

Drug Resistance Trends in *M. tuberculosis*: Blackburn 2000-2009 Completion of 50 Years Continuous Surveillance

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Abstract

Setting: Blackburn, East Lancashire, a high TB prevalence district of the United Kingdom.

Methods: Continuous prospective monitoring of all isolates of *M. tuberculosis*, with their drug susceptibility profiles.

Results: Of the 382 isolates in 2000-2009, 54 were of white ethnic origin, 319 of South Asian ethnic origin and 9 of other ethnic origin. There was no isoniazid resistance in the white ethnic patients in the 10-year cohort, whereas the rate of isoniazid resistance was nearly 6% in the South Asian group. 4/319 (1.25%) of isolates in the South Asian cohort had MDR-TB.

Conclusion: Drug resistance remains very low in the local white population, but in the South Asian population continues at a level of isoniazid resistance of 6%, with 4/19 with isoniazid resistance having MDR-TB. The drug resistance profile of the non-white population continues to reflect that of South Asia, with MDR-TB now appearing in previously untreated recent arrivals.

Introduction

Continuous drug resistance data for *M. tuberculosis* isolates is available for the Blackburn, Hyndburn and Ribble Valley local government areas of East Lancashire, UK (United Kingdom), from 1960 onwards. Those for 1960-84 [1], 1985-89 [2], and 1990-1999 [3] have been published, and these show drug resistance declining to very low levels in the white ethnic group, but remaining consistently between 6.5 and 15% in the South Asian ethnic group, mainly to isoniazid (H), Streptomycin (S) or to these combined (SH). The Blackburn district of East Lancashire remains one of the high TB incidence districts in the UK, being over 28/100000 per annum in 1998 [4], and 37/100000 in 2009 [5].

Methods

Isolates of *M. tuberculosis* were cultured locally, by Lowenstein-Jensen slope until May 2004, and then by MGIT (Becton Dickinson) from June 2004 onwards. After local isolation, all samples were sent to the Newcastle Regional Centre for Mycobacteriology, for species identification and drug susceptibility testing. The results of such tests have been continuously prospectively collated (by LPO) since 1981, and are reported here for isolates from 01.01.00 to 31.12.09 inclusive.

Results

In 2000-04, there were 172 isolates overall, 22 white, 149 South Asian and 1 in other ethnic groups. For 2005-09 there were 210 isolates overall, 32 white, 170 South Asian and 8 in other ethnic groups. Details of drug resistance are given in (Table 1), and comparison with earlier data [1-3] in (Table 2). None of the Multi-Drug-Resistant TB (MDR-TB; resistant to isoniazid/rifampicin +/- other drugs) had prior TB treatment in the United Kingdom. One MDR-TB case in 2005-2009 had been a close contact 18 months earlier of a local MDR-TB case, occurring in a recent arrival from South Asia. A further close contact of the second MDR

case subsequently developed MDR-TB approximately two years later in 2005-2009. Both of the other MDR-TB cases (n=2) were born in either Pakistan or India and had subsequently emigrated to the UK.

Discussion

This cohort completes 50 years of continuous drug resistance data, in an area of the UK, which went from below national average TB rates in 1960-1965 to the highest rate of TB in England and Wales in 1970 [6]. No cases of drug resistance were seen in the white ethnic cases over this 10 year (2000-2009) cohort. With these data, and those from previous

| Resistance (n=) | | | | | | | % total resistance | % isoniazid resistance |
|-----------------|-----------------|---|---|----|-------|-----|--------------------|------------------------|
| Period | Number isolates | H | S | HS | Other | MDR | | |
| White | | | | | | | | |
| 2000-04 | 22 | - | - | - | - | - | 0% | 0% |
| 2005-09 | 32 | - | - | - | - | - | 0% | 0% |
| South Asian | | | | | | | | |
| 2000-04 | 149 | 2 | - | 7 | - | - | 6.16% | 6.16% |
| 2005-09 | 170 | - | - | 5 | 1* | 4 | 5.88% | 5.88% |

Table 1: Drug resistance 2000-2009

*HS+Ethambutol

(Other ethnic groups 1 isolate in 2000-04, and 8 in 2005-09, all fully susceptible)

*HS+Ethambutol

(Other ethnic groups 1 isolate in 2000-04, and 8 in 2005-09, all fully susceptible)

H= Isoniazid S=Streptomycin E=Ethambutol

| Period | Number isolates | H | S | HS | HSP | Other | MDR | % Total Resistance | % isoniazid Resistance |
|----------------------|-----------------|----|----|----|-----|-------|-----|--------------------|------------------------|
| White | | | | | | | | | |
| 1960-69[1] | 525 | 17 | 13 | 6 | 3 | 10 | - | 9.33% | 6.1% |
| 1970-79[1] | 271 | 6 | 4 | 1 | - | - | - | 4.06% | 2.58% |
| 1980-89 [1,2] | 131 | - | 1 | - | - | - | - | 0.76% | nil |
| 1990-99[3] | 6 | 3 | - | - | - | - | - | 4.47% | 4.47% |
| 2000-09 (these data) | 54 | - | - | - | - | - | - | nil | nil |
| South Asian | | | | | | | | | |
| 1960-69[1] | 125 | 2 | 4 | 5 | - | 2 | - | 10.40% | 7.20% |
| 1970-79[1] | 301 | 9 | 16 | 7 | 1 | 5 | - | 12.62% | 6.64% |
| 1980-89 [1,2] | 175 | 3 | 12 | 7 | 1 | - | - | 11.43% | 4.57% |
| 1990-99[3] | 229 | 9 | 1 | 7 | - | - | 1 | 7.9% | 7.4% |
| 2000-09 (these data) | 319 | 2 | - | 12 | - | 1 | 4 | 5.95% | 5.95% |

Table 2: Drug resistance 1960-2009 in newly diagnosed patients

H= Isoniazid S= Streptomycin P=Para-amino-salicylic acid MDR= Multidrug resistance

cohorts [1-3], this means only 3 cases of isoniazid resistance were reported in 30 years in the white cohort. In contrast, the rate of drug resistance, particularly to isoniazid (approximately 6.0% in these data), has remained between 4.5-7.4% consistently since 1960 in the South Asian group (Table 2). These data, therefore, continue, together with the previous data [1-3], to provide substantial indirect evidence of the lack of transmission, using isoniazid resistance as a surrogate marker, between the main White and South Asian ethnic groups over nearly 50 years. Analysis of MIRU-VNTR (multiple interspersed repetitive units; variable number tandem repeat) profiles of the whole East Lancashire TB isolates for 2001-9, has also recently directly confirmed this lack of inter-ethnic transmission [7].

The first case of MDRTB was seen in our South Asian population in 1990-1999 [3]. In this 10 year cohort there were 4 cases, 2 previously untreated new entrants from India (A) and Pakistan (B). The 2 further cases were (C) in a household contact of (A), and (D) a close social contact of case (C). A, C and D had identical MIRU-VNTR profiles [7]. All have been cured and remain under long term follow-up. The occurrence of the MDR-TB cases highlights the significance of rising drug resistance rates in South Asia, with primary resistance rates of 0-51.2% reported including 0-14.2% MDR-TB in untreated patients and 10.7-58.3% in those with a prior treatment history [8-12]. Since the South-Asian cohort currently make up 90% of all local TB cases, and this cohort, particularly those born abroad, have an annual incidence 20-30 times that of the UK born, either white or South-Asian, it is not surprising that drug resistance, and particularly MDRTB is detected more frequently in this group. The types and incidence of drug resistance, of the overseas born, will continue to drive the drug resistance profile of low burden countries, such as the UK with a high proportion of TB cases born abroad [5].

Conflicts of Interest

None

Author Contributions

LPO prospectively collated the data, and ran the clinical service and treated the patients. The other authors provided the bacteriology service and quality control of the isolation of mycobacteria.

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