Characterization of HIV-1 drug resistance mutations among HIV-1 infected paediatric patients in Malaysia

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Abstract

Mother-to-child transmission (MTCT) has been identified as a significant HIV transmission route in children in Asia. Despite all efforts to achieve zero prevalence rate of HIV infection among infants born to HIV positive mothers, cases of HIV positive infants are still reported each year in Malaysia. Currently, figures on the drug resistance mutations (DRMs) among HIV-1 infected Malaysian children are inadequate. In this study, we have characterized DRMs among HIV-1 infected children from various parts of Malaysia. A total of 89 HIV-1 paediatric patients’ plasma with virological failure from the year 2014-2015 was received from major and state hospitals throughout Malaysia. Virological failure is defined as patient with HIV-1 viral load ≥ 1000 copies/mL. HIV-1 viral load assay was performed in viral load centres in Malaysia prior to sending to the laboratory. The entire HIV-protease and up to codon 335 of the HIV-reverse transcriptase regions of the pol gene were sequenced to cover all known DRMs. The results were submitted to the Stanford University HIV-1 Drug Resistance Database to yield associated DRMs and susceptibility to each of antiretroviral drugs tested. Of 89, 78 samples were successfully amplified and sequenced. Majority of patients (41/78) was from the age group of 10-14 years, followed by age group 15-19 years (19/78), 5-9 years (17/78) and age group of 0-4 years (1/78). Measured viral load of HIV-1 in this study ranged between 2.94 to 6.66 log copies/mL. Overall, 16.7% of patients had Protease Inhibitor (PI) major resistance while 33.3% of patients exhibited PI Minor resistance. Meanwhile, resistance towards Nucleoside Reverse Transcriptase Inhibitors (NRTI) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) was 70.5% and 73.1%, respectively. The most common DRMs, M46I and L10V/I/F were detected for major PI and Minor PI, respectively. Meanwhile, the combination of M184V/MV mutations were the most frequent mutations detected for NRTIs. In addition, for NNRTIs group, the combination of K103N/KN/S mutations were noted to be the most common. Most of the major resistance mutations are highly correlated with the resistance pattern of antiretroviral drugs. A high level of resistance based on the drug resistance mutations demonstrated towards all three classes of ARV by Stanford University HIV-1 Drug Resistance Database was shown in this analysis.

Keywords: HIV-1, resistance mutation, paediatric, Malaysia

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