Karakterisasi molekular mutasi-mutasi gen penyandi resistensi obat antituberkulosis menggunakan Whole-Genome Sequencing pada isolat klinik Multidrug-Resistant Tuberculosis = Molecular characterization of mutations associated with resistance to antituberculosis drugs using Whole-Genome Sequencing among Multidrug-Resistant Tuberculosis clinical isolates

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Abstrak

Latar Belakang : Multidrug-resistant tuberculosis (MDR-TB) adalah masalah kesehatan masyarakat yang utama di dunia, termasuk di Indonesia. Analisis menggunakan whole-genome sequencing (WGS) masih jarang digunakan untuk investigasi penyakit TB dan MDR-TB di Indonesia.
Tujuan: Mengevaluasi potensi penggunaan WGS untuk melakukan drug susceptibility testing (DST) dan mengetahui strain Mycobacterium tuberculosis resisten obat antituberkulosis di Jawa, Indonesia.
Metode: Tiga puluh isolat MDR-TB dilakukan DST menggunakan Mycobacteria Growth Indicator Tube 960 (MGIT) dan WGS. Analisis filogenetika dilakukan menggunakan data dari WGS. Hasil DST yang didapatkan dengan menggunakan MGIT dan WGS dibandingkan.
Hasil:. Kesesuaian antara WGS dan MGIT adalah 93,33% untuk rifampicin, 83,33% untuk isoniazid, dan 76,67% untuk streptomycin tetapi hanya 63,33% untuk ethambutol. Kesesuaian yang moderat ditemukan pada obat antituberkulosis lini kedua termasuk amikacin, kanamycin, dan fluoroquinolone (73,33%-76,67%). MDR-TB lebih sering ditemukan pada isolat yang berasal East Asian Lineage (63,33%).
Kesimpulan: Penelitian ini menunjukkan penerapan dari WGS untuk DST dan epidemiologi molekular dari TB resisten obat di Jawa, Indonesia.
.....Background: Multidrug-resistant tuberculosis (MDR-TB) is a major public health problem globally, including in Indonesia. Whole-genome sequencing (WGS) analysis has rarely been used for the study of TB and MDR-TB in Indonesia.
Aim: We evaluated the use of WGS for drug susceptibility testing (DST) and to investigate population structure of drug-resistant Mycobacterium tuberculosis in Java, Indonesia.
Method: Thirty suspected MDR-TB isolates were subjected to MGIT-960 system (MGIT)-based DST and WGS. Phylogenetic analysis was done using the WGS data. Results obtained using MGIT-based DST and WGS-based DST were compared.
Result: Agreement between WGS and MGIT was 93.33% for rifampicin, 83.33% for isoniazid and 76.67% for streptomycin but only 63.33% for ethambutol. Moderate WGS-MGIT agreement was found for second-line drugs including amikacin, kanamycin, and fluoroquinolone (73.33-76.67%). MDR-TB was more common in isolates of the East Asian Lineage (63.33%).
Conclusion: This study demonstrated the applicability of WGS for DST and molecular epidemiology of DR-TB in Java, Indonesia.