Even though, molecular genotyping techniques have been developed, they provide less discriminatory power to differentiate the genetic diversity, transmission dynamics and outbreak of MTB strains. Even in clustered isolates these methods could not distinguish the recent from past transmissions [10]. Furthermore, genomic heterogeneity among the drug susceptible or drug resistant strains could also not be accurately detected using conventional genotyping methods [11]. Whole-genome sequencing (WGS) based on next-generation sequencing (NGS) has been emerging as a very powerful tools for detection of genetic diversity, outbreak analysis, surveillance and determination of drug resistance [12]. Recently, WGS is considered as a gold standard method because of its high resolution allowing for in-depth characterization about the dynamics of evolution, transmission and exogenous infection [13].

The main importance of this book chapter was to provide overview and also understand about the molecular epidemiology pattern, transmission dynamics, host response, mechanisms associated with increasing trends of drug resistant TB including MDR-TB, evolution, molecular biology, pathogenesis mechanism and development of anti-mycobacterial drugs about the *Mycobacterium tuberculosis* complex. The purpose of book chapter will be help to provide the updating research information to the policy maker or planner for further diagnosis and treatment with genotyping tools, control and prevention for MTB disease. This book chapter main theme are to explore the vigorous approaches in novel designing of anti-tubercular drugs, diagnosis and treatment of latent tuberculosis infection to measure their quality of life, laboratory diagnosis by identification of novel SNPs, tracing of outbreak isolates, study of various chemically and structurally diverse currently clinically used and recently developed for anti-mycobacterial drugs, molecular characterization of *Mycobacterium* spp. isolated from cattle and wildlife in Poland, challenges in drug discovery against tuberculosis and genealogy of resistant TB in Latin American territories.

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