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Multi-drug resistant tuberculosis

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INTRODUCTION

Mycobacterium tuberculosis as a causative agent of TB was indicated by Robert Koch in 1882. Commencement of BCG vaccine after 39 years for the benefit of mankind which was used for the prevention of TB worldwide. Symptoms of TB are pyrexia, loss of appetite, loss of weight, sweating in night. Cough is the commonest symptom of pulmonary Tuberculosis. The most common sign of lymphatic TB is swelling in the neck. Low temperature and headache was commonest sign of pleural and CNS TB respectively^[1]. In many forms of tuberculosis, fever is a common symptom. Tuberculosis should always be considered in differential diagnosis of patients presenting with unexplained low grade fever and weight loss. Death rate was decreased by the innovation of first-line anti-MDR TB drugs. The modern therapy that is short caused for the management of TB in which there are four-drugs that are used for the treatment of drug resistance. *Mycobacterium* shows high degree of resistance to drug because of low permeability of cell wall and mutation in strain^[2].

Treatment is for tuberculosis is complex. Drugs that are used to treat TB are less valuable and more toxic, and are used for longer time period but with the passage of time efficacy is decreased and severely decreasing probability of success^[3]. Resistant *Mycobacterium tuberculosis* is a threat for Global Tuberculosis Control.

Drug resistance in *Mycobacterium* is actually a man made dilemma. Incomplete and reduced treatment led towards new form of drug resistant known as Extensively drug resistance tuberculosis caused by *Mycobacterium tuberculosis* strain, which has resistance to rifampicin and isoniazid among the first-line anti-tuberculosis drug and resistance also to any fluoroquinolone and at least one of three injectible second-line anti-tubercular drugs i.e. amikacin, kanamycin and/or capreomycin.

Appearance of extensively drug resistance is reported globally. Rate of frequency reported about XDR-TB of total MDR cases are; 6.6% all over the world, 6.5% in developed nation state, 13.6% in Russia and Eastern Europe, 1.5% in Asia, 0.6% in Africa and Middle East and 15.4% in Republic of Korea. Researchers are working how to control the spread of TB that is Multi drug resistance^[4].

In 1993, World Health Organization declared that TB as a big threat in the world. Treatment was available even then one third of world's population was affected by *Mycobacterium tuberculosis*. Due to multi drug resistance (MDR) *Mycobacterium tuberculosis* strains, it spread worldwide, thus need for more effectiveness of anti-mycobacterial drugs. HIV-positive patients are known to have an increased rate of poor effects of first-line TB drugs and the prevalence of adverse effects of second-line TB drugs may be bigger as well. People with low income can't afford the treatment because drugs are costly^[5].

Review

PREVALENCE

Tuberculosis causes millions of deaths every year. These deaths somewhat explain the worldwide TB hazard. More than 80% of TB patients which are going to be affected mostly by TB are in age between 15-42 years. In this contact, we report as area of multi drug resistant tuberculosis which thinks to see the role of clinical mycobacteriology laboratory in the administration of such cases^[8].

The increasing appearance of MDR-TB (Multidrug resistance-Tuberculosis) XDR-TB (Extensively drug resistance-Tuberculosis) in the era of human immunodeficiency virus infection presents a most important threat to effectual control of TB. Drug resistant in Mycobacterium occurred as a result of variable drug supply to patients.

The threat factors for MDR-TB are originated from previous incomplete curement or begin from "hot spot" areas, homelessness and probably also HIV virus. The management of multidrug-resistant tuberculosis is complicated due to adverse effect and cure which require 3 years treatment for complete cure. Therefore, new plans for the cure and impediment of MDR-TB are without more ado essential. This requires functioning of tuberculosis control programmed (directly observed treatment short course), and, in some dominant countries, the introduction of second-line drugs on the basis of appropriate liability testing (directly observed cure short course-Plus). Only the coming time will reveal whether this "ticking time bomb" can be resolved^[23]. In an experiment, anti-microbial vulnerability of the isolates was tested against the four first-line anti-tuberculosis medicine (rifampicin, isoniazid, streptomycin and ethambutol). Fifteen percent of the strains were resistant to only one drug; the percentage of multi drug resistant 28% included 7% which has resistant to all the 4 drugs. The over all resistance against individual drugs was rifampicin 32%, isoniazid 37%, streptomycin 19% and ethambutol 17%^[6].

In an other study, high confrontation is seen in opposition to isoniazid and rifampicin, 25% each, followed closely by streptomycin 24.12% and pyrazinamide and 21.49%. Primary resistance was much lesser than Acquired drug resistance. The difference was statistically significant for all drugs tested except isoniazid, MDR was 7.3% and acquired MDR was 25.7%. This differ-

ence is statistically significant. MDR tuberculosis is increasing in this part of the world. Previous disclosure to anti-tuberculosis drugs emerged as an important forward planner of drug resistance. The MDR-TB is also threatening World Health Organization's intention of tuberculosis removal by 2050^[7].

