Estimating the burden of Hepatitis B in Aboriginal and Torres Strait Islander peoples

Dr Jane Davies
Senior Clinical Research Fellow
Menzies School of Health Research
Physician in Infectious Diseases & General Medicine
Royal Darwin Hospital
Disclosures

Unrestricted educational grant from Gilead Sciences
What do we mean by burden........

- Prevalence of Hepatitis B infection
  - Chronic, acute
  - Pre and post universal vaccination

- Burden
  - Morbidity – genotype likely to be important
  - Mortality – cirrhosis, hepatocellular carcinoma
  - Social impact on individuals
  - Impact on communities
  - Stigma & psychological burden
Chronic HBV prevalence

Mathematical Modeling
  Risk based deterministic

Sero-survey
  Gold Standard

Collating existing data
  National & State & Territory Notifiable disease registers
  Surveillance reports
  Laboratory data
  Data linkage

Chronic HBV prevalence
What do Aboriginal and Torres Strait Islander people think?

- “Only your blood can tell the true story”
- “we have so much blood taken all the time – we want you to use the results you have before asking us for more blood”
- “we want to know the full story about this Hep B before we agree to give more blood – tell us the true story”
ASHM mapping data Indigenous Australians make up 9.3% of those living with chronic hepatitis B in Australia

Graham et al

Table 2.6: Meta-analysis data to estimate the prevalence of CHB in Indigenous adults/pregnant women in Australia before and after universal vaccination. Data from Graham et al. [53]

<table>
<thead>
<tr>
<th></th>
<th>Pooled HBsAg prevalence in adults/pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall (95% CI)</td>
</tr>
<tr>
<td>Pre-2000</td>
<td>6.47% (4.56-8.39)</td>
</tr>
<tr>
<td>Post-2000</td>
<td>2.25% (1.26-3.23)</td>
</tr>
<tr>
<td>Author and year published</td>
<td>Study population</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Barrett 1972</td>
<td>Children Adults</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Gardner 1992</td>
<td>School children, Teachers</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Wood 2005</td>
<td>General age 1-84 years</td>
</tr>
<tr>
<td>Schultz 2008</td>
<td>Pregnant women</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Wood 2008</td>
<td>Pregnant women</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Carroll 2010</td>
<td>Adults</td>
</tr>
<tr>
<td>Dent 2010</td>
<td>Adolescents</td>
</tr>
<tr>
<td>Liu 2012</td>
<td>Pregnant women</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevalence of Hep B by region and Indigenous status 2012 (CDC data)
NT Government Pathology service
92,589 testing episodes
Jan 1998-July 2012

Western Diagnostic Pathology Service
226,336 testing episodes
Dec 1991-July 2012

SA Pathology
28,062 testing episodes
Jan 1998-Jan 2012

346,587 lines of data
Those with no identifying details removed

329,425 testing episodes
Linked to client master index to obtain Indigenous status

247,196 results returned
194,321 unique testing episodes
91,227 unique individuals – dropped if Indigenous status unknown

