

lineages and sub lineages, relationship between strains, underline mutations conferring drug-resistant TB, which may not be shown by molecular and phenotypic tests. As far as we know this is the first study that describes genetic diversity of *M. tuberculosis* strains causing DR-TB and using WGS in central region of Mozambique. We aim to describe genetic diversity of *M. tuberculosis* strains causing DR-TB in central Mozambique.

**Methods.** A total of 35 strains from Beira Mozambique were evaluated with genotypic tests (Genotype MTBDRplus™, and MTBDRsl™); phenotypic (MGIT-SIRE™) and DST. All isolates resistant to isoniazid (H) or rifampicin (R) or both were submitted to WGS Illumina HiSeq 2000 and analyzed with TB profiler database and phylogenetic tree was done using Figtree tool. This was a descriptive cross-sectional study.

**Results.** WGS shown that strains analyzed, belongs to three of six major lineages, with Lineage 4: 25(71.4%); Lineage 1: 5(14.3%); and Lineage 2 Beijing family: 5(14.3%). All pre-XDR strains 3(8.6%) were from lineage 4.3. By WGS, all 35 strains had any mutations conferring DR-TB while in one strain, mutation was not shown by genotypic neither phenotypic DST. Compared with genotypic tests, WGS had best performance in showing mutation conferring resistance to etambutol 12/35 (34.3%) and 7/35 (20%).

**Conclusion.** The DR-TB disease in Beira Mozambique is mainly caused by *M. tuberculosis* strains of Lineage 4, sub-lineage 3 although lineage 1 and 2 are also present. WGS shows underline mutations causing DR-TB that are not detected by genotypic and phenotypic DST test.

**Disclosures.** All authors: No reported disclosures.

### 800. Drug-Resistant TB: An Experience From Qatar

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**Session:** 70. Tuberculosis and Other Mycobacterial Infections  
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**Background.** Drug-resistant tuberculosis (DR-TB) is an important issue for public health. This study was conducted to evaluate the characteristics, treatment outcome, and risk factors associated with 223 DR-TB cases in the State of Qatar.

**Methods.** A descriptive records-based retrospective study was conducted on patients registered at Communicable Disease Centre (CDC), Qatar to all consecutive microbiologically confirmed tuberculosis cases for the period January 2010–March 2015. Demographic and clinical data extracted included: patient's age, sex, and country of origin; disease site (pulmonary or extra-pulmonary); presence of comorbidities, HIV/AIDS status, previous chemoprophylaxis and/or previous treatment for TB, and anti-TB drug resistance the resistance pattern of isolated mycobacteria. The sputum culture conversion rate and treatment outcome was assessed for the patient who completed their treatment in Qatar

**Results.** Of 3,301 patients with positive *M. tuberculosis* culture were analyzed; 223 (6.7%) were resistant to one or more first-line drugs, to isoniazid in 3.1% ( $n = 102$ ), streptomycin in 1.2% ( $n = 41$ ), rifampicin in 0.2% ( $n = 6$ ), ethambutol in 0.15% ( $n = 5$ ), and multi-drug resistance in 1.2% ( $n = 38$ ) of patients. Among the resistant TB patients, more common demographic characteristics were former resident of Indian subcontinent (64.1%). A history of anti-TB treatment was not a risk factor with drug resistance in our cohort. Only 111 (49.7%) patients were tested for HIV antibodies and the results were all negative. There was significant correlation between the type of drug-resistance and CXR finding (23.3% had cavity— $P = 0.019$ ). Sputum culture conversion to negative at 2 month of therapy was 94% ( $n = 101$ ), whereas 122 cases lost follow-up. The outcome of treatment was assessed for 85 resistant cases with follow-up after completion of treatment, show cure rate of 97.6%, and relapse of 2.4%. However, 137 cases (61.4% from total) they left the country before completion of therapy.

**Conclusion.** Drug-resistant TB in Qatar is influenced by migration, especially from the Indian subcontinent, where the patients were probably infected. Rapid sputum sampling performed in the early stages of the disease, patient isolation, and drug susceptibility testing should be the standard of care to avoid further transmission and improve TB control.

