2103. Detection of KatG/inhA Mutation to Guide Isoniazid and Ethionamide Use for Drug-resistant Tuberculosis
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**Session:** 239. Diagnostics Mycobacteriology
**Saturday, October 7, 2017: 12:30 PM**

**Background.** Both Mozambique and Brazil are countries with a high burden of tuberculosis. Isoniazid (INH) is one of the cornerstones of tuberculosis treatment and, depending on the mutated gene (katG or inhA), the organism may be susceptible to high doses of INH (inhA mutation) or to ethionamide (Eth-KatG mutation).

**Methods.** To analyze isoniazid genotypic resistance profile in *Mycobacterium tuberculosis* to guide decision making about management of resistant tuberculosis. Descriptive study of MTB tuberculosis isolates from Ribeirão Preto, Brazil (2011-2014) and 155 isolates from Beira, Mozambique (2014-2015). Drug resistance patterns and the specific genes mutations were determined using Genotype MTBDRplus (Hain Lifescience GmbH, Germany).

**Results.** Mutations in katG gene were detected in 13/22 (59%) of Brazilian and in 32/38 (84.2%) of Mozambican isolates. Unique inhA mutations were observed in 8/22 (36%) isolates in Brazil and 4/38 (10.5%) in Mozambique. Both katG and inhA mutations were detected in 1/22 (5%) and 2/38(5.2%), respectively. katG mutations were more frequent among INH previously treated patients.

**Conclusion.** There is a geographical variation of INH mutations and the new molecular tests can be used to guide and accelerate decision making towards the use of ETH or high doses of INH based on detected mutations.

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2104. Does Disseminated Nontuberculous Mycobacterial Disease cause False-positive Results on the QuantiFERON®-Tb Gold In-Tube Assay? Results
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**Session:** 239. Diagnostics Mycobacteriology
**Saturday, October 7, 2017: 12:30 PM**

**Background.** The Determine TB-LAM (LF-LAM) can detect liparabinomannan, a glycolipid found in mycobacteria, in the urine of HIV-infected patients with disseminated TB. Whether disseminated nontuberculous mycobacterial (NTM) infection causes false-positive results has not been adequately assessed.

**Methods.** We retrospectively reviewed the LF-LAM results and the evidence for tuberculosis (TB) coinfection among HIV-infected subjects with microbiologically confirmed disseminated NTM infection seen by the infectious diseases consultation service at a tertiary hospital in Johannesburg, South Africa.

**Results.** 26 patients had disseminated NTM infection, and 83 mycobacterial cultures and Xpert Mtb/RIF assays were performed on these patients. All patients had specimens collected from a minimum of two different sites (e.g., blood and sputum), and the median number of specimens taken per patient was three. On the basis of this, three subjects were diagnosed with TB-NTM coinfection. LF-LAM was performed on 23 out of 26 subjects with disseminated NTM disease, and was positive in 21 cases (95.8%, 95% CI 92.9-97.4). Excluding subjects in which coinfection was diagnosed, LF-LAM was positive in 19/21 cases (90.5%, 95% CI 71.1-97.4).

**Conclusion.** Our study revealed an unexpectedly high rate of LF-LAM positivity in patients with disseminated NTM infection. While it cannot be definitively determined whether disseminated nontuberculous mycobacterial (NTM) infection causes false-positive results, this has not been adequately assessed.

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2105. Evaluation of the High Indeterminate Rate of the QuantiFERON®-Tb Gold In-Tube Assay in a Children’s Hospital
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**Session:** 239. Diagnostics Mycobacteriology
**Saturday, October 7, 2017: 12:30 PM**

**Background.** The QuantiFERON®-Tb Gold In-Tube (QFT) assay is an in vitro diagnostic test for Mycobacterium tuberculosis infection. We observed a high indeterminate rate among inpatients at Steven and Alexandra Cohen Children’s Medical Center of New York. We hypothesized this was caused by incorrect specimen collection. We educated healthcare workers in proper collection techniques and studied the effect on the indeterminate rate.

**Methods.** We recorded the results of the QFT test for pediatric inpatients from November 2012 to December 2016 from a laboratory specimen log. Beginning in April 2015, multimedia education was implemented using an instructional card that accompanied the QFT tubes, presentations, and an instructional video. We used an electronic survey to assess knowledge of healthcare workers before and after the education intervention. We abstracted demographic, clinical, and laboratory factors to analyze correlation with the indeterminate rate.

