HBV IN YOUNG MAORI

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AUCKLAND, NEW ZEALAND
NEW ZEALAND

- Maori are indigenous people of New Zealand
- First sighted by Dutch sailor Abel Tasman in 1642
- First circumnavigated by captain James Cook in 1769
- European settlement started in early 1800
- Today we are 4 million plus people with Maori 14.9%
- Pacific Islanders 7.4%
- European 74%
- Asian 11.8%
MIDDLE EARTH
HEPATITIS B NATURAL HISTORY

- Studied in Asian population mostly
- Vertical transmission
- Genotype B and C
- REVEAL Study showed increased rate of cirrhosis, HCC and liver related death
- Low spontaneous HBs Ag clearance of 0.5 – 1.4% annually
- At mean age of 48 years
CHB IN NEW ZEALAND

- Different genotype
- Predominantly C and D
- Some A
- Mostly horizontal transmission
STORY FROM KAWERAU
1981 CENSUS

- 8568 total population
- 61% European
- 35% Maori
- 2% Pacific Islander
- 2% Asian/other
- In 1984, 7901 of 8514 residents were tested for HBV markers
STUDY IN 1984

Demographics

- European: 57%
- Maori: 41%
- Pacifica: 2%
- Asian: 0%
STORY FROM KAWARAU

• 572 have CHB on viral marker tests
• CONFIRMED on retesting six months later
• Median age was 17 years (1-71)
• 41 % E antigen positive at enrolment
DEMOGRAPHICS OF CHB CASES

- Maori
- European
- Pacifica
VERTICAL VS HORIZONTAL TRANSMISSION

• 66 children aged between six and 12 month tested

• Only 1 Positive for HBsAg

• Low rate of HBV in NZ women

• Plus low rate of vertical transmission

• 2.8 % prevalence in pregnant Maori women vs 16 % in Taiwan
HORIZONTAL TRANSMISSION

S AG PREVALENCE

European | Non-European

- <1 yr: 4% | 5%
- 5 yr: 10% | 30%
- 10 yr: 60% | 70%
2012 FOLLOW UP

- Total 572 cases of CHB identified in 1984
- 509 (89%) Followed up 28 years later
- 98% cases had interval data available
- Only 4% had antiviral
- 1140 Non CHB cases from Kawarau chosen as control
RATE OF LIVER RELATED DEATH & HCC

• 15 Developed HCC (2.6%) i.e. 101 per 100,000 person years
• Liver related death occurs in 12 cases (all from HCC)
• Baseline predictors are higher HBV DNA, Older age and Maori ethnicity
LIVER RELATED DEATH

HBsAg neg controls
No liver-related deaths

HBsAg pos cases
12 liver-related deaths

Cumulative survival (%)

p<0.0001 (Log-rank test)

Years of follow-up
Figure 3.5: Incidence of HCC

Cumulative incidence of HCC (%) vs Years of follow-up

- HBsAg pos cases
  15 HCCs (2.6%)

- HBsAg neg controls
  No HCCs

p<0.001 (Log-rank test)
CONCLUSION ONE

- Natural history of CHB in Maori is similar to Asians with vertical transmission
- Though absolute incidence rates of HCC or liver death are lower
SEROLOGIC OUTCOMES – REVEAL

- Clearance of E Ag and/or S Ag leads to reduction of HCC and ESLD
- Low spontaneous annual clearance rate of S Ag
- Rate varies from 0.5 to 1.4
- Mean age of Sag clearance is 47.8 yrs in Taiwan study in E Ag negative cohort
- Antiviral therapy S Ag clearance is 2.4% to 5%
KAWARAU FOLLOW UP

- 41% were e ag positive in 1984
- E Ag positive patients were young (median age 10)
- Predominantly Maori 82%
- High HBV DNA (Median log 10)
2012 STUDY