88,175 individuals for analysis
Cross-sectional analysis

- 2007-2011 inclusive
- 35,633 individuals
- De-identified – unique study number
- Latest result for HBsAg, anti-HBs, anti-HBc with date of test
- DOB, sex, Indigenous status, community of residence
<table>
<thead>
<tr>
<th>Age group</th>
<th>Indigenous</th>
<th></th>
<th></th>
<th></th>
<th>Non-Indigenous</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>tested</td>
<td>ERP</td>
<td>Proportion of ERP tested (%)</td>
<td>tested</td>
<td>ERP</td>
<td>Proportion of ERP tested (%)</td>
<td>tested</td>
<td>ERP</td>
</tr>
<tr>
<td>Under 10 years</td>
<td>78</td>
<td>7924</td>
<td>1:0</td>
<td>71</td>
<td>7326</td>
<td>1:0</td>
<td>82</td>
<td>10678</td>
</tr>
<tr>
<td>10-19 years</td>
<td>996</td>
<td>7290</td>
<td>13:7</td>
<td>1542</td>
<td>6829</td>
<td>22:6</td>
<td>493</td>
<td>9973</td>
</tr>
<tr>
<td>20-29 years</td>
<td>1880</td>
<td>6452</td>
<td>29:1</td>
<td>2233</td>
<td>6423</td>
<td>34:8</td>
<td>1994</td>
<td>15562</td>
</tr>
<tr>
<td>30-39 years</td>
<td>1451</td>
<td>4869</td>
<td>29:8</td>
<td>1400</td>
<td>5015</td>
<td>28:1</td>
<td>2195</td>
<td>14422</td>
</tr>
<tr>
<td>40-49 years</td>
<td>1110</td>
<td>3873</td>
<td>28:7</td>
<td>1105</td>
<td>4135</td>
<td>26:7</td>
<td>1723</td>
<td>13581</td>
</tr>
<tr>
<td>50-59 years</td>
<td>605</td>
<td>2498</td>
<td>24:2</td>
<td>715</td>
<td>2602</td>
<td>27:5</td>
<td>1269</td>
<td>11989</td>
</tr>
<tr>
<td>60-69 years</td>
<td>270</td>
<td>1079</td>
<td>25:0</td>
<td>312</td>
<td>1279</td>
<td>24:4</td>
<td>592</td>
<td>7596</td>
</tr>
<tr>
<td>Over 70 years</td>
<td>104</td>
<td>494</td>
<td>21:1</td>
<td>146</td>
<td>762</td>
<td>19:2</td>
<td>210</td>
<td>3203</td>
</tr>
<tr>
<td>Overall</td>
<td>6494</td>
<td>34479</td>
<td>18:8</td>
<td>7524</td>
<td>34371</td>
<td>21:2</td>
<td>8498</td>
<td>87004</td>
</tr>
</tbody>
</table>
Table 5.1 Summary of demographics and HBsAg, anti-HBs and anti-HBc positive results broken down by Indigenous status and sex.

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Indigenous</th>
<th>Non-Indigenous</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=35,633</td>
<td>n=14,025</td>
<td>n=21,608</td>
</tr>
<tr>
<td>Median age in years at sample date (IQR)</td>
<td>32.4 (24.5-43.7)</td>
<td>30.8 (21.5-43.3)</td>
<td>33.2 (26.3-44.0)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female % (95% CI)</td>
<td>57.8 (57.3-58.3)</td>
<td>53.7 (52.8-54.5)</td>
<td>60.5 (59.9-61.2)</td>
</tr>
<tr>
<td>HBsAg positive % (95% CI)</td>
<td>3.40 (3.19-3.61)</td>
<td>6.08 (5.65-6.53)</td>
<td>1.56 (1.38-1.76)</td>
</tr>
<tr>
<td>HBsAg positive men % (95% CI)</td>
<td>4.99 (4.59-5.40)</td>
<td>8.27 (7.53-9.05)</td>
<td>2.22 (1.86-2.62)</td>
</tr>
<tr>
<td>HBsAg positive women % (95% CI)</td>
<td>2.35 (2.13-2.59)</td>
<td>4.31 (3.83-4.84)</td>
<td>1.18 (0.99-1.40)</td>
</tr>
<tr>
<td>Anti-HBs &gt;10IU/ml % (95% CI)</td>
<td>58.0 (57.3-58.7)</td>
<td>60.7 (59.7-61.6)</td>
<td>55.4 (54.4-56.3)</td>
</tr>
<tr>
<td>Anti-HBc positive % (95% CI)</td>
<td>25.2 (24.7-25.8)</td>
<td>38.3 (37.4-39.1)</td>
<td>11.7 (11.1-12.3)</td>
</tr>
</tbody>
</table>
Multivariate logistic regression