**Results.** There were 216 subjects, 101 during the pre-education period and 115 during the post-education period. Ninety-three (43.1%) were indeterminate, 8 (3.7%) were positive, and 115 (53.2%) were negative. There was no significant difference in indeterminate result rate between pre and post-education groups, 46% and 40%, respectively (P = 0.33). In a multivariable model of factors associated with an indeterminate result, there was no significant association with education (P = 0.86), immuno-compromised status (P = 0.6), age (P = 0.0007), absolute lymphocyte count (ALC) (P = 0.0016), and recent receipt of immunosuppressive medication (IS) (P = 0.0001) were significantly associated with an indeterminate result. Among those surveyed after the education period there was a significantly lower proportion of positive results seen in indeterminate result rate between pre and post-education groups, 46% and 40%, respectively (P = 0.33).

**Conclusion.** Although education resulted in an increase in knowledge of correct specimen collection, the indeterminate rate remained high. Younger patient age, recent receipt of IS, and lower ALC are factors associated with an indeterminate result.

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2106. Utilization and Performance of a Laboratory Developed Nucleic Acid Amplification Test for the Diagnosis of Pulmonary and Extrapulmonary Tuberculosis in a Low Prevalence Area: A 14 Year Study
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**Session:** 239. Diagnostics Mycobacteriology
**Saturday, October 7, 2017: 12:30 PM**

**Background.** Tuberculosis (TB) is a significant global health problem. Nucleic acid amplification tests (NAATs) are valuable in reducing delays in initiation of ther- apy and infection control protocols. A retrospective study was performed to assess the utilization and performance of a laboratory developed test molecular targeting a 123 bp region of the IS6110 insertion sequence of MTBC was performed on smear positive samples or if ordered by physician. Clinical and laboratory data was compared with TBPCR results for all culture confirmed cases.

**Results.** There were 151 culture positive patients and 2186 TBPCR performed. Median age of patients at diagnosis was 49 years (IQR 33–66), 74 (49%) were female. The organism may be susceptible to 3 were MDR; ordering of TBPCR was higher in specimens from PTB source (58.4%) as compared with EPTB source (37%). Combined sensitivity of the TBPCR on all specimen types was 86.6% (95% CI 76.3–93.1); 90.3% for PTB specimens alone (58.4%) as compared with EPTB source (37%). Sensitivity of TBPCR was 97% in smear positive and 79% in smear negative PTB specimens. The median time to culture positivity was 7 days longer in specimens that were TBPCR negative compared with those that were positive (P = 0.14, NS), however, TBPCR shortened time to diagnosis by 13 days.

**Conclusion.** We found TBPCR to be underutilized in both PTB and EPTB although it was found to be a rapid and reliable method for early diagnosis. Education regarding utility of NAATs could be useful in low burden areas where paucibacillary disease is more common, especially in EPTB.

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2107. Correlation of Specific Mutations in Line Probe Assay (LPA) and Drug Susceptibility Test (DST) with Respect to Fluoroquinolone Resistance in Drug Resistant Mycobacterium tuberculosis
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**Session:** 239. Diagnostics Mycobacteriology
**Background.** This study was done to investigate the utility of specific fluoroquinolone mutations in LPA in predicting the susceptibility in DST at WHO recommended Critical Concentrations of 0.5 and 2 μg/dL of moxifloxacin within a short time frame as provided by LPA.

**Methods.** In a retrospective study performed at a tertiary care hospital of Mumbai, India from October 2015 to February 2017, consecutive samples demonstrating fluorquinolone resistance by LPA were selected. The LPA kit used was Hain Lifescience Genotype MTBDRsl (Version 1). It detects the following mutations in gyrA gene: MUT1: Ala90Val, MUT2: Ser91Pro, MUT3A: Asp94A1a, MUT3B: Asp94/Asn/Tyr. MUT3C: Asp94Gly, MUT3D: Asp94His. The causal mutation was noted. For 85 of these samples, DST had been requested and results with Critical Concentration of 0.5μg/dL and 2μg/dL for moxifloxacin were available

