Introduction: Cryptococcus is a worldwide mycosis caused by Cryptococcus neoformans and Cryptococcus gattii. Although resistance to amphotericin is infrequent, isolates with decreased susceptibility to fluconazole have been reported globally, including Colombia, which may be due to 1) heteroresistance, defined as the ability to adapt to increasing concentrations of the drug, amphotericin, and 2) point mutations in the ERG11 gene encoding the fluconazole target enzyme, lanosterol 14α-demethylase.

Objective: To determine the development of heteroresistance to fluconazole in C. neoformans and C. gattii clinical isolates from Brazil and to amplify and sequence the ERG11 gene of the isolates to seek for mutations that may contribute to resistance or heteroresistance phenotypes.

Methods: The minimal inhibitory concentration (MIC) of fluconazole was determined in 12 and 42 isolates of C. neoformans and C. gattii, respectively, using broth microdilution. Heteroresistance was evaluated by plating each isolate on YPD agar that contained fluconazole at concentrations equal to the MIC of each isolate. Heteroresistant clones were then regrown in the presence of concentrations of fluconazole, and the MIC was determined.

Results: All isolates were susceptible to fluconazole with MICs of 1 μg/ml (n = 12, 2 μg/ml (n = 4), 4 μg/ml (n = 17), 8 μg/ml (n = 25), 16 μg/ml (n = 5), and 32 μg/ml (n = 1)). However, all isolates developed heteroresistance clones, with increases in MIC from 2 to 128 μg/ml. The MIC for the parental C. neoformans and 8.5 (3.3%) of the C. gattii, grew up to 64 μg/ml of fluconazole, which is in the MIC that define resistance to this drug, and 1,126 (3%) of C. neoformans and 4,17 (3%) of C. gattii, grew up to 128 μg/ml of fluconazole, which is the MIC of resistance to the drug.

Conclusion: Clinical isolates of C. neoformans and C. gattii that develop heteroresistance to fluconazole in high concentrations circulate in Colombia, which is important since this characteristic contributes to the edge of cryptococcosis during therapy with this drug.

5.1d Chronic pulmonary aspergillosis in post-TB and retuberculosis patients in Lagos, Nigeria

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Objection: Chronic pulmonary aspergillosis (CPA) is a common complication of post-TB treatment. It is a progressive disease characterized by progressive cavitation, fibrosis, and pleural thickening among others. Globally, as estimated 3 million people are affected. This study determined the burden of CPA among the post-TB and retuberculosis patients in two facilities in Lagos, Nigeria.

Methods: This was a prospective longitudinal study that was carried out at two TB clinics (UTH and NSMR) in Lagos, Nigeria between February 2011 and March 2012. The study population were those who had been previously diagnosed 2-3 years before and who were clinically diagnosed as post-TB disease. Patients were followed every 3 months for a period of 6 months. The data collected were quality of life (QOL) and SGRQ questionnaire used, microbiological data, and the outcome of treatment.

Results: A total of 112 post-TB treatment patients were recruited, 65 (57.8%) were men and 47 (42.2%) post-TB patients were women. The mean age of the patients was 41.6 years, with the majority of the age between 25-50 years. The male/female ratio was 0.91, 98.5% (67) were HIV negative, and only 8 patients had GenXpert tests done. In all 32 (40%) were GenXpert negative, of which 24/32, 7.5% were sputum positive, and 19/24 positive to retuberculosis. Cough was the predominant symptom with 39 (34.8%) having productive cough. Hemoptysis occurred in 11/19 (57.9%). In 18/19 (94.7%) the patients had no sputum positive tuberculosis. Chest X-ray was done in all patients of which 8/19 (42.1%) had bilateral infiltrates and 11/19 (57.1) had pleural thickening. Sputum culture yield growth of Aspergillus sp., with A. fumigatus (11; 67.6%) being the predominant species followed by A. flavus (6; 33.3%), and A. smoking (0; 0%). In all 88/191 (46.2%) had Aspergillus IgG titres above the cut-off level, while 8/19 patients had positive Aspergillus IgG titres. The cut-off for IgM was 1000 IU/ml.

Conclusion: The results of the study showed a high prevalence of chronic pulmonary aspergillosis among post-TB and retuberculosis patients. The results also showed that CPA is underdiagnosed as treatment failure at TB or TB relapse. There is a need for further follow-up post-TB patients for early identification of post-TB lung disease. It is also imperative to educate our clinicians to screen patients who have persistent symptoms and are GenXpert negative for other post-TB lung diseases.