A Retrospective Nationwide Study on Hepatitis B Epidemiology and Genotypes; The Canadian Hepatitis B Network


Canadian Liver Meeting, February 9 – 11, 2018

Financial Interest Disclosure
(over the past 24 months)

Name: Dr. Carla Coffin

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSK</td>
<td>advisory board, consultant, research support (Canadian Institutes of Health Research Industry partnered funding)</td>
</tr>
<tr>
<td>Gilead Sciences</td>
<td>advisory board, consultant, research support (investigator initiated), clinical trial</td>
</tr>
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</table>
Background/Aims

- Most recent published epidemiologic data on hepatitis B in Canada are either single-centre / large urban referral centers or in Canadian indigenous population
- CanHepB: Multisite Canadian network focused on advancing HBV care and research
- Aim: To obtain an overview of demographic and clinical data of HBV patients followed nationwide


- 21 sites
- CASL endorsement
- Academic & community, Provincial laboratories
- National Microbiology Laboratory, Winnipeg
- University of Calgary, Alberta
  - Dedicated research coordinator, Data Custodian
  - Ethics, Data Transfer Agreements / Data management plan

* Represent other ID / Hepatology/GI at their site
Mission Statement

• To improve treatment and control of hepatitis B in Canada.

• To advance our understanding of hepatitis B disease processes and natural history.

• To promote collaboration on national HBV studies and databases.

Methods

• Retrospective cohort study
• 7 Provinces, 21 sites
• N=5157 unique patient records
• N= 2138 Alberta Health Services Administrative Data for 4 clinics (2010-2017): comorbidities, hospitalizations, labs
• Available data elements
  – Demographics (Age, Sex, Ethnicity)
  – HBV DNA, HBV E Antigen / HBV E Antibody, ALT
  – Antiviral therapy
  – Administrative data labs: HBA1C, eGFR, Fasting Lipid (Alberta)
  – Genotype (retrospective or prospectively done at National Microbiology Laboratory, include data from previous study\(^1\))
• Data summarized via frequencies and percentages for categorical variables and median and quartiles for continuous variables (P<0.05)

1. Congly S et.al., Liver Intl. 2013
Comparison of HBV Patient Demographics

<table>
<thead>
<tr>
<th>Province (N)</th>
<th>Median Age</th>
<th>Male (%)</th>
<th>Asian (%)</th>
<th>Caucasian (%)</th>
<th>Black (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia (N=1186)</td>
<td>49</td>
<td>59 %*</td>
<td>92 %*</td>
<td>4 %*</td>
<td>1 %*</td>
</tr>
<tr>
<td>Alberta (N=1342)</td>
<td>42</td>
<td>51 %*</td>
<td>73 %*</td>
<td>10 %*</td>
<td>15 %</td>
</tr>
<tr>
<td>Saskatchewan (N=124)</td>
<td>44</td>
<td>62 %</td>
<td>63 %</td>
<td>15 %</td>
<td>16 %</td>
</tr>
<tr>
<td>Manitoba (N=1064)</td>
<td>44</td>
<td>53 %</td>
<td>69 %</td>
<td>7 %*</td>
<td>22 %</td>
</tr>
<tr>
<td>Ontario (N=1093)</td>
<td>41</td>
<td>58 %</td>
<td>47 %*</td>
<td>21 %*</td>
<td>28 %*</td>
</tr>
<tr>
<td>Quebec (N=120)</td>
<td>48</td>
<td>60 %</td>
<td>10 %*</td>
<td>68 %*</td>
<td>12 %</td>
</tr>
<tr>
<td>Nova Scotia (N=11)</td>
<td>55</td>
<td>82 %</td>
<td>40 %</td>
<td>50 %*</td>
<td>10 %</td>
</tr>
<tr>
<td>National averages</td>
<td>44</td>
<td>55 %</td>
<td>66 %</td>
<td>14 %</td>
<td>17 %</td>
</tr>
<tr>
<td>n (total known) = 5168</td>
<td>2229</td>
<td>491</td>
<td>571</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* = P<0.05

Interprovincial differences: more Asian especially in BC

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Comparison of HBV Genotypes in Canada (N=951)

