Prevalence and Incidence of Liver Dysfunction in Asian Children with Human Immunodeficiency Virus

Linda Auprich, MD, Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand, 1. The Golden Group, Chiang Mai University, Chiang Mai, Thailand, 2. Thammasat University, Bangkok, Thailand, 3. National Pediatric Hospital, Phnom Penh, Cambodia, 4. The Khmer Institute, University of Sydney, Australia, 5. Children’s Hospital, University of Sydney, Australia, 6. National Hospital of Pediatrics, Hanoi, Vietnam, 7. National Center for HIV/AIDS, Dermatology and STDs, Bangkok, Thailand, 8. National Center for HIV/AIDS, Dermatology and STDs, Bangkok, Thailand, 9. National Center for HIV/AIDS, Dermatology and STDs, Bangkok, Thailand, 10. Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, 11. Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 12. Children’s Hospital, Chulalongkorn University, Bangkok, Thailand, 13. Children’s Hospital, Siriraj Hospital, Mahidol University, Bangkok, Thailand, 14. Children’s Hospital, Chulalongkorn University, Bangkok, Thailand, 15. Children’s Hospital, Prince of Wales Hospital, Sydney, Australia, 16. Pediatric Institute, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, 17. Chiang Mai University Hospital, Chiang Mai, Thailand, 18. Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, 19. Penang Hospital, Penang, Malaysia, 20. TREAT Asia/IeDea – The Foundation for AIDS Research, Bangkok, Thailand

Background

Chronic liver disease has emerged as an important problem in HIV-infected adults, especially in the Asia-Pacific region where hepatitis B and C are endemic.

Data on the incidence and prevalence of liver dysfunction among children with HIV infection are sparse. Many studies report the proportion of patients with abnormal liver tests, but a limited number provide data on the incidence of liver dysfunction. The use of liver biomarkers, including aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (APRI) and FIB-4 index, has been advocated to identify children at risk of developing severe liver disease.

A retrospective data analysis: data were from 18 clinical sites in 6 Asian countries participating in the TREAT Asia Pediatric HIV Observational Database (TAP-HOD), which is a multicenter study of children and adolescents living with HIV in Asia, enrolled before 18 years of age, established in 2008.

Data transfer to a central data management and biostatistical analysis center is performed at 6-month intervals. Data transferred up to September 2012 were used for this analysis.

Inclusion criteria were: 1) children and adolescents with confirmed diagnosis of HIV infection, 2) aged between 2-18 years at the time of first-line cART initiation, 3) receiving cART - defined as a regimen of ≥3 antiretroviral agents, and 4) with baseline ALT tests within six months prior to cART.

Results

Prevalence

- Prior to cART, the prevalence of ALT ≥5 times the upper limit of normal (ULN) was 1.9%.
- The median APRI score was 0.34 (IQR 0.18-0.67) and 8.5% of children had an APRI >1.5 pre-cART.
- Although liver chemistries are inconsistently available, they represent a more accessible method of assessing liver dysfunction.

Incidence

- The incidence of ALT ≥5ULN after cART was 0.40/1,000 person-months (PM; 95% CI 0.27-0.61).
- The incidence after cART of APRI scores >1.5 was 0.77/1,000 PM, and for FIB4 index scores >1.3 was 0.44/1,000 PM.
- Two (0.2%) met Hy’s law, defined as ALT ≥3ULN and total bilirubin ≥2ULN.

Discussion

- The potential toxicities of life-long CART and HIV infection on organ function are a concern among perinatally HIV-infected children in resource-limited settings who are now growing up into adolescence; especially when known hepatotoxic antiretroviral agents were commonly prescribed in the setting of severe immunosuppression.

- Although liver chemistries are inconsistently available, they represent a more accessible method of assessing liver dysfunction when compared to other non-invasive evaluations (e.g., liver fibroscan).

- The prevalence of transaminase elevation reflecting liver injury or inflammation in our study were comparable to a previous study on HIV-infected children.

- The potential toxicities of life-long CART and HIV infection on organ function are a concern among perinatally HIV-infected children in resource-limited settings who are now growing up into adolescence; especially when known hepatotoxic antiretroviral agents were commonly prescribed in the setting of severe immunosuppression.

Conclusion

- A low incidence of liver dysfunction in this regional, observational pediatric HIV cohort was observed.
- Increased liver transaminases after cART initiation was seen in a small number of cases.
- Use of liver-related biomarkers may help identify those at higher risk of active disease and guide further clinical evaluation.

Acknowledgements

The TREAT Asia Pediatric HIV Observational Database is an initiative of TREAT Asia, a program of amfAR, The Foundation for AIDS Research, with support from the U.S. National Institutes of Health’s National Institute of Allergy and Infectious Diseases, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and National Cancer Institute as part of the International Epidemiology Observational Studies Collaboration (I-EOS). The Databases to Evaluate AIDS (IeDEA) is an initiative of the National Institute of Allergy and Infectious Diseases, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and National Cancer Institute. The IeDEA Asia Pacific Regional Initiative is sponsored by the TREAT Asia/IeDea – The Foundation for AIDS Research, Bangkok, Thailand.

References