Combining Mycobacterium Testing Methods to Deliver Enhanced Laboratory Diagnostics and Clinical Patient Outcomes: A Proposed Algorithm Using MycoDDR™ & Xpert® MTB/RIF

Candelaria WJ, Namdarian SV, Magee CM, Maneclang KJ
Clinical Laboratory, Maricopa Integrated Health System, Phoenix 85008, USA

abstract

Active pulmonary tuberculosis (TB) is a highly infectious disease and an important worldwide public health issue. Effective surveillance and detection of TB is crucial to managing active cases and reducing exposure. The traditional algorithm for TB management relies heavily on culture confirmation of infection and can take up to 14 days for definitive diagnosis from the date of presentation with the disease. This can have a significant impact on the health of the patient and can result in substantial healthcare costs to the patient and treating facility. Here we present a new algorithm for TB diagnosis, utilizing the specimen processing system, IMMY MycoDDR™, and the Cepheid® Xpert® MTB/RIF nucleic acid amplification test (NAAT), for improved time to confirmed diagnosis and treatment. The results of this study suggest that the new proposed algorithm for TB diagnosis results in an increased positive patient outcome by providing confirmed diagnosis faster, which could result in a significant cost savings to the treatment facility and ultimately, the patient.

introduction

Diagnosis of TB is important not only for correct treatment of the disease but also for containment of the highly contagious infected individual. Traditionally, clinical laboratory testing includes AFB smear, culture, and on-site NAAT testing, if sufficient bacterial growth is present, and/or offsite HPLC or NAAT confirmatory testing. Culture confirmation of Mycobacterium infections can take up to 17 to 20 days, which is not ideal for the patient or treatment facility. NAATs, such as the Cepheid® Xpert® MTB/RIF, have been recommended for presumptive diagnosis of TB as a means to reduce the time to treatment. Regardless of which of these diagnostic methods is used, pre-processing of the sample specimen is highly beneficial in that it facilitates concentration of the sample and removal of any contaminating organisms that may interfere with the test results. We had previously shown that use of the MycoDDR™ specimen processing system facilitated positive culture results up to one day sooner than a competitor (Candelaria, et. al., 2014). Given these factors, a new diagnostic algorithm was developed and evaluated using the MycoDDR™ for specimen processing and the Cepheid® Xpert® MTB/RIF as a tool for initial diagnosis in an effort to reduce the time to confirmed diagnosis of disease. This algorithm was compared to the traditional algorithm for length of time to confirmed diagnosis and hospital cost savings.

The results of this study show that the new proposed algorithm utilizing the MycoDDR™ sample processing system and the Xpert® MTB/RIF, for presumptive diagnosis prior to culture results, should be more widely utilized as the new algorithm for TB diagnosis as it provides confirmed positive diagnosis faster, which translates to a significant cost savings to the treatment facility, and may ultimately allow for a significant health and cost savings to the patient.

observations & conclusions

Use of the MycoDDR™ specimen processing system reduced the total specimen processing time by approximately 30 minutes and reduced the time to positive culture results.

The MycoDDR™ specimen processing system was validated for complete compatibility with the Xpert® MTB/RIF and provided positive confirmed diagnosis in a new proposed algorithm in less time than the traditional algorithm utilizing offsite NAAT (1-3 days vs. 16-18 days respectively).

Utilization of the new proposed algorithm resulted in a significant cost savings to the hospital (~$33,000.00).

