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Frequency and implications of ofloxacin resistance among previously treated tuberculosis patients

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Sir,

The fluoroquinolones (FQ) are an important class of antibiotics and with the global emergence of multidrug resistant TB (MDR-TB), they are used in combination with other drugs for the clinical management of MDR TB patients. Increased use of FQ for other respiratory infectious diseases and its availability without prescription has resulted in acquisition of FQ resistance among *M. tuberculosis* strains. A recent metaanalysis has reported three fold higher risk of FQ resistant MTB in patients prescribed FQ before TB diagnosis [1]. The resistance to FQ is a key defining condition of XDR-TB and is associated with poor treatment outcomes, a potential threat to control programmes [2]. Knowledge of FQ resistance is necessary since new FQ based regimens are being introduced and high cross resistance among FQs is a concern.

We retrospectively analyzed the laboratory data to assess the extent of ofloxacin resistance among previously treated (failure/relapse/return after default) pulmonary TB patients at Department of Microbiology, National Reference Laboratory, National Institute of Tuberculosis and Respiratory Diseases, New Delhi. Prevalence of ofloxacin resistance was determined among 1548 pulmonary *M. tuberculosis* complex isolates from retreatment cases (out patient department and wards) whose samples were received for culture and DST from January 2011–December 2013. Drug susceptibility testing was performed by Mycobacterial growth indicator tube (MGIT 960) liquid culture system (Becton Dickinson, Franklin Lakes, NJ, USA) at the following critical concentrations: streptomycin 1.0 μg/ml, isoniazid 0.1 μg/ml, rifampicin 1.0 μg/ml, ethambutol 5.0 μg/ml and ofloxacin, 2.0 μg/ml.

991 (64.0%) patients were male and 557 (36%) were female with a male female ratio of 1.8:1. The mean age of patients was 31 year. A total of 102 (6.6%) isolates were infected with *M. tuberculosis* strains susceptible to all four I line drugs of which 11 (10.85%) were resistant to ofloxacin. Among isolates resistant to one of more first line drugs 66% (954/1446) were ofloxacin resistant. The resistance increased to 70.60% (879/1245) among MDR TB cases. When z test for proportion was applied among isolates pan susceptible to four first line drugs and isolates with resistance to one or more drugs, p value was statistically significant ($p < 0.001$). The present analysis shows alarming rate of ofloxacin resistance among previously treated TB patients 965/1548 (62.3%). The findings are consistent with the data reported by earlier study from Mumbai, India which showed 69.1% of MDR isolates were resistant to ofloxacin, mainly due to high level of baseline floroquinolone resistance.

A few other studies from India have also reported ofloxacin resistance of 11–20% in non MDR cases and 24–54% in MDR patients [3–5]. Our findings have reported increase rate of ofloxacin resistance as compared to these which may be due to the fact that 1245/1548 (80.42%) of isolates were MDR. Furthermore, since the hospital is a referral center sampling bias cannot be ruled out.

Treatment failure patients, who turn to be MDR, receive ethambutol and PZA and are on functional monotherapy with ethambutol for atleast 3 months. Previous studies from India have reported PZA resistance among MDR isolates to be in the range of 60%–70% [6,7]. In absence of DST results for ethambutol and PZA, with high level of resistance to ofloxacin may lead to suboptimal treatment leading to low cure rates and amplification of drug resistance. Addition of ofloxacin in the treatment regimen of MDR-TB patients without susceptibility testing would have less benefit and might increase the risk of XDR-TB development or render treatment ineffective. These results emphasize the need for rapid and accurate molecular test for detection of pre XDR TB for their timely and proper management.

Competing interests

None.

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