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>OR of being HBsAg positive</th>
<th>OR adjusted for other tabulated variables</th>
<th>P value for the adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indigenous Australia</td>
<td>4.08 (3.54-4.71)</td>
<td>3.81 (3.29-4.44)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.53 (1.42-1.66)</td>
<td>1.56 (1.44-1.70)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Living remotely</td>
<td>1.93 (1.78-2.10)</td>
<td>1.21 (1.05-1.39)</td>
<td>P&lt;0.0001</td>
</tr>
</tbody>
</table>
Birth cohort analysis HBsAg positivity

The graph shows the prevalence of Hepatitis B surface antigen (HBsAg) among different birth cohorts over time. The y-axis represents the percentage prevalence, and the x-axis represents the birth cohort years ranging from 1930 to 2010.

- **Overall** line: Shows a steady decline in HBsAg prevalence over time.
- **Indigenous** line: Displays a similar trend but with potentially higher baseline levels compared to the overall population.
- **Non-Indigenous** line: Indicates a lower prevalence and a more steady trend over time.

Key events marked on the graph:
- 1990: Introduction of birth vaccination for all.
- 1990: Catch up program.

The data suggests a significant decrease in HBsAg positivity, particularly after the implementation of vaccination programs.
Interrupted time series analysis

Birth cohort analysis HBsAg positivity
HBsAg positivity in the NT:
- 3.4% overall
- 6.08% Indigenous Australians
- 1.56 non-Indigenous Australians

Hepatitis B test positivity rates were falling before the introduction of universal vaccination

Big gaps in testing in the young (especially those born after universal vaccine introduction) and over 60’s
Galiwin’ku Sero survey:

Know your Hep B status
- To determine prevalence of HBsAg and occult infection in Galiwinku
- To determine the field sensitivity, specificity and acceptability of novel diagnostics for Hepatitis B serology
- To assess vaccine efficacy in the context of sub-genotype C4 Hepatitis B

Study duration
- March 2015 to December 2017

Number of Participants
- 2000 (estimated) – overall data collection
- 800 (estimated) – serological testing

Inclusion Criteria
- All individual residents in Galiwin’ku and surrounding homelands/outstations (for checking and recording of existing serology)
- All individuals who have no available HBsAG results within the 5 years preceding the recruitment date (for collection of blood and saliva)

Exclusion Criteria
- Unable to give consent/assent
- Children <1 year of age
Seek individual consent/assent to participate in Hep B study

- No HBsAg results available in the 5 years prior to recruitment
  - Blood sample collected
    - Participant HBV negative but not immune
      - Participant referred to clinic for HBV vaccination
    - Participant HBV positive (HBsAg +ve)
      - Ensure Participant put on appropriate care pathway

- Saliva sample collected and medical records checked for HBsAg serology
  - HBsAg results available in the 5 years prior to recruitment
    - Individual immune - no further action
    - Individual HBV positive (HBsAg +ve)
      - Confirm Individual on appropriate care pathway
      - Individual referred to clinic for HBV vaccination
    - Individual HBV negative but not immune
      - Individual referred to clinic for HBV vaccination
60-70 people recruited so far

Learning points:
- True informed consent regarding hepatitis B in this setting takes a long time and multiple visits to achieve.
- Stigma and shame still very widespread
- Blame – important to be aware of and try to minimize
Acknowledgements

- The people of Galiwin’ku
- Associate Professor Josh Davis
- Sarah Bukulatjpi
- Shu Li
- Professor John Condon
- Associate Professor Ben Cowie
- Associate Professor Steven Tong
- Associate Professor Rob Baird
- Clinical Professor Miles Beamen
- Dr Geoff Higgins
- Paula Binks
- Melita McKinnon
- Professor Steven Locarnini
- Dr Margaret Littlejohn
- Dr Lilly Yuen
- Dr Renae Walsh
- Suresh Sharma
- Mathew Maddison
- VIDRL
- Doherty Institute
- NHMRC
- Sidney Myer Foundation
- And many more....
References


Questions?