results

1) Algorithms of Mycobacterium Testing Methods

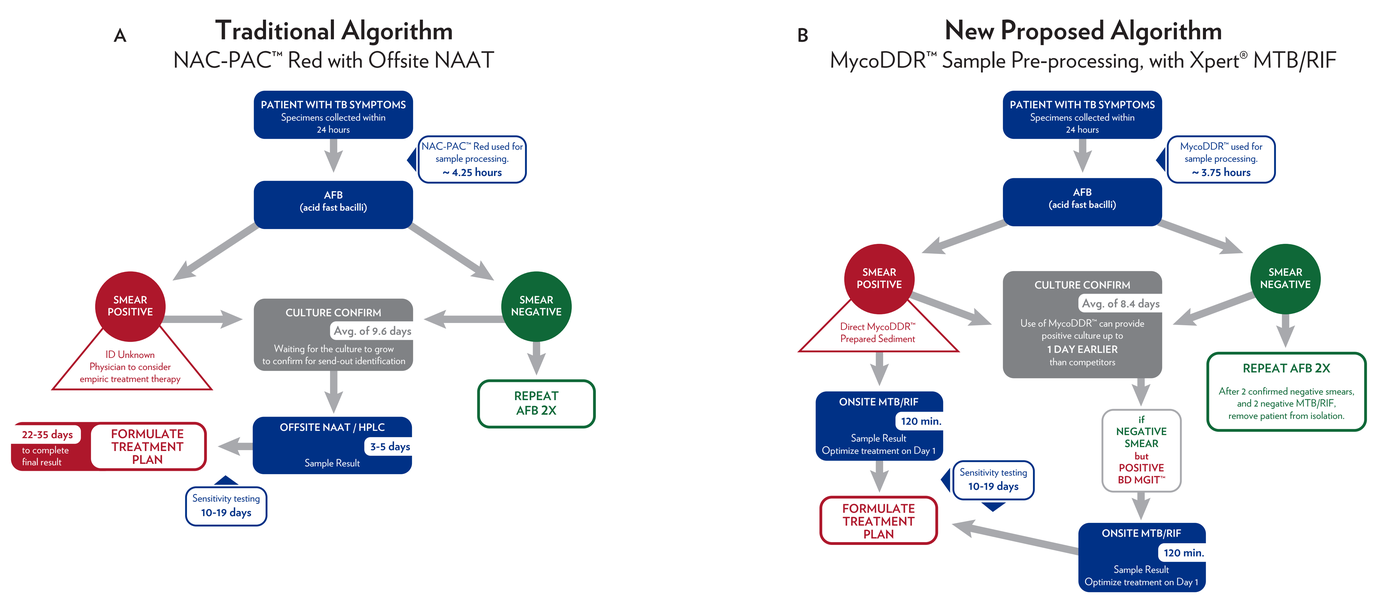

Figure 1. New proposed algorithm vs. the traditional method of Mycobacterium testing. A) The traditional algorithm utilizes the NAC-PAC™ Red specimen pre-processing system for sample preparation. This algorithm relies on offsite NAAT and sensitivity testing, which results in a significant delay in confirmed diagnosis and the initiation of treatment. Additionally, the patient can remain in isolation longer due to the delay in confirmed diagnosis, which can have a significant impact on the cost of care to the patient and the treating facility. B) The new proposed algorithm utilizes the MycoDDR™ specimen pre-processing system for sample preparation an on-site NAAT (Cepheid® Xpert® MTB/RIF) as an aid to culture results, in order to provide confirmed diagnosis in less time so that treatment can be initiated without delay.

2) MycoDDR™ Facilitates Quicker Time to Diagnosis

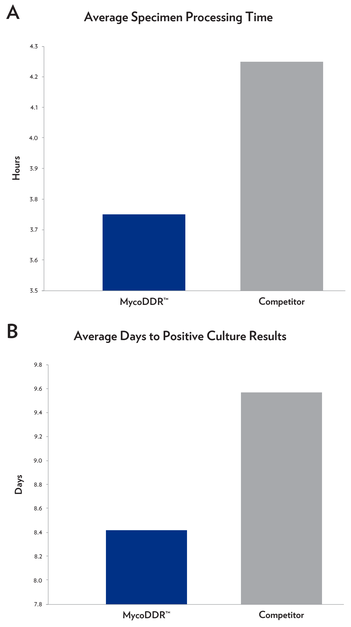

Figure 2. Faster results to diagnosis.
A) Positive MTB specimens were split and processed using the MycoDDR™ specimen processing system and a competitors specimen processing system following the respective protocols for each system. B) The samples were then followed until positive culture results were obtained n=8.

3) Confirmed Positive Results Obtained Quicker with New Algorithm Utilizing MycoDDR™ and Xpert® MTB/RIF.