**Results.** The 89 samples studied were as follows: Sputum (n = 60), paravertebral soft tissue (n = 2), bronchoalveolar fluid (n = 2), cerebrospinal fluid (n = 1), endotracheal tube secretion (n = 1), pleural fluid (n = 1) and site not recorded (22). 3 of these samples had double mutations. Results are as follows.

| Mutation in gyrA gene | Number of Susceptible at 0.5 μg/dL [n (%)] | Susceptible at 2 μg/dL samples [n (%)] |
|-----------------------|------------------------------------------|-------------------------------------|
| MUT1 (Ala90Val)       | 18 (63.33)                                | 16 (88.89)                          |
| MUT2 (Ser91Pro)       | 2 (0)                                    | 1 (50)                              |
| MUT3A (Asp94A1a)      | 13 (52.00)                               | 11 (48.91)                          |
| MUT3B (Asp94/Asn/Tyr) | 6 (11.11)                                | 4 (66.67)                           |
| MUT3C (Asp94Gly)      | 61 (48.15)                               | 43 (84.31)                          |
| MUT3D (Asp94His)      | 2 (0)                                    | 2 (100)                             |

**Conclusion.** This study showed a higher proportion of *M. tuberculosis* susceptibility at 2 μg/dL rather than at 0.5 μg/dL, to moxifloxacin for gyrA mutations Ala90Val (MUT1), Asp94A1a (MUT3A), Asp94Gly (MUT3C), Asp94His (MUT3D) but not for Ser91Pro (MUT2) and Asp94A1a/Asn/Tyr (MUT3B). However, the number of samples with Ser91Pro (MUT2) and Asp94A1a/Asn/Tyr (MUT3B) mutations was too small for meaningful conclusion. This susceptibility at a higher critical concentration of moxifloxacin may have clinical implications for use of high dose moxifloxacin. Since this information is available within a short time frame as provided by LPA, a more effective regimen could be devised 4 to 8 weeks earlier than after results of DST. This may result in faster sputum conversion and prevent amplification of resistance.

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**2109. Improved Detection and Accuracy of Mycobacterium Species Identification from Paraffin Embedded Tissues of Patients by Using Multigege Targeted PCR and Sequencing**

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**Saturday, October 7, 2017: 12:30 PM**

**Background.** Prompt and accurate identification and differentiation of Mycobacterium tuberculosis-complex (MTBC) from non-tuberculous mycobacteria (NTM) is crucial for the selection of antimicrobial treatment and appropriate public health response. Diagnosis and characterization of mycobacteria is challenging due to diverse clinical presentations, lack of sensitivity of smear microscopy, and fastidious culture identification. Moreover, because of clinical suspicion of noninfectious conditions, specimens are often not processed for culture and formalin-fixed, paraffin-embedded (FFPE) tissues are the only specimens available. For rapid and accurate identification of Mycobacterium spp. from patient tissues, sensitive and specific molecular assays combined with other tissue-based methods are vital.

**Methods.** We extracted DNA from FFPE tissues from 931 patients with clinical and histopathological suspicion of mycobacterial infection (received during 2013–2016) and evaluated by multistage, multigene targeted Mycobacterium-genus, complexes-and species-specific PCR assays (targets including 16S rRNA, rpoB, groEL, IS6110, RLEP and sequencing). Tissues were also examined by acid-fast bacilli (AFB) stains and mycobacteria immunohistochemistry (IHC). Assays to detect mutations associated with drug resistance were performed on MTBC cases.

**Results.** A *Mycobacterium* species was detected in 465 (50%) cases by PCR and sequencing. Of these, 380 (82%) were positive by *Mycobacterium* PCR targeting 16S rRNA. 85 cases (18%), including 9 MTBC, 12 *M. avium complex* and 3 *M. leprae* were positive by other PCRs. Co-infection of MTBC and NTM spp. was detected in 5 cases. Of 465 PCR positive cases, 327 (70%) showed immunostaining and 223 (48%) were AFB-positive. Molecular markers for drug resistance were detected in 9 out of 88 (10%) tested MTBC cases.

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**Figure 1. Mycobacterium Species Identified by PCR and Sequencing**

![Mycobacterium Species Identification diagram](image-url)