DC-SIGN and L-SIGN repeat-region polymorphisms influence HIV-1 disease progression in slow and rapid progressors among perinatally-infected children in India

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Background: Among human host factors known to modulate HIV disease progression, the C-type lectins, dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin, DC-SIGN and the liver/lymph node-specific L-SIGN have been poorly described in children with HIV. We aimed to study the exon 4 repeat-region polymorphisms, and assess the impact of DC/L-SIGN homozygous and heterozygous genotypes among pediatric slow and rapid progressors.

Methods & Materials: We defined slow progressor children as perinatally-infected, asymptomatic, with known HIV infection for >10yrs, ART-naive, and CD4>500 cells/mm³ and rapid/pronormal progressors as HIV infection<10 years, on ART, CD4<500 cells/mm³. Genomic DNA isolated from whole blood was genotyped for DC/L-SIGN homozygous and heterozygous genotypes among pediatric slow and rapid progressors.

Results: Among 25 slow progressors included, mean age was 10.8±2.42 years, 64% females, median CD4 count was 751 cells/mm³ (IQR 575–1036.75) and viral load, 4.36 log copies/ml (IQR 4.09–4.84). Among 40 rapid progressors, mean age was 6.07±2.4 years, 45% females, median CD4 was 462.5 cells/mm³ (IQR 291–663) and viral load, 5.42 log copies/ml (IQR 4.97–5.95). The exon-4 repeat-region DC-SIGN polymorphism was not observed in our population as all samples showed 7/7 homozygous DC-SIGN genotype. In the L-SIGN repeat region, eight genotypes were found. The total L-SIGN heterozygosity in slow (7/5, 7/6, 9/5, 9/6 and 9/7 genotypes) and rapid (6/5, 7/5, 7/6, 9/5, 9/6 and 9/7 genotypes) progressors was 76% and 45% respectively (P=0.02; OR=3.87; 95%CI 1.3–11.7). Rapid progressors had a significantly higher occurrence of 7/7 homozygous L-SIGN genotype (P=0.03; OR=3.1; 95%CI 1.16–10.6). The L-SIGN allele frequency in slow progressors was 14% for allele 5, 14% for allele 6, 54% for allele 7 and 18% for allele 9. L-SIGN alleles 6 and 7 were significantly more frequent in rapid progressors than slow progressors (P=0.03, OR=0.16, 95%CI=0.03–0.8 and P=0.03, OR=2.24, 95%CI=1.07–4.72 respectively).

Conclusion: This is the first study to determine the DC-SIGN and L-SIGN polymorphisms in HIV-1 positive children in India. While heterozygous DC-SIGN genotypes were not seen in this population, the higher prevalence of heterozygous L-SIGN genotypes among slow progressors suggests their protective role in HIV disease progression among children in India.

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CD4 Levels >350 cell/μl at initiation of option B+ Predict retention in care amongst mothers in urban health facilities in Uganda

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Background: Uganda like most countries is providing Option B+ to HIV+ mothers. However, patients who start ART with a high immunity are often thought to be poorly retained in care (Tayler et al, 2010). Poor retention in care predicts poorer survival with HIV infection (Thomas et al, 2007). Patients with CD4 >350 cells/μl are asymptomatic and presumed to be comfortable with their status quo. The study hypothesized that CD4 <350 cell/μl at initiation of Option B+ would also predict higher retention compared to CD4 >350 cell/μl.

Methods & Materials: A retrospective cohort study was done on mothers that were initiated on Option B+ between December 2012 and January 2013 in six urban public health facilities in Uganda. Patients were observed starting at Option B+ initiation to patient outcome such as at death, transfer out, loss to follow-up and 12 months after initiation. Only mothers whose CD4 was recorded at initiation of Option B+ were considered for analysis.

Results: A total of 601 mothers with mean age 25.0 years (95% CI: 21-28) were enrolled and of these 65% were still in care one year after option B+ initiation. At the time of enrollment, 313 mothers had CD4 > 350, 74 had CD4 <350 while 212 had no CD4 done. Majority (80%) mothers had no prior exposure to ARVs at the time of initiation. There was a significant relationship between retention and prior treatment, age of mother >20yrs, and CD4 levels. After regression modelling, the odds of being in care among CD4 >350 were 2.21 (p=005) times more likely to stay in care compared to those with lower CD4. There was no significant relationship between retention and age or prior ART.

Conclusion: Contrary to the study hypothesis and knowledge among the general HIV patients, our study revealed that women started on option B+ with CD4 >350 cell/ul were 2.21 times more likely to stay in care, one year after ART initiation.

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