Mutasi genetik dan resistensi obat HIV (HIVDR) golongan NRTI, NNRTI, dan PIi pada HIV 1 dari pasien gagal terapi setelah mendapat enam bulan terapi antiretrovirus di RSUPN dr Ciptomangunkusumo periode September 2013 - Maret 2014 = Hiv drug resistance after failure of 6 months first line therapy in RSUPN dr Ciptomangunkusumo September 2013 to March 2014

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Abstrak

Latar Belakang : Implementasi penggunaan terapi antiretrovirus aktif (highly active antiretroviral therapy/HAART) di Indonesia meningkat sejak tahun 2004. Namun demikian, perlu disadari bahwa resistensi obat HIV, salah satu konsekuensi pemberian antiretrovirus, dapat menurunkan keberhasilan terapi. Ketersediaan data mengenai resistensi terhadap obat golongan NRTI, NNRTI dan PI dapat memberi keuntungan dalam program pengendalian dan pencegahan HIV/AIDS nasional.
Tujuan : Penelitian ini dilakukan untuk mengetahui profil resistensi genotip HIV-1 terhadap antiretrovirus pada pasien terinfeksi HIV-1 yang gagal terapi lini pertama.
Metode : Mutasi gen penyandi resistensi obat HIV dievaluasi pada pasien HIV di RSUPN Dr. Ciptomangunkusumo, Jakata, setelah mengalami gagal terapi lini pertama. Pasien dengan viral load > 200 kopi/ml setelah enam bulan terapi antiretrovirus dimasukkan dalam penelitian ini. Hasil resistensi secara genotip dan subtipe HIV-1 diinterpretasi menggunakan Viroseq dan database Stanford DR.
Hasil : Sebelas pasien diperoleh selama periode penelitian dengan nilai tengah usia 31 tahun, 54,55 % pasien laki – laki dan sebaran transmisi yaitu heteroseksual (45,45 %), homoseksual (9,09 %), pengguna jarum suntik yang tidak aman (27,27 %) dan tidak diketahui (18,18 %). Infeksi oportunistik ditemukan pada 72,73 % pasien yang didominasi oleh tuberkulosis paru. Sekitar 27,27% memiliki kepatuhan minum obat yang baik. Subtipe HIV yang ditemukan 81,81 % CRF01_AE, 9,09% C dan 9,09 % tidak dapat dinilai. Nilai tengah hitung sel CD4(+) dan viral load sebesar 116 (6 - 274) sel/mm3 and 104.000 (385 - 326.595) kopi/ml. Resistensi secara genotipik ditemukan pada seluruh pasien gagal terapi. Berdasarkan rejimen antiretrovirus yang diterima, ditemukan manifestasi resisten terhadap rejimen lamivudine (90%), tenofovir (83%), nevirapine (100%) dan efavirenz (100%). Menarik untuk diperhatikan bahwa tidak ditemukan manifestasi resistensi terhadap zidovudine, termasuk pada empat pasien HIV/AIDS yang mendapatkan zidovudine dalam rejimen terapinya. Mutasi NRTI yang banyak ditemukan adalah M184VI dan K65R, sedangkan mutasi NNRTI adalah Y181CFGVY, K103N, A98AG, E138GQ dan G190AGS. Tidak ditemukan mutasi mayor terhadap PI.
Kesimpulan : Pada penelitian ini ditemukan proporsi resistensi obat HIV yang cukup tinggi. Hal ini memperkuat urgensi monitoring virologi, survey resistensi obat HIV serta akses pilihan terapi yang sesuai pada kasus gagal terapi.
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Background : The administration of highly active antiretroviral therapy (HAART) has rapidly increased in Indonesia since 2004. The emergence of HIV-1 drug resistance, however, may limit the benefits of antiretroviral therapy in settings with limited laboratory monitoring and drug options. The availability of

data concerning resistance towards NRTI, NNRTI, and PI will be beneficial for the national HIV/AIDS prevention and control program.

Objective : To determine genotypic resistance profiles in HIV-1 infected patients failing first line therapy.

Methods : HIV drug resistance mutations were assessed among patients from RSUPN Dr. Ciptomangunkusumo, Jakarta, following failure of their first line antiretroviral therapy. Virology failure was defined as value > 200 copies/ml after six months therapy. Genotypic resistance results and HIV-1 subtype were interpreted by Viroseq and Stanford DR database.

Results : A total of 11 adults were included. Median (IQR) age was 31 years, 54,55 % were male and mode of transmission were heterosexual (45,45 %), MSM (9,09 %), IVDU (27,27 %) and unknown (18,18 %). Opportunistic infections were found in 72,73% patients and TB were the most common infection. Only 27,27 % patients have good adherence. HIV subtypes were 81,81 % CRF01_AE, 9,09% C and 9,09 % undefined. Median (IQR) CD4(+) T-cell count and HIV-RNA were 116 (6 - 274) cells/mm3 and 104.000 (385 - 326.595) copies/ml, respectively. All patients with virological failure were resistant to at least one antiretroviral drug. Genotypic resistance towards the antiretroviral drugs being used was observed in lamivudine (90%), tenofovir (83%), nevirapine (100%) dan efavirenz (100%). It is interesting that no zidovudine resistance were found, including in four patients receiving zidovudine in their HAART. The common NRTI mutations were M184VI and K65R, while NNRTI mutations were Y181CFGVY, K103N, A98AG, E138GQ and G190AGS. No mayor PI mutations were found.

Conclusion : Our study found a high proportion of drug resistance and supports the need for appropriate virology monitoring and HIV drug resistance survey in clinical practice and access to drug options in case of virology failure.