

Monitoring tuberculosis treatment response with conventional laboratory tests during the first 14-days of therapy has no clinical value

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Background. Every year more than 6 million people are declared as having tuberculosis (TB) and started on treatment. Monitoring treatment response in those individuals is required to confirm adequate therapy, identify those at risk of adverse outcomes, and to inform infection control. However, response to treatment is currently assessed after several months of therapy, causing much anguish to TB-affected individuals.

Objective. To assess the utility of available tools during early treatment for pulmonary TB.

Methods. In a prospective cohort study in Callao, Peru, before and after the first 14-days of treatment, patients were weighed, interviewed about their symptoms and were requested to provide sputum. Sputum was tested for the number of acid-fast bacilli (AFB) in microscopy, colony-forming units(CFU) and time to positivity(TTP) in culture and PCR cycle times(CT) in GeneXpert. Patients were followed for 2 years to determine clinical outcome.

Results. Over an 18-month period, 356 pairs of samples were collected, 97%(n=345) of which were during empirical first-line therapy. Sputum culture from patients with drug-susceptible TB after 2-weeks of first-line therapy demonstrated that CFU counts decreased by median 63-times and TTP increased by median 14-days (n=264, both $p < 0.0001$), whereas AFB and CT had minor changes. The changes in culture results was similar between these patients versus those later found to have mono-resistance to either isoniazid or rifampicin (n=62, $p=0.9$), and also for those on second-line therapy (n=11, $p=0.5$). However, no change was demonstrated in culture results for individuals taking first-line therapy but in fact had multi-drug resistance (n=19, $p > 0.3$). After 14-days of therapy further weight loss or loss of appetite was associated with incorrect therapy ($p=0.04$ and $p=0.03$ respectively).

For those with confirmed drug-sensitive disease, n=2 died, n=4 had failing treatment, and n=1 had another confirmed episode of TB within 2-years. Suffering from loss of appetite ($p=0.03$) or self-reported debilitating cough ($p=0.01$) after 14-days of treatment were the only variables associated with these outcomes (see Figure).

Conclusion. Once drug susceptibility has been confirmed by rapid testing, at 2-weeks of therapy there should be more emphasis on an individual's symptomatic response and not laboratory results to aid clinical decision-making.

Adverse outcomes in patients on 1st line therapy with confirmed drug sensitive TB