<table>
<thead>
<tr>
<th>Province</th>
<th>n=</th>
<th>A %</th>
<th>B %</th>
<th>C %</th>
<th>D %</th>
<th>E %</th>
<th>F %</th>
<th>G %</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>139</td>
<td>8%*</td>
<td>47%*</td>
<td>32%</td>
<td>12%</td>
<td>2%*</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Alberta</td>
<td>484</td>
<td>20%</td>
<td>27%</td>
<td>26%</td>
<td>19%</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Sask.</td>
<td>15</td>
<td>7%</td>
<td>40%</td>
<td>33%</td>
<td>13%</td>
<td>7%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Manitoba</td>
<td>201</td>
<td>43%*</td>
<td>12%*</td>
<td>17%*</td>
<td>15%</td>
<td>10%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Ontario</td>
<td>130</td>
<td>2%*</td>
<td>45%*</td>
<td>42%*</td>
<td>8%*</td>
<td>2%*</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Quebec</td>
<td>119</td>
<td>9%*</td>
<td>31%</td>
<td>36%</td>
<td>16%</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Total</td>
<td>1088</td>
<td>19%</td>
<td>30%</td>
<td>28%</td>
<td>16%</td>
<td>7%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

* = P<0.05

Interprovincial differences: more Genotype B in BC

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Results
Region Specific: HBV Genotypes in Canada

Comparison of HBeAg status, antiviral treatment and fibrosis data of HBV patients in Canada

<table>
<thead>
<tr>
<th>Province</th>
<th>% HBeAg +</th>
<th>% &gt;F2 Fibrosis</th>
<th>% &gt; F3 – F4 Fibrosis</th>
<th>Antiviral Therapy (if known)</th>
<th>% LMV</th>
<th>% TDF</th>
<th>% ETV</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>34%*</td>
<td>23%</td>
<td>9%</td>
<td>57%*</td>
<td>54%</td>
<td>13%*</td>
<td></td>
</tr>
<tr>
<td>Alberta</td>
<td>22%</td>
<td>29%*</td>
<td>13%v</td>
<td>13%*</td>
<td>54%</td>
<td>25%*</td>
<td></td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>20%</td>
<td>N/A</td>
<td>N/A</td>
<td>8%</td>
<td>75%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Manitoba</td>
<td>14%*</td>
<td>9%</td>
<td>9%</td>
<td>26%</td>
<td>82%*</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>Ontario</td>
<td>20%</td>
<td>14%*</td>
<td>3%*</td>
<td>54%*</td>
<td>24%*</td>
<td>4%*</td>
<td></td>
</tr>
<tr>
<td>Quebec</td>
<td>25%</td>
<td>N/A</td>
<td>N/A</td>
<td>6%*</td>
<td>78%*</td>
<td>3%*</td>
<td></td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>100%*</td>
<td>N/A</td>
<td>N/A</td>
<td>13%</td>
<td>50%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>National averages</td>
<td>24%</td>
<td>23%</td>
<td>9%</td>
<td>31%</td>
<td>51%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>n (total known)</td>
<td>2860</td>
<td>452/1988</td>
<td>183/1988</td>
<td>551/1774</td>
<td>913/1774</td>
<td>320/1774</td>
<td></td>
</tr>
</tbody>
</table>

* The most common antiviral therapy used was TDF
* Interprovincial differences: more lamivudine in BC (some on multiple Rx)  
  * = P<0.05
Administrative Data – Alberta Health Services
Comorbidities

• N = 2138 HBV patients, median Age 41 y, 53%
  – 4 clinics (Community mix GI/Liver, Academic Infectious
    Diseases, Hepatology and Liver Transplant)
• In those tested:
  – median DNA 2.4 log, 83% HBeAg (-), median ALT 27 U/L
  – 5% Type 2 DM (HBA1C), 2.6% eGFR <60, most normal
    lipid profile
• 71% ambulatory care visits liver related, 27%
  hospitalized, 4% liver related (median LOS 3 days)
  – Inter-cohort variation in comorbidities reflect expertise /
    interest (i.e., HCC, transplant, pregnancy etc.)

