

# DEVELOPMENT OF MDR TB IN SHORT DURATION IN A PATIENT RECEIVING TREATMENT FOR SIMPLE TB: A CASE REPORT

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## Abstract

Multidrug resistant (MDR) tuberculosis (TB) is becoming more cumbersome especially in developing countries. Already supportive infrastructures are weak as compared to disease burden. Numerous diagnostic techniques for early diagnosis of TB and MDR TB have brought incremental improvements however; the technical intricacies of these assays and their reliance on enthusiastic laboratory infrastructure have restricted their implementation, particularly in low – resource and high – burden settings. Recently introduced Gene-

Xpert MTB / RIF assay simultaneously detects the presence of MTB, and its susceptibility to the important first – line drug rifampicin. Aim of this report is to understand the role of physician in prompt diagnosis and its control in spread of MDR TB and conversion of normal TB to MDR TB using available resources. Watchfulness of physician is an important factor in treating TB patients and early diagnosis of MDR TB using available resources. A good skilled team work is necessary to locate such cases in early stages and prompt treatment can save many lives and ultimately serve as a big barrier in spreading primary MDR TB.

**Keywords:** MDR TB, Tuberculosis, Prompt Diagnosis, GeneXpert.

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## Introduction

Multidrug resistant (MDR) tuberculosis (TB) has become common especially in developing countries already suffering from fewer infrastructures compared to the disease burden. By increasing the drug resistance TB patients around the world, prompt, accurate and appropriate diagnosis and treatment of various presentations of disease require special attention.<sup>1</sup> About one third of the global population is infected with *Mycobacterium tuberculosis* (MTB) main cause of TB and at risk of developing MDR TB.<sup>2</sup> Multi drug resistant (MDR) TB is the disease caused by the strain of MTB complex which is resistant to at least isoniazid and rifampicin with or without resistance to any other first

line anti TB drugs.

Numerous diagnostic techniques for early diagnosis of TB and MDR TB have brought incremental improvements however; the technical intricacies of these assays and their reliance on enthusiastic laboratory infrastructure have restricted their implementation, particularly in low – resource and high – burden settings<sup>3</sup> where ZN smear and conventional culture on Lowenstein Jensen (LJ) media are still method of choice. Although culture on LJ is standardized but slow and requires 6 – 8 weeks for isolation of organism and further 4 – 6 weeks for drug susceptibility testing; hence comprehensively delays in confirmation of MDR TB suspects.

Recently introduced GeneXpert MTB/RIF assay simultaneously detects the presence of MTB, and its susceptibility to the important first-line drug rifampicin.<sup>4</sup> This system of sample processing is based on an automated hemi – nested and real – time PCR assay is integrated into a single disposable cartridge. The assay can be performed directly from a clinical specimen or from a decontaminated specimen's pellet and can generally be completed in 2 hours<sup>4</sup>. World Health Organization (WHO) has recommended and endorsed the utility of GeneXpert MTB / RIF assay and expected threefold increase in diagnosis of drug resistant TB cases.<sup>5</sup>

Treatment and curing drug resistant TB is quite difficult. Inappropriate treatment can be fatal therefore such cases should be managed in close consultation with and an expert in disease.<sup>6</sup> Rifampicin is an important drug and a part of four core drugs being used for treatment of first line TB. Rifampicin is being used from the beginning of the treatment to the end till 6 – 8 months.<sup>6</sup> Therefore resistance to rifampicin is considered the individual is suffering from MDR TB and now it has become a national protocol to treat rifampicin resistant cases as MDR TB and GeneXpert has been recommended to rule out the rifampicin resistant. Present case report will help to understand the role of physician in prompt diagnosis and efficient control of MDR TB and conversion of normal TB to MDR TB using available resources.

## Case Report

A 42 years old, male health worker was suffering from sick conditions like weakness and lethargy. He was advised by the senior to get his proper medical checkup done. On physicians inquiry he gave history of

cough, fever, anorexia, lethargy and weight loss of 4 – 5 kg in 2 months. He was diabetic and on insulin therapy however his blood sugar levels are under good control as shown by HBA<sub>1c</sub>. Moreover he had taken the treatment of acute renal failure about a year ago and anti-tubercular treatment (ATT) about 4 years back.

