Evaluating the Impact of Molecular Diagnostics for Tuberculosis within the Public
Health Laboratory System

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BACKGROUND

Of the five participating laboratories, 4 evaluated molecular detection of MTBC. The assay sensitivity and specificity was reported for the laboratories performing the Xpert MTB/RIF assay. Sensitivity ranged from 72-92%, and specificity ranged from 97-98%. Additionally, the sensitivity and specificity for AFB smear negative specimens was calculated for all laboratories. Sensitivity for the Xpert MTB/RIF assay ranged from 50-72%; specificity remained high, ranging from 97-98%. Sensitivity for the RT-PCR was substantially higher at 81.4%, while the specificity was comparable at 96.7% (Figure 1).

METHODS

In July 2012, the Association of Public Health Laboratories (APHL), in cooperation with the U.S. Centers for Disease Control and Prevention (CDC) Division of Tuberculosis Elimination (DTE), awarded one-time funding to five (5) county and four (4) state public health laboratories. The evaluation period was July 2012 through June 2013. Funds were used to support laboratory operational initiatives aimed at improving current molecular diagnostic services and/or develop efficient and effective laboratory algorithms incorporating these tests into the overall laboratory system. One laboratory evaluated a real-time PCR assay for detection of Mycobacterium tuberculosis Complex (MTBC) and detection of mutations associated with resistance to first-line drugs Rifampin (RIF) and Isoniazid (INH). Three laboratories evaluated the Cepheid Xpert MTB/RIF assay, and another evaluated a pyrosequencing (PSQ) assay for detection and sequencing of mutations associated with first and second line drug resistance. The laboratories assessed various outcomes including performance characteristics, turnaround time, and contribution to the overall testing algorithm. Additionally, laboratories worked with submitters and the TB Control Program within their jurisdictions to evaluate the clinical impact of molecular detection and drug resistance testing results.

RESULTS

In order to quantify the value of molecular testing for MTBC on AFB smear negative patient specimens, the laboratories determined the total number of AFB smear negative specimens tested and percent yield of culture confirmed TB patients that had AFB smear negative/NAAT positive results. For specimen tested with the Xpert MTB/RIF assay, the percent yield ranged from 1.7-4.4%; the RT-PCR assay displayed the highest percentage yield at 5% (Figure 2).

CONCLUSIONS

The participating laboratories demonstrated the average turnaround time (TAT) from specimen receipt to reporting of molecular detection results. For laboratories performing the Xpert MTB/RIF assay, the average TAT was compared to that of culture. The reduction in TAT is substantial with molecular testing, going from weeks (range 17-40 days) to 1-2 days. The Xpert MTB/RIF assay simultaneously detects MTBC and the presence of mutations associated with resistance to the first-line drug Rifampin, and therefore the TAT for these results are equivalent, ranging from 1-2 days. Conventional data was not provided or not applicable for Site D (RT-PCR) and E (PSQ). TAT for RT-PCR and PSQ was 7 and 1 days, respectively (Figure 3).

For More Information

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