CS Coffin, A Shaheen, KE Doucette, RJ Bailey, M-M Ma, Abstract accepted EASL 2018

Conclusion

• First report from the Canadian HBV Network
• Majority Asian, Genotype B or C
  – Demographics similar to data in the US HBV
    research network (all untreated)
• Retrospective / Cross-sectional study
  – ~13% >Stage 3 Fibrosis
  – Majority on Tenofovir therapy
• Provides a snapshot in Canada of similarities
  and region-specific differences in HBV patients
• Large-scale high quality prospective data
  collection ongoing
Online portal
http://partnernet.ucalgary.ca/research/liver/SitePages/Home.aspx

• Web-based Clinician Intake Form (“live” ~June 2017)
• Retrospective “data dump”
• Prospective data entry ongoing

https://evisualuat.ucalgary.ca/#/workbooks/343/views

Acknowledgements

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Laval University: Ms. Chantal Legris

Memorial University: Mr. Chris Corkum

Gilead Sciences, Canada, - Mr. Mark Khan, Sr Manager Medical Affairs

Alone we can do so little, together we can do so much, Helen Keller
Mission Statement

• To improve treatment and control of hepatitis B in Canada.

• To advance our understanding of hepatitis B disease processes and natural history.

• To promote collaboration on national HBV studies and databases.

Thank you – Questions?
Variations in Current HBV Management

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Coverage / Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleos(t)ide Analog therapy</td>
<td>Tenofovir, Entecavir in Alberta &amp; Quebec, Ontario (2016). Not in British Columbia until fail LAM</td>
</tr>
<tr>
<td>Pegylated-Interferon therapy</td>
<td>Not reimbursed in Ontario or British Columbia</td>
</tr>
</tbody>
</table>
| HBV Vaccination Schedule       | - Infant schedule (birth or 2 months) – New Brunswick, British Columbia and territories  
                              |  - Pre-adolescent in other 8 provinces                                            |
| Quantitative HBV surface antigen| - Available in Ontario (larger centers), Alberta and Quebec provincial laboratories |

* Variation in demographics due to regional immigration and migration patterns (i.e., French vs. non-French speaking etc.)
Background – HBV Epidemiology

~240 million HBV? 1-3

~200,000 HBV? 2-4

1. WHO. WHO factsheet (2017)
2. Reditt et al., Hepatitis B Can Fam Physician. 2015;
4. Wong WL et al., Liv Int 2011; Can J Gastro 2013

Background

Canada’s *universal* health-care system

- Canada Health Act – Medicare
- Federal and provincial publicly funded health care
  - 10 province + 3 territories = 13 insurance plans
  - Direct federal health care for First Nations, Inuit, Canadian Forces, Federal penitentiaries, some refugee groups
  - “Reasonable access to medically necessary services”
- “Medically necessary” is not defined in the Canada Health Act
  - Significant variation in anti-HBV prescription medication coverage
  - Variation in childhood HBV immunization schedules

www.canada.ca / health / health care system
Characterization of hepatitis B virus genotypes and quantitative hepatitis B surface antigen titres in North American tertiary referral liver centres

Stephen E. Congly, Philip Wong, Said A. Al-Butail, Karen Doucette, Scott K. Fung, Peter Ghali, Kevin Fonseca, Robert P. Myers, Carla Olsowy and Carla S. Coffin

Liver International 2013

The North American Hepatitis B Research Network

The North American Hepatitis B Research Network is currently seeking patients for a multi-center prospective studies of the natural history of chronic hepatitis B. Details of the entry criteria for these studies can be obtained from the clinical centers outlined on the map below.

http://www.hepbnet.org
### Summary of 630 CHB Patients in Canadian Liver Clinics

<table>
<thead>
<tr>
<th>Clinic</th>
<th>Median Age</th>
<th>Male (%)</th>
<th>Asian (%)</th>
<th>HBe Ag+ (%)</th>
<th>Inactive CHB (%)</th>
<th>Stage &gt;F2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calgary n=340</td>
<td>42</td>
<td>55</td>
<td>72</td>
<td>16</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Montreal n=120</td>
<td>43</td>
<td>60</td>
<td>67</td>
<td>25</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Edmonton n=88</td>
<td>34</td>
<td>50</td>
<td>51</td>
<td>14</td>
<td>23</td>
<td>9</td>
</tr>
<tr>
<td>Toronto n=82</td>
<td>48</td>
<td>68</td>
<td>85</td>
<td>39</td>
<td>0</td>
<td>52</td>
</tr>
<tr>
<td>Total n=630</td>
<td>42</td>
<td>57</td>
<td>70</td>
<td>21</td>
<td>11</td>
<td>14</td>
</tr>
</tbody>
</table>

Congly S et al., *Liver Intl*. 2013