He was advised to provide a spot specimen of sputum for smear microscopy and a chest X-ray. Spot specimen for acid fast bacilli (AFB) was negative by Ziehl Neelsen (ZN) staining while there was a suspicious lesion spotted on the x-ray chest. Physician advised him to provide first morning specimen for smear microscopy, AFB culture and GeneXpert MTB Rif assay. Smear microscopy was found to be positive (1+) and GeneXpert was conferring MTB which was sensitive to rifampicin. After five weeks his TB culture was also positive which was already inoculated on the slants of LJ medium. Patient was prescribed treatment regimen as approved by the World Health Organization (WHO) and Centre for Disease Control (CDC)<sup>6</sup> through DOTS. Patient was given medical leave and sent home. After one month he took his medicine again and went home. After six weeks from starting ATT patient came again with complaint that his blood sugar is not under control even with higher dose of insulin. Physician examined him and again advised a chest x-ray again. There was an improvement in size of lesion and patient claimed relief from the symptoms of TB as mentioned earlier. Physician was not satisfied and asked the attendant to check the weight of patient again. He improved his weight about 2 kg from the start of ATT. Physician again advised him to give a spot specimen of sputum for AFB smear microscopy and GeneXpert MTB Rif assay.

AFB smear showed few bacilli and about 8AFB/100 high power fields were reported but physician was shocked to see the GeneXpert MTB Rif assay report which was positive for not only MTB but rifampicin was also resistant. Physician started thinking about the previous reports especially of Genexpert. Another sputum specimen for GeneXpert MTB Rif assay to check if there is any personnel error again it was positive for MTB and resistant to rifampicin. Then colonies from TB culture positive slant were used as sample for GeneXpert to check rifampicin resistance in previous samples and whether there is any mistake running previous sample on GeneXpert. It was clearly positive for MTB and sensitive to rifampicin showing no error in previous run. It was confirmed that this rifampicin resistance was developed during 6 weeks of treatment

by first line anti tubercular drugs. He was put on second line ATT and improvement in symptoms has started to appear within one month. Vigilance of physician and GeneXpert helped in prompt diagnosis of MDR TB.

## Discussion

Multidrug resistant tuberculosis has developed as a noteworthy global health due to alarming reports of growing drug resistance which potentially threaten to disrupt the gains attained in treatment of TB during last decade or so.<sup>1</sup> Although MDR TB has been considered essentially a man-made disease due to inadequate treatment is not true in case of present findings as the patient had good compliance and dose was also prescribed according to the weight of the patient but patient had other non-communicable diseases like diabetes and renal failure which in turn might be the reasons of poor response to drugs ultimately resulted in the drug resistance.

Elevation in the prevalence of MDR TB cases during recent years has been reasoned to increased awareness of the disease, increased access to the culture and drug sensitivity testing, earlier suspicion of MDR cases among previously treated cases.<sup>1</sup> Although conventional methods for diagnosis of TB and MDR TB are useful and reliable however modern techniques including GeneXpert has revolutionized the diagnosis of rifampicin resistant TB in only two hours which in turn briskly diagnose MDR TB as is shown in present. Hence there is an urgent need for increasing awareness of physician to such presentations.<sup>7</sup> Present case report also focuses the attentiveness of the physician in observing his patient and deliberately discussing the issue with his team that includes disease consultant, radiologist and microbiologist. It is also important how to utilize the available resources to save the lives of poor patients. If patient continues with first line ATT in this case hence he has relief from symptoms and showing radiographic improvements it was also possible that patient may become ZN smear negative as sensitivity of AFB smear is very low. And in continuation phase he can deteriorate suddenly and make management of disease more difficult in presence of co-morbidities.

Few facts about MDR TB must be discussed to create awareness among the people as well as clinicians to understand the depth of this disease. An estimated 480,000 people develop MDR TB and there were 210,000 deaths which makes mortality rate due

to this disease was about 43% in 2013. According to WHO MDR TB case detection rate was tripled during 2009-2013 even then this was equivalent to only 45% of total estimated cases. Only 71% of diagnosed MDR TB cases were provided treatment in 2013 and remaining 29% were on waiting. Extensively drug resistant TB has been reported by 100 countries by 2013 and an estimated about 9% MDR TB cases develop extensively drug resistant TB.<sup>8</sup>

Various healthcare systems factors influence treatment results of patients having MDR TB. The most important is timely diagnosis by implementation of rapid molecular drug susceptibility testing in accordance of national guidelines, secondly favorable financial support system for MDR TB patients to avoid economic obstacle, inter-sectoral liaison to manage patient's emotional, social and clinical needs and lastly motivated, devoted healthcare staff with sufficient mandate and means to support the patient<sup>9</sup> is of significance importance. Focus of physician and related healthcare workers played an important role to utilize available resources, equipment and investigate this case for sensible management of this case.

## Conclusion

Treating TB patients especially prompt diagnosis and treatment of MDR TB plays a vital role in good prognosis of disease. A good skilled team work equipped with latest diagnostic tools is necessary to find such cases in early stages and quick second line treatment can save many lives and ultimately can prevent spread of MDR TB.

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