MOLECULAR BIOLOGY

Researchers from the Hamburg Outstation of the European Molecular Biology Laboratory (EMBL) and Max Planck Institute for Infection Biology (MPIIB) have currently achieved the structural figure of protein that is needed by the bacterium for the endurance in human cell. *Mycobacterium tuberculosis* lives in immune cells. A protien that is called LipB that controlls the cellular metabolism of bacterium. LipB is highle active in multidrug resistant tuberculosis patients.

In HIV patients it was seen that in genes there is a mutation as reported earlier which are present in drug resistance, and the mutation too which are not reported untill. There is a shift in nucleotide and aminoacids. There is mutation in three strains AGC→ACC at codon 315 of *katG* gene (Ser→Thr) it is the commonest change in gene in INH-resistant strains^[34,35].

In MDR tuberculosis, along with the above mutation, there is also a mutation at codon 531 of the *rpoB* gene (TCG→TTG), resulting in aminoacid change from Ser to Leu. Rifampin resistant isolates also have a mutation at codon 469 of the *rpoB* gene: GAG→TCG (Glu→Ser)^[36].

DIAGNOSIS

Previously, the recognition and test of the vulnerability of *Mycobacterium tuberculosis* complex (MTBC) strains take too many days to complete. Hasty recognition of adherence using the PCR-based Genotype MTBDR test (Hain Lifescience GmbH, Nehren, Germany) has the noticeable power to remarkably shorten the gyrate time from specimen reception to reporting of results of vulnerability test. There after the intention of the study by Somoskovi et al.^[32] it was verified (i) the delicateness and exactness of the Genotype MTBDR assay for the revealing of MTBC strains and (ii) the ability of the analyzer to detect the occurrence of INH and RIF's resistance-associated change in gene

in *katG* and *rpoB* from samples taken directly from smear-positive experimental specimens.

TREATMENT

Currently, none of the usually used candidate agents have proof of effectiveness for used in MDR-TB or XDR-TB.⁹ However; immunotherapies have the potential to recover the outcome in all patients with tuberculosis including those with MDR-TB and XDR-TB. Potentially preventing reappearance.

The W.H.O. has suggested a multifaceted programme, known by the short form DOTS (directly observed therapy, short course), that upholds valuable treatment of drug-prone TB as the chief method of off-putting drug resistance. DOTS was part of prosperous MDR-TB control programme in New York City, which also integrated cure of prevalent MDR-TB cases. Chemotherapy is not as such effective^[25,33].

The hexanic extract of *A. taliscana* was tested by microdilution alamar blue assay against *Mycobacterium* strains and bioguided fractionation led to the separation of the neolignans Licarin A, Licarin B and Eupomatenoid-7, all of which had antimycobacterial action. Licarin A was the most active compound, with least inhibitory concentrations of 3.12-12.5 microg/mL against the following *M. tuberculosis* strains: H37Rv, four mono-resistant H37Rv variants and 12 clinical MDR isolates, as well as against five non-tuberculous mycobacteria (NTM) strains. In ending, Licarin A represents a potentially active anti-TB agent to treat MDR *M. tuberculosis* as well as NTM strains^[13].

The influence of pigmented cells for treatment is limited by their high price and lethal. But, the appearance of XDR-TB, for which therapy by chemicals is unsuccessful, has again made cytokine-based therapy effectual as one of the previous available preferences. The results of clinical assessment to treat pulmonary tuberculosis with cytokines have not been promising, making it clear that treatment policy use a single cytokine is not enough. To expand effective cytokine-based XDR TB rehabilitation, essential investigation will be needed to achieve a better perceptible of how cytokines promote a successful immune response. We must investigate other cytokines that may enhance the action of already present cytokines. They may also have the bacteriostatic and bactericidal effect and also improve im-

mune system. The legitimacy of these patents needs to be reassessed from a clinical point of view, and new applications of patents concerning cytokines potentially supportive in XDR TB treatment should be expectant^[21].

Recently thioridazine (TZ) has proved a potential drug for the treatment of MDR-TB and XDR-TB and has less risks^[16].

CONCLUSION

BCG was that first drug that was used to treat tuberculosis then an additional drug was introduced that was more effective. After re-emergence of tuberculosis, its treatment was not so effective.

The mounting level of resistance in drug among mycobacterial isolates is more frightening. Strict accomplishment of control measures is required to conflict this unfolded crisis. Measures to improve the treatment completion rates are urgently needed. Research is going on to treat the multi drug resistant. Licarin A is used to treat MDR-TB.

TB is yet a worldwide health dilemma. The selection and spread of MDR-TB and XDR-TB *Mycobacterium tuberculosis* strains be a symbol of a menace for universal TB control. The re-emergence of TB has obsessed greater than before unease in indulgent the method of action of drug and drug resistance, which could offer a major input in the development of latest antimicrobials. Cure of infected people with MDR-TB by means of the DOTS-Plus strategy and individualized drug regimens can be reasonable, reasonably valuable, and purchasable for low income people and middle income countries.

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