

ABSTRACT

The Molecular Epidemiology of Tuberculosis in the Caribbean

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This study represents the first molecular epidemiological study of *Mycobacterium tuberculosis* in the Caribbean. The study was aimed among other objectives to: describe the several comorbidities or characteristics associated with and seen in patients with *Mycobacterium tuberculosis* infections in the Caribbean using Trinidad and Tobago as a representative of countries in the Caribbean; determine the susceptibility patterns of these *Mycobacterium tuberculosis* isolates and their genetic relatedness, and comparing their clonal relatedness with other isolates in the international database.

This was a prospective cross-sectional laboratory based study on clinical and cultured specimens from 15 countries in the Caribbean as well as target groups of individuals in Trinidad & Tobago. Over 1260 specimens were collected over a 2 year period, September 2006 to October 2008. Culture and identification was performed using the BACTEC 460 TB system. Drug susceptibility tests on isolates were performed using both the BACTEC 460 TB system and the Hain Lifesciences Line probe assay, MTBDR*plus*. Genotyping of tuberculosis isolates were conducted using spoligotyping and MIRU-VNTR. Analysis of data was performed using Epi Info and SITVIT2 database.

Results showed that tuberculosis in the Caribbean is characterized by a very high male to female ratio (3:1) and in some countries up to 4:1 ratio. The mean age was 39.9 years, which was significantly higher for the age group 25-44 years ($p < 0.01$) when compared to the other age groups. There was a very high TB/HIV co-infected rate of 26.8% (range 13.5%-44.4%). Drug resistance was relatively low with one country (Guyana) having over 85% of the resistance seen. Jamaica, Bahamas and Suriname had few cases of mono-resistance, while isolates from the other Caribbean countries were mostly susceptible to the major first line drugs used. The Hain Lifesciences Line probe assay, *MTBDRplus*, showed excellent results for identification of *Mycobacterium tuberculosis*. Detection of rifampicin resistance from clinical specimens showed excellent correlation with the phenotypic method (95.8%) and the assay was cheaper to use than culture. However detection of INH resistance was disappointing showing only 34.6% correlation with the phenotypic method.

Spoligotyping of 480 isolates generated 104 distinct patterns suggesting that there is a wide diversity of strains present in the Caribbean and that there is ongoing and active transmission of tuberculosis due to the large percentage of clustering of the isolates. When compared to 2653 other strains from neighbouring countries, the results revealed that many of the strains found in Trinidad and Tobago were different from the other Caribbean and South American countries where data were available. The Spoligotyping and MIRU genotyping results also revealed that a predominant strain SIT566 belonging to

the X family was mainly responsible for the spread of tuberculosis in Trinidad & Tobago. The strains from the rest of the Caribbean including the predominant strain, SIT53 were consistent with the historical evolution of the Caribbean where strains predominant in Europe were present. This could be because of the colonization history of the Caribbean where strains could be brought by persons who travelled to the Caribbean as settlers. Strains present in the Indian sub continent were also seen in Trinidad and Tobago, Guyana and Suriname where there is a large percentage of East Indians who were brought to these islands during the indentureship period which began in the Caribbean during the 1830's.

In conclusion, many of the Caribbean countries have low to moderate incidence of tuberculosis with the exception of Guyana which can be described as high and increasing. Overall, in countries where the incidence is moderate such as Trinidad and Tobago, Suriname, Guyana and Bahamas, HIV co-infection is high and this could be the driving force behind the tuberculosis epidemic in these countries. Drug resistance was very low in the countries surveyed except for Guyana where the majority of resistance (both mono-resistance and multi-drug resistance) was seen. Tuberculosis infection was more predominant in males and the age group most affected was the 25-45 years old. Like studies in other developing countries, HIV is a major risk factor in tuberculosis infections in the Caribbean. The high level of clustering of the isolates suggests that the tuberculosis epidemic in the Caribbean is ongoing and that new infections are spreading with several outbreaks of tuberculosis in many of these countries. Lack

of proper epidemiological tools for identifying these outbreaks caused these outbreaks to go un-noticed. The tuberculosis lineage distribution in Trinidad and Tobago was completely different from its neighbours but overall the majority of strains seen in the Caribbean are consistent with the history of the Caribbean evolution.

Keywords: Tuberculosis, Mycobacterium, Spoligotyping, MIRU-VNTR, MTBDRplus, Molecular, Epidemiology