Hepatitis B antiviral therapy in the Top End, Northern Territory: the ANTLER study

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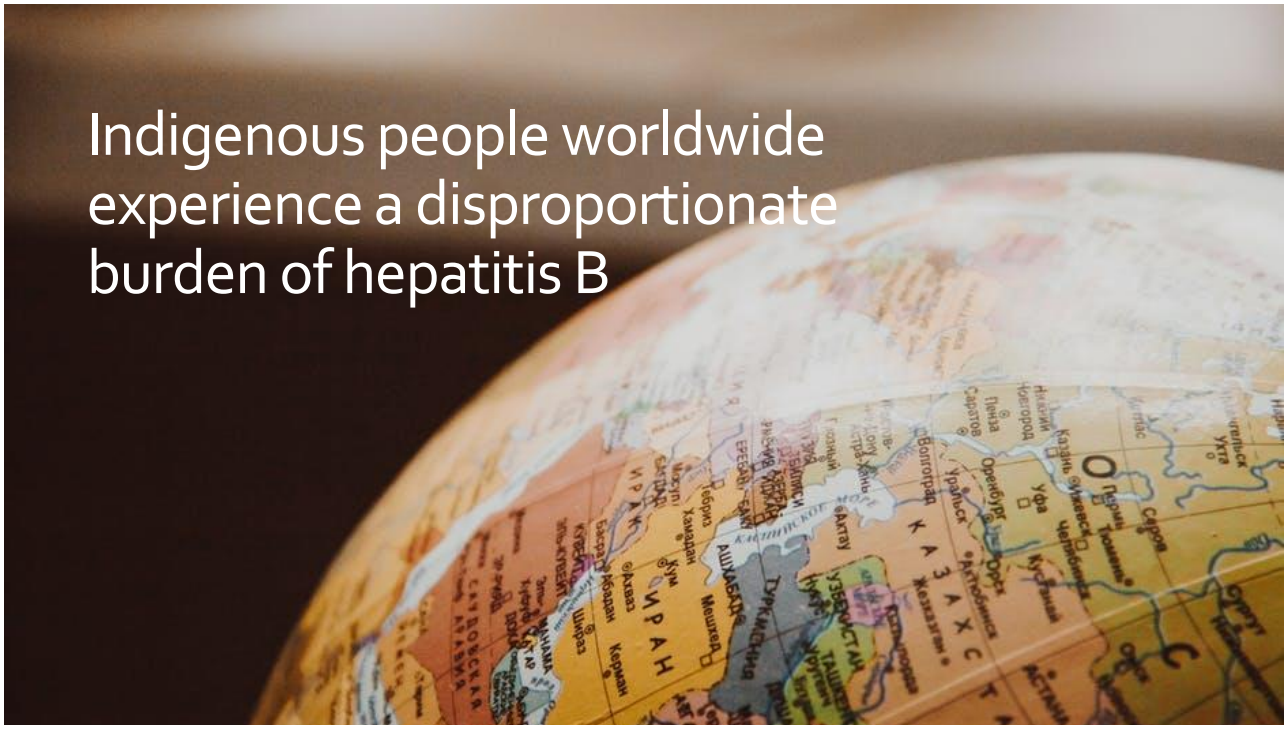


Hepatitis B amongst Indigenous Australians

- Prevalence 4x higher amongst Indigenous than non-Indigenous Australians (Graham et al., 2013)
- Higher in rural > urban (Deng et al, 2017)
- Rates of hepatocellular carcinoma 2-8x higher (Zhang et al, 2011)
- 7% of people with CHB in Australia received antiviral therapy (Kirby Institute, 2016)
  - Indigenous Australians – exact % unknown but likely lower

Hepatitis B in the Top End, Northern Territory

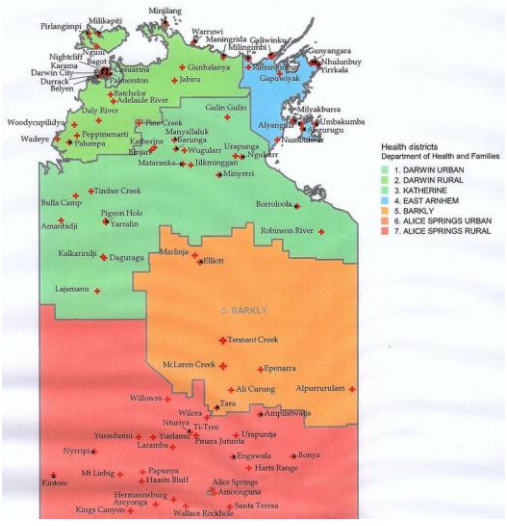


Image Source: Kruavit A, Fox M, Pearson R, Heraganahally S. Chronic respiratory disease in the regional and remote population of the Northern Territory Top End: A perspective from the specialist respiratory outreach service. Australian Journal of Rural Health. 2017 Oct;25(5):275-84.

Hepatitis B in the Top End, Northern Territory

- Universal HBV immunisation since 1990
- 6-12% HBsAg prevalence (Davies et al, 2017; Carroll et al 2010)
- HBV C4 sub-genotype (Littlejohn et al, 2014)

Adherence to HBV antiviral therapy

- Important – prevent viral breakthrough & resistance
- "Degree to which a patient's behaviour corresponds with agreed recommendations from a health provider" (WHO, 2003)
- 20-24% patients in Australian urban centres (Sydney, Melbourne) hospitals poorly adherent to HBV medications, none/few Indigenous patients (Allard et al., 2017; Sheppard-Law et al., 2017)

Is medication adherence lower amongst Indigenous Australians?

- Often based on anecdote, not evidence
- Recent systematic review of adherence amongst Indigenous Australians (de Dassell et al., 2017)
  - 47 articles meeting inclusion criteria
  - Only 6 measured adherence quantitatively
  - Adherence 2/3, comparable with general population

Gaps in literature

No studies to date about adherence or virological outcomes to HBV antiviral medications amongst Indigenous Australians, especially not in remote settings

Aim

To describe the adherence and virological outcomes of all Indigenous and non-Indigenous patients receiving HBV antiviral therapy in the Top End, NT

Methods

- Retrospective audit of pharmacy dispensing data matched to clinical records
  - All patients on oral antiviral therapy agent(s)
  - July 2012 – October 2015
  - Royal Darwin Hospital Pharmacy, Top End Health Network
- Part of the "**A**dherence to a**NT**ivira**L** th**ER**apy for hepatitis B in the Northern Territory (ANTLER) study"
  - Feasibility and effectiveness of antiviral therapy in the Top End, NT

Methods

- Variables
  - Demographics
  - Treatment: indication, prescribed agent(s), duration
  - HBeAg status, HBV DNA
- Outcomes
  - Virological response: HBV DNA IU/ml
    - Complete: undetectable viral load
    - Partial response: 20-2000 IU/mL
    - Failure: >2000 IU/mL
  - Ongoing engagement with treatment: proportion of patients dispensed medication within 2 months of end of study period or date of death
- Stata 14

Results: Baseline characteristics

219 patients prescribed antiviral therapy from 2012-2015

Indigenous (n=86)

- Mean age 42 yrs
- Males 52%
- Most born in Australia (90%)
- Most living remote (79%)
- HBeAg+ (31%)

Non-Indigenous (n=127)

- Mean age 45 yrs
- Males 58%
- Most born in Asia-Pacific (67%)
- Most living in Darwin (88%)
- HBeAg+ (19%)