- 85% (201) of E Ag positive patients had blood tests in 2012
- Total 3051 person years follow up
- 184 (92 %) underwent seroconversion
- Median age 23 ( range 6-66)
- Annual E Ag loss was 3.3 %
- Lower E Ag loss rate with increasing age at baseline
Figure 6.1: HBcAg loss
# Predictors of eAg Loss

<table>
<thead>
<tr>
<th>Variables</th>
<th>HBeAg loss (n=184)</th>
<th>HBeAg + (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (yrs)</td>
<td>10.6 (0.5-57.1)</td>
<td>8.8 (1.2-30.9)</td>
<td>0.43</td>
</tr>
<tr>
<td>Gender M:F</td>
<td>121:63</td>
<td>11:6</td>
<td>1.0</td>
</tr>
<tr>
<td>Maori ethnicity (%)</td>
<td>155 (84%)</td>
<td>11 (65%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Baseline ALT level, median (range) (IU/L)</td>
<td>23 (3-178)</td>
<td>18 (5-38)</td>
<td>0.08</td>
</tr>
<tr>
<td>Baseline HBsAg level, median (IU/mL)</td>
<td>68653.1 (0.01-80632.1)</td>
<td>232273 (0-216522)</td>
<td>0.57</td>
</tr>
<tr>
<td>Baseline HBV DNA level, median (IU/mL)</td>
<td>10 logs (1.88-10)</td>
<td>10 logs (2.5-10)</td>
<td>0.64</td>
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</tbody>
</table>
SAG LOSS

• 438 (77) patient has Sag test in 2012
• 10849 person years follow up
• 145 (33) lost sAg
• Median age 40 (4-80) years
• Rate of Sag clearance 1.34 per 100 person years
• Increased with increasing age at baseline
• Detectable anti HBs in 95 % of these patients
HB S AG LOSS
# BASELINE PREDICTOR OF S Ag LOSS

<table>
<thead>
<tr>
<th>Variables</th>
<th>HBsAg + (n=293)</th>
<th>HBsAg - (n=145)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (yrs)</td>
<td>14.8 (0.5-59.8)</td>
<td>20.6 (0.9-57.1)</td>
<td>P&lt;0.0001</td>
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<tr>
<td>Gender M:F</td>
<td>178:115</td>
<td>91:54</td>
<td>P=0.75</td>
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<tr>
<td>Maori ethnicity (%)</td>
<td>236 (81%)</td>
<td>104 (72%)</td>
<td>P=0.039</td>
</tr>
<tr>
<td>HBeAg negativity (%)</td>
<td>143 (49%)</td>
<td>121 (83%)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Baseline ALT level, median (range) (IU/L)</td>
<td>18 (2-178)</td>
<td>15.5 (2-95)</td>
<td>P=0.18</td>
</tr>
<tr>
<td>Baseline HBsAg level, median (IU/mL)</td>
<td>18612.6 (0-232273)</td>
<td>3521.4 (0-175260)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Baseline HBV DNA, median (IU/mL)</td>
<td>6.76 logs</td>
<td>4.15 logs</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>(undetected-10)</td>
<td>(undetected-10)</td>
<td></td>
</tr>
</tbody>
</table>
PREDICTORS OF S AG LOSS

- Univariate analysis HBsAg loss associated with
  - Increasing age
  - Caucasian
  - E Ag negative at baseline
  - Lower baseline HBV DNA
- Multivariate analysis ONLY older age and lower HBsAg level at baseline
NEW ZEALAND AND ALASKA
HOW NZ DIFFERENT FROM ALASKA

• Alaska study showed higher clearance of HBeAg
• Similar horizontal transmission
• 7.3 % per annum HBeAg loss
• But lower HBsAg loss (0.5 % per annum)
TAKE HOME MESSAGE

- In young Maori, CHB is associated with increased liver related death and HCC
- Baseline HBV DNA level is associated with this increased Risk
- Incidence rate of HCC, ESLD and liver related death lower than Asian population
- Spontaneous clearance of HBe Ag and HBs Ag higher than Asians
- Predictors of S Ag loss are older age and lower baseline HBsAg level