Title	ASSOCIATION OF HLA GENOTYPES AND ABACAVIR NEVIRAPINE AND STAVUDINE INDUCED ADVERSE DRUG REACTIONS: A SYSTEMATIC REVIEW AND META- ANALYSES
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ABSTRACT

Introduction: Antiretroviral therapy has substantially decreased mortality and morbidity from HIV infection. However, these therapeutic response and to drug therapy is compromised by drug resistance, poor patient adherence and adverse drug reaction (ADR). Their ADR include hypersensitivity reactions (HSR) (3-50%), lipoatrophy and lipodystrophy (59%), hepatotoxicity (2-18%), and neuropathy (20-57%). Among the previously mention ADRs, there are genetic linkages associated with antiretroviral drug therapy. Recently, several studies implicated a possibility that genetic factors may play an important role in its adverse drug reactions (ADR), particularly the polymorphic human leukocyte antigen (HLA) genotypes. The adverse drug reactions induced by certain anti-HIV drugs such as abacavir, nevirapine, and stavudine may also be associated with some HLA genotypes as shown in recent studies. However, these associations remain inconsistent. This study aims to systematically review and quantitatively synthesize an association between HLA genotypes and abacavir and nevirapine and stavudine -induced ADRs.

Methods: We searched for studies investigating the association between HLA genotypes and abacavir and nevirapine and stavudine induced ADRs and

providing sufficient information on frequency of carriers of HLA genotypes among cases and controls. Meta-analysis with a random-effects model was performed.

Results: There were 9, 9 and 2 studies included in our meta- analysis for abacavir, nevirapine, and stavudine, respectively. Odds ratio (OR) and 95% confidence interval (95% CI) for HLA-B*5701 and abacavir-induced HSR was 157.91 (95% CI = 31.99-779.40). For HLA-Cw*04 and nevirapine-induced skin reaction, ORs were 2.66 (95% CI = 1.88 – 3.76). For HLA-B*4001 and stavudine-induced lipodystrophy, we did not find any statistically significant association between association between HLA-B*4001 and stavudine-induced lipodystrophy (overall OR = 3.13; 95% CI = 0.40-24.14). However, the association between HLA-B*4001 and stavudine-induced lipodystrophy was significant in Thai population (OR = 9.44; 95% CI = 2.04-43.60).

Conclusions: We found a strong association between the HLA-B*5701 and abacavir-induced HSR in White and Asian populations. These results were supporting the US-FDA recommendations for screening HLA-B*5701 allele in patients before starting an abacavir therapy among high risk populations. For HLA-Cw*04 and nevirapine-induced skin reaction and HLA-B*4001 and stavudine-induced lipodystrophy in Thai populations, more studies are required.