Epidemiologic analysis of pyrazinamide drug resistance in TB patients enrolled in a cohort study in Lima, Peru.

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Introduction: Multi-drug resistant tuberculosis (MDR-TB) is a global threat with high mortality due to limited access to effective treatment. Pyrazinamide (PZA) is usually included in MDR TB treatment. However, data are limited on prevalence of PZA resistance in representative populations of TB patients in high burden countries. The major constraint is the limited reliability of PZA drug susceptibility testing (DST). Objective: To estimate the prevalence of and risk factors for PZA resistance among TB patients in Lima-Peru. Methods: The study included patients with pulmonary TB diagnosed in health centers in Lima between Sept 2009 and Aug 2012. First-line DST was performed using the proportion method in LJ, and PZA DST was performed by the Wayne method. To measure the reliability of Wayne method, a sample of isolates was tested by BACTEC MGIT 960 as reference. Association of socio-demographic and clinical characteristics with PZA resistance was evaluated in multivariable logistic regression. Results: Overall PZA resistance prevalence was 6.6% (95% CI 5.8 – 7.5) among all TB cases, 47.7% (42.7 – 52.6) among MDR-TB cases and 0.6% (0.1 – 1.9) in non-MDR-TB cases. Wayne method showed a substantial concordance with BACTEC MGIT 960 (*kappa* value = 0.65; IC 95% 0.54 – 0.75). In the multivariable analysis, the prevalence of PZA resistance was independently associated with MDR-TB (OR: 84.9; 95% CI: 53.3 – 135.1); previous treatment (OR: 1.39; IC 95% 0.93 – 2.07), with residence in Eastern Lima (OR: 1.30; IC 95% 0.8 – 2.11) and LAM lineage (OR: 3.27 IC 95% 2.24 – 4.79). Conclusion: Evidence from this study and other similar studies reveal that usual susceptibility to PZA cannot be reliable in MDR-TB patients or in patients with prior treatment exposure. The Wayne method can be useful to identify patients whose regimens should be adjusted to compensate for detected loss of PZA activity and to avoid future toxicity due to the addition of a likely ineffective drug.

Keywords: Pyrazinamide, drug resistance, multidrug-resistant tuberculosis, Wayne Method