**Disclosures.** All authors: No reported disclosures.

### 801. Emergence of Multi-Drug Resistance Tuberculosis During the Treatment Course of Pan-Susceptible TB: A Case Series

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**Session:** 70. Tuberculosis and Other Mycobacterial Infections  
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**Background.** Successful treatment of tuberculosis (TB) requires monitoring for clinical, radiographic, and microbiologic improvement. Even after negative cultures are obtained, there should be continued monitoring of sputa. If cultures become positive during treatment of drug susceptible TB (DS-TB), there should be concern for multi-drug-resistant tuberculosis (MDR-TB). We present two cases diagnosed with DS-TB who developed MDR-TB during treatment. Case Report: Case 1 is a 33-year-old male who was incarcerated in Peru. During incarceration in 2008, three of his

cellmates had MDR-TB and he was diagnosed with DS-TB and treated with directly observed therapy (DOT) for 7 months. In Texas in 2015 he was diagnosed with DS-TB and was initiated on rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE). Five months into DOT, his sputa became culture positive with molecular detection of drug resistance (MDDR) and drug susceptibility testing (DST) revealing resistance to all of RIPE. Repeat MDDR and DST of the 2015 isolate showed no resistance. Genotyping of the two isolates were identical by mycobacterial interspersed repetitive units (MIRU) and spoligotyping. However, whole genome sequencing showed two different isolates. Case 2 is a 63-year-old female diagnosed with DS-TB in Saipan and started on RIPE in April 2017. She was on DOT until July when she moved to Texas and was lost to follow-up until September. She claims adherence with rifampin and isoniazid during this time. All sputa collected between diagnosis and September were smear and culture negative. Six months into therapy, she had sputa that was culture positive with MDDR and DST showing MDR-TB. Her isolates from Saipan and Texas were sent for genotyping. The MIRU and spoligotyping showed two different isolates.

**Conclusion.** These cases show the importance of following cultures throughout treatment. Traditionally, MDR-TB is thought to be due to poor adherence. However, in high prevalence areas, heterogeneous infection with two different strains is an important consideration for the cause of MDR-TB. Concomitant infection of DS and MDR-TB can occur with MDR-TB not being detected until far into therapy. These cases represent heterogeneous exogenous infection of DS and MDR-TB—only discovered after meticulous culture monitoring.

**Disclosures.** All authors: No reported disclosures.

### 802. Use of N-Acetylcysteine for Prevention and Treatment of Isoniazid Induced Liver Injury During Treatment of Mycobacterial Infections

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**Session:** 70. Tuberculosis and Other Mycobacterial Infections  
Thursday, October 4, 2018: 12:30 PM

**Background.** Hepatotoxicity secondary to therapy for *Mycobacterium tuberculosis* (MTB) is a common complication that may lead to treatment interruption. N-Acetylcysteine (NAC) exerts a hepatoprotective effect by replenishing glutathione stores and enhancing the cellular antioxidant defense mechanism. NAC has been found to be protective against liver toxicity in animals treated for MTB infection. Randomized controlled trials have shown that its use in humans also decreases the risk of hepatotoxicity associated with anti-MTB treatment but there is minimal data regarding its utility for treatment of liver toxicity.

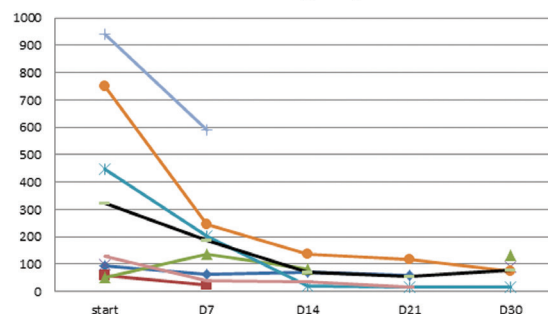
**Methods.** Patients who received NAC from January 2012 to March 2018 for prophylaxis and treatment of increasing liver function tests (LFTs) while on isoniazid (INH) were included. A retrospective review of the medical record system was performed.

**Results.** Nineteen patients were included. Eight received NAC for treatment. The average age was 49 years. Seventy percent of patients were male. The mean BMI was 25. Five patients had underlying liver cirrhosis and two had hepatic steatosis. Eleven patients had Hepatitis C (HCV) and one had active Hepatitis B infection. Ten patients had MTB pulmonary infection, three had latent TB infection, two meningitis, and three had disseminated disease. One patient was treated for atypical mycobacterial infection. The dose of NAC used was 600 mg oral twice daily and the duration was variable.

The prophylaxis group had stable LFTs during treatment, except for two patients whose enzymes increased more than three times the upper limit of normal. These two patients had underlying HCV and liver cirrhosis. Only one required discontinuation of INH. This group received NAC for an average of 47 days. The treatment group had a favorable trend of liver enzymes after NAC initiation, with levels significantly improving by day 14 (Figures 1 and 2). Three patients did not require discontinuation of antibiotics. INH was stopped prior to NAC initiation in four patients. No side effects of NAC were documented in any patient.

**Conclusion.** NAC is a safe and effective measure to prevent and treat hepatotoxicity secondary to INH therapy. More studies are needed to determine its optimal dose and duration for this indication.

**Treatment group AST trend**



**Figure 1.**