HIV-1 subtypes and drug resistance mutations among infected patients in Kelantan, Malaysia

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Introduction
The use of antiretroviral (ARV) therapy has greatly reduced the rate of morbidity and mortality among human immunodeficiency virus type-1 (HIV-1) infected patients. However, high-mutation and recombination rates of HIV-1 lead to the emergence of various subtypes and drug resistance viruses, rendering ARV therapy ineffectual in many patients. In Malaysia, molecular epidemiology studies on HIV-1 were carried out mainly in Kuala Lumpur; thus data pertaining to the prevalence of HIV-1 subtypes and primary drug resistance in other states including in the east coast of Peninsular Malaysia is insufficient. Therefore, this study was undertaken to determine for the first time the prevailing HIV-1 subtypes and the patterns of drug resistance mutations among HIV-1 infected patients in Kelantan, Malaysia.

Materials and methods
50 blood samples of adult HIV-1 infected patients (naive and treated) were collected from Hospital Raja Perempuan Zainab II, Kelantan, Malaysia from Jan 2010 to Dec 2012.

Reverse transcriptase-PCR (RT-PCR) and Nested PCR
DNA sequencing
Alignment and editing nucleotide sequences
Phylogenetic analysis (neighbour-joining method; Kimura 2 parameter, 1000 replicates) and Bootscanning analyses (SimPlot 3.2)

Drug resistance analysis using Stanford HIV drug resistance database

Results: subtypes
CRF01_AE was found to be the most predominant variant (76%) (Figure 1).

CRF03_B1 was replaced subtype B and CR01_AE as the most predominant HIV-1 in Malaysia (Sarawathy et al., 2000; Tee et al., 2006). Recent study done in Kelantan among paediatric patients reported similar finding with the present study (Mohamed et al., 2012).

CRF02_AG was not present among the patients in the present study, indicating subtype shifting had occurred.

The newly identified CRF35_01B also present in the current study. First emergence was reported in Kuala Lumpur in 2012.

The present study reported Thai strain, CRF15_01B, existed in Kelantan albeit at a low prevalence, demonstrating a mix presence of HIV-1 of Malaysia and Thailand strains or origin in this state.

Results: naive patients

Among the 19 treatment naive patients, the (26.3%) had resistance to at least one drug group; one patient had resistance to protease inhibitor (PI) and non-nucleoside reverse transcriptase inhibitor (NNRTI) and one to three patients to nucleoside reverse transcriptase inhibitor (NRTI) and NNRTI only, respectively (Table 1).

All mutations conferring resistance to PI were contributed by a single patient (Figure 2). This treatment-naive patient who was highly resistant to PIs carried M46I, K103N, and Y181C (minor mutation) resistance (Figure 3).

Conclusions

The frequency of primary drug resistance mutation was high in HIV-1 patients (naive and treated) in Kelantan suggesting that ARV resistance testing is essential prior to commencing and during ARV therapy in these patients.

Literature cited


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