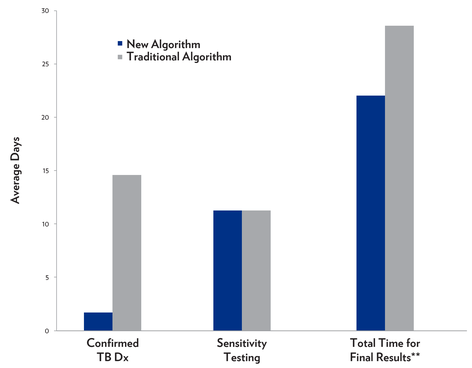

Figure 3. New Algorithm provides confirmed positive results in less time than the traditional algorithm.
Specimens were processed and followed through the diagnostic stages of the traditional and new proposed algorithms.

**Calculated as the average total time to obtain confirmed final diagnosis of disease (specimen processing, culture, sensitivity, and ID).

4) New Algorithm Facilitates Overall Cost Savings to the Hospital

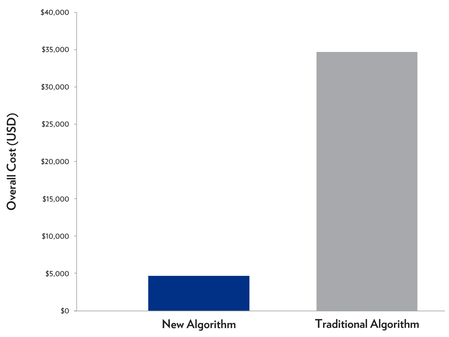

Figure 4. New Algorithm provides estimated overall cost to the hospital.
Hospital cost was estimated based on the average cost of an isolation room and the average number of days of isolation following each algorithm (n=31). Use of MycoDDR™ infers a cost savings of approximately 25% over other specimen processing systems, however, this was not included in the cost savings analysis.

materials & methods

Three specimens were collected 8-24 hours apart, with one specimen collected in the early morning. Both the traditional algorithm and new proposed algorithm followed the same specimen criteria for testing. A retrospective study of specimens processed utilizing the traditional algorithm (n=24) was evaluated to determine the time associated for detection and identification of mycobacterium. The traditional algorithm did not utilize the MycoDDR™ preprocessing reagents; NAAT and HPLC testing were performed off-site at either a reference laboratory or local state laboratory. The new proposed algorithm (n=31) incorporated MycoDDR™ preprocessing reagents and Xpert® MTB/RIF onsite testing.

Traditional algorithm testing utilized Alpha-Tec NAC-PAC™ Red system for specimen decontamination and concentration. The processed samples were inoculated onto solid LJ media and liquid BD MGIT™ media. All cultures were incubated at 35-37°C and held for a total of 6 weeks. Flurochrome screening of the concentrated specimens were examined, and positive screens confirmed with Acid-Fast staining. Positive AFB smears were flagged and the physician notified. Cultures were monitored daily for growth and upon sufficient growth the culture was sent to a local state laboratory for organism identification (HPCL or NAAT) and sensitivity testing.

New proposed algorithm testing utilized IMMY MycoDDR™ system for specimen decontamination and concentration. The processed samples were inoculated onto solid LJ media and liquid BD MGIT™ media. All cultures were incubated at 35-37°C and held for a total of 6 weeks. Flurochrome screening of the concentrated specimens were examined, and positive screens confirmed with Acid-Fast staining. Positive AFB smears were reflexed to onsite Xpert® MTB/RIF testing directly from the concentrated MycoDDR™ sediment. Physicians were notified with smear and Xpert® MTB/RIF results the same day. Specimens that were not initially positive by flurochrome smear screening, however were BD MGIT™ culture detected days later underwent repeat flurochrome screening and then confirmed with AFB staining. Positive AFB BD MGIT™ samples were reflexed to the onsite Xpert® MTB/RIF testing directly from the BD MGIT™. As with direct specimen detection the BD MGIT™ detection results were relayed to the physician to initiate patient management.

The hospital cost savings was determined based on the average number of days that a patient would be isolated until diagnosis (~$2400/day).

references

Candelaria, W., Maneclang, K., Magee, C. (2014, May). *Clinical Evaluation of IMMY Myco DDR-Digestion/Decontamination Reagents for the Recovery of Mycobacterium.* Poster session presented at the 114th annual meeting of the American Society for Microbiology, Boston, MA.

MARICOPA INTEGRATED HEALTH SYSTEM
Count on us to care.