Standard Genotyping Overestimates Transmission of Mycobacterium tuberculosis among Immigrants in a Low-Incidence Country

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Immigrants from regions with a high incidence of tuberculosis (TB) are a risk group for TB in low-incidence countries such as Switzerland. In a previous analysis of a nationwide collection of 520 Mycobacterium tuberculosis isolates from 2000 to 2008, we identified 35 clusters comprising 90 patients based on standard genotyping (24-locus mycobacterial interspersed repetitive-unit-variable-number tandem-repeat [MIRU-VNTR] typing and spoligotyping). Here, we used whole-genome sequencing (WGS) to revisit these transmission clusters. Genome-based transmission clusters were defined as isolate pairs separated by ≤12 single nucleotide polymorphisms (SNPs). WGS confirmed 17/35 (49%) MIRU-VNTR typing clusters; the other 18 clusters contained pairs separated by >12 SNPs. Most transmission clusters (3/4) of Swiss-born patients were confirmed by WGS, as opposed to 25% (4/16) of the clusters involving only foreign-born patients. The overall clustering proportion was 17% (90 patients; 95% confidence interval [CI], 14 to 21%) by standard genotyping but only 8% (43 patients; 95% CI, 6 to 11%) by WGS. The clustering proportion was 17% (67/401; 95% CI, 13 to 21%) by standard genotyping and 7% (26/401; 95% CI, 4 to 9%) by WGS among foreign-born patients and 19% (23/119; 95% CI, 13 to 28%) and 14% (17/119; 95% CI, 9 to 22%), respectively, among Swiss-born patients. Using weighted logistic regression, we found weak evidence of an association between birth origin and transmission (adjusted odds ratio of 2.2 and 95% CI of 0.9 to 5.5 comparing Swiss-born patients to others). In conclusion, standard genotyping overestimated recent TB transmission in Switzerland compared to WGS, particularly among immigrants from regions with a high TB incidence, where genetically closely related strains often predominate. We recommend the use of WGS to identify transmission clusters in settings with a low incidence of TB.
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