

Type: Poster Presentation

Final Abstract Number: 43.230

Session: Poster Session III

Date: Saturday, March 5, 2016

Time: 12:45–14:15

Room: Hall 3 (Posters & Exhibition)

Genetic variability and molecular evolution of hepatitis B virus in HIV co-infected patients on lamivudine based anti-retroviral therapy: A 5 year longitudinal studyE. Amponsah-Dacosta¹, G. Selabe^{1,*}, M.P. Gededzha¹, J.N. Rakgole¹, J. Blackard², J. Mphahlele¹¹ Sefako Makgatho Health Sciences University, Pretoria, South Africa² University of Cincinnati College of Medicine, Cincinnati, USA

Background: Reports on the concomitant impact of HIV infection and long term cross-reactive HAART on the genetic variability and molecular evolution of HBV over time are limited. This longitudinal study retrospectively investigated the molecular characteristics of chronic HBV in HIV co-infected patients on lamivudine (3TC)-based HAART, over the course of a 5 year period.

Methods & Materials: Four HIV co-infected patients consecutively recruited and followed-up from 2004 to 2008 were screened for complete hepatitis B seromarkers and viral loads determined. HBV full length genome isolates were amplified and directly sequenced from serial samples. Evolutionary analyses were then conducted and prediction of phenotypic drug resistance and escape mutations carried out.

Results: All patients exhibited persistent chronic HBV infection at baseline, prior to 3TC-based HAART initiation and over the course of follow-up. Based on phylogenetic clustering, it could be determined that all but one patient were infected with HBV subgenotype A1. The greatest evolutionary distance determined was 0.008 (~25 base substitutions within the 3.2 Kb genome) after 5 years of persistent chronic HBV infection with exposure to 3TC-based HAART. Positive selection pressure, based on dS/dN ratios <0.05 , was evident within structural genes (pre-S/S and Pre-C/C). It was noted that the *pol* ORF in all study patients' isolates was relatively variable prior to HAART initiation at baseline and during the course of follow-up.

Conclusion: Overall, HBV exhibited limited evolutionary rates even after 5 years, which could be attributed to the minimal genetic diversity observed. The impact of current TDF-based HAART regimens on the molecular evolution of HBV in HIV co-infected South African patients should be investigated.

<http://dx.doi.org/10.1016/j.ijid.2016.02.966>

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Elevation in liver enzymes are associated with increased IL-2 and may predict severe outcomes of dengue virus infection in a Sri Lankan cohortT. Senaratne^{1,*}, J. Carr², F. Noordeen³¹ University of Peradeniya, Peradeniya, Sri Lanka² School of Medicine, Flinders University, Adelaide, Australia³ University of Peradeniya, Kandy, Sri Lanka

Background: A synergistic effect of host genetic factors, host immunity and the virulence of dengue viruses (DENV) contribute to the pathogenesis of DENV infections. In severe DENV infections, the hepatic transaminase AST level increases more than the hepatic transaminase ALT.

IL-2 and TNF- α are both elevated in DENV infection as a part of the body's early response to infection. The objective was to assess the correlation between changes in IL-2 and TNF- α levels with changes in liver enzymes in dengue patients with varying clinical severity.

Methods & Materials: A total of 67 DENV infected patients (DF=24 and DHF=43) either confirmed by ELISA or RT-PCR from July 2011 to February 2012 from General Hospital Kandy were selected for the IL-2 and TNF- α evaluation using a single analyte ELISArray (Qiagen, Germany). Clinical, haematological parameters and hepatic transaminases (AST and ALT) were recorded on admission. Five mL of blood was collected from DENV suspected patients on fever days 5 or less (onset of fever was considered as day 1).

Results: Of the patients, 47.76% (n=32) showed AST: ALT >2 . AST: ALT mean \pm SD among DF was 1.64 ± 0.74 U/L while it was 3.18 ± 4.50 U/L for DHF/DSS patients.

No significant correlation was noted between AST: ALT and TNF- α and also with IL-2. A significant positive linear correlation was observed between AST and IL-2 levels ($r = 0.31$ $p = 0.01$) and also between ALT and IL-2 levels ($r = 0.27$ $p = 0.02$). No significant correlation was noted between AST and TNF- α and ALT and IL-2.

Conclusion: Almost half of our study population showed AST: ALT >2 indicating acute changes in liver function and the potential for liver derangement due to DENV infection. There was a statistically significant positive correlation between the IL-2 with AST and ALT levels, although no correlation was noted between AST and ALT with TNF- α . The positive correlations between elevations of AST and ALT with IL-2, and the association of higher levels of these factors in DHF/DSS compared with DF suggest that these measurements may be useful predictors for the progression of DENV infection to severe DF/DHF.

<http://dx.doi.org/10.1016/j.ijid.2016.02.967>

