Relevance of Hepatitis B Virus genotypes of HBV/HIV coinfected Patients from Sudan

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Overview

- Global distribution of HBV genotypes and subgenotypes
- Impact of HBV genotypes on disease progression and therapy (in Africa)
- Funding of African research
- HBV genotypes in Africa (Khartoum/Sudan)
- HBV and HBV/HIV coinfection in Khartoum/Sudan

Hepatitis B virus

- HBV has been classified phylogenetically into 9 genotypes
  A, B, C, D, E, F, G, H, I
- Potential 10th genotype "J" (single isolate)
- Genotypes must show nucleotide divergence of greater than 7.5 %
- Subgenotypes have at least more than 4 % genomic divergence
- Over 35 Subgenotypes in A-D, F, H and I, but not in E and G
- (Sub)-genotypes show distinct geographical distributions

Clinical differences of HBV sub/genotypes (selection)

- HBV genotypes A1, C, B2-B4, F1 show higher risk of serious complications during chronic HepB, like cirrhosis and HCC, compared to A2, B1, B5
- South Africans infected with A1 have 4.5 higher risk for HCC development (6.5 years earlier) compared to other genotypes
- Similar results from A1 infected persons in Southern India.
- Genotype F is often seen during sexual transmission with vaccine breakthrough (anti-HBs lower than 100 IU/L) and severe acute and chronic hepatitis B.
- Genotypes A and B respond better to interferon-based therapy, compared to genotype C or D

For review see: Kramvis, A. Intervirology 2014; 57:141-150

Disclosures

- D. Glebe received a research grant from GILEAD
HBV genotypes summary

Table 1. Comparison of Clinical, Virological and Geographical Distribution Differences among HBV Genotypes

<table>
<thead>
<tr>
<th>AL D</th>
<th>AL A, E, D'</th>
<th>B, C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ins:</td>
<td>Others above</td>
<td>Short</td>
</tr>
<tr>
<td>Allelic</td>
<td>Early</td>
<td>Very early</td>
</tr>
<tr>
<td>Distribution</td>
<td>Western Europe</td>
<td>Africa</td>
</tr>
<tr>
<td>Allelic</td>
<td>Low</td>
<td>Intermediate to high</td>
</tr>
</tbody>
</table>

The African perspective

- Africa is the 2nd largest continent
- Covers 20% of the world's land area
- Currently 54 countries
- Population: 1.1 billion (2013)
- 15% of the world's total human population
- Has the youngest population of all continents
- 50% of Africans are younger than 20 years

Hepatitis B – from an African perspective

- Improvement of preventive, diagnostic and therapeutic intervention is urgently needed, esp. for indigenous population

Improving Research in African countries

- DFGs “Africa initiative” to study “neglected infectious diseases” in Africa
- Consolidation of mutually beneficial equal partnerships between German and African researchers.
- Provide support and funding for the academic and professional careers of young African researchers in their home countries in order to contribute to building research capacities in Africa.
- Strengthens research networks within Africa
The main goal of the initiative is to allow for African scientists to work on elucidating fundamental biological principles of neglected tropical diseases relevant for their countries, including indigenous population.

So far, 30 projects are being funded with 71 partners in 20 African countries.

Hepatitis B is a neglected infectious disease in Africa.

Project for cooperation of labs from South-Africa, Sudan and Germany started in 2009.

Hepatitis B exposure rate: 47% - 78%

HBsAg-prevalence: 7% - 18.7%

The Regional committee for the WHO Eastern Mediterranean Region (EMR), to which Sudan belongs, urged member states to:

- Improve the epidemiological surveillance systems, develop a hepatitis registry and implement sero-surveys in order to produce reliable data to guide prevention and control measures and monitor impact of preventive strategies.

Build up of a molecular biology lab in Khartoum/Sudan (including equipment, personnel and consumables funded by DFG).

Training of Sudanese PhD students and technicians was done in Johannesburg, South Africa (lab of Anna Kramvis).

A cross-sectional, laboratory based study was conducted to molecular analyze chronic hepatitis B cases.

We collected 100 sera from HBV-monoinfected patients from medical clinics at IbnSina Hospital, Soba University Hospital and Khartoum Teaching Hospital in Khartoum State between August 2008 and March 2009.

Distribution of HBV genotypes in Africa

Sudan

South Africa

Genotypes of HBV-monoinfected patients in Sudan

HBV genotypes in Sudanese blood donors

HBV genotypes in Sudanese liver disease patients and asymptomatic carriers (our study)
HBV/HIV coinfections in Africa

- HIV infection is a serious health problem in Africa.
- 34 Mio HIV-infected persons globally, 69% reside in Sub-Saharan Africa.
- HBV/HIV co-infection causes rapid progression of liver disease, cirrhosis, and HCC. HIV prevalence in Sudan is 0.52% (2011).
- No study on HBV/HIV coinfection in Sudan has been done before.
- Cross-sectional study in Khartoum, Sudan with 358 (100%) treatment-naive HIV-positive adults.
  - 62% showed evidence of current or past HBV infection.
  - 42 patients (11.7%) HBsAg positive.
  - No difference of HBV exposure rate between HBV-mono or HBV/HIV co-infected persons (similar to other Sub-Saharan countries).
  - Mode and timing of transmission of HBV in Africa is independent to HIV.
  - HBV in childhood, long before exposure to HIV.

Yousif et al., IJID 2014, in press; Mudawi et al., IJID 2014, in press.

HBV/HIV coinfections in Khartoum/Sudan

- Cross-sectional study in Khartoum, Sudan with 358 (100%) treatment-naive HIV-positive adults.
  - 62% showed evidence of current or past HBV infection.
  - 96 patients (26.8%) were HBV-DNA positive, of those 42 patients (11.7%) HBsAg positive.
  - 54 patients (15.1%) HBsAg negative → indicating occult HBV infection.

Yousif et al., IJID 2014, in press; Mudawi et al., IJID 2014, in press.

Occult hepatitis B virus infection (OBI)

- OBI: absence of HBsAg and low viral replication of HBV (< 200 IU/ml HBV DNA).
- Usually referred to “anti-HBc-only” or “isolated anti-HBc”.
- OBI can reactivate during immunosuppression (e.g. caused by HIV/AIDS).
  - Can cause serious (fulminant) liver disease.
  - HIV treatment in case of HIV/HBV co-infection should include Tenofovir.

Yousif et al., IJID 2014, in press; Mudawi et al., IJID 2014, in press.

Conclusions

- HBV has been classified phylogenetically into at least 9 genotypes and over 35 (sub)-genotypes.
- (Sub)-genotypes show distinct geographical distributions.
- In Africa, genotypes A, D and E prevail, in Khartoum D>E>A.
- Differences in clinical manifestation and response to antiviral therapy.
- Genotyping can predict risk for development of severe liver disease and response to antiviral therapy.
- HBV/HIV coinfections should be carefully monitored.
- In Khartoum, 26% of HIV-infected adults are HBV coinfected.
- 15% of HIV-infected adults have an OBI.
- Support and funding of African research labs is urgently needed.

Yousif et al., IJID 2014, in press; Mudawi et al., IJID 2014, in press.
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2015 International Meeting
Molecular Biology of Hepatitis B Viruses
DECEMBER 4 — 6, 2015

Location:
Dolce Bad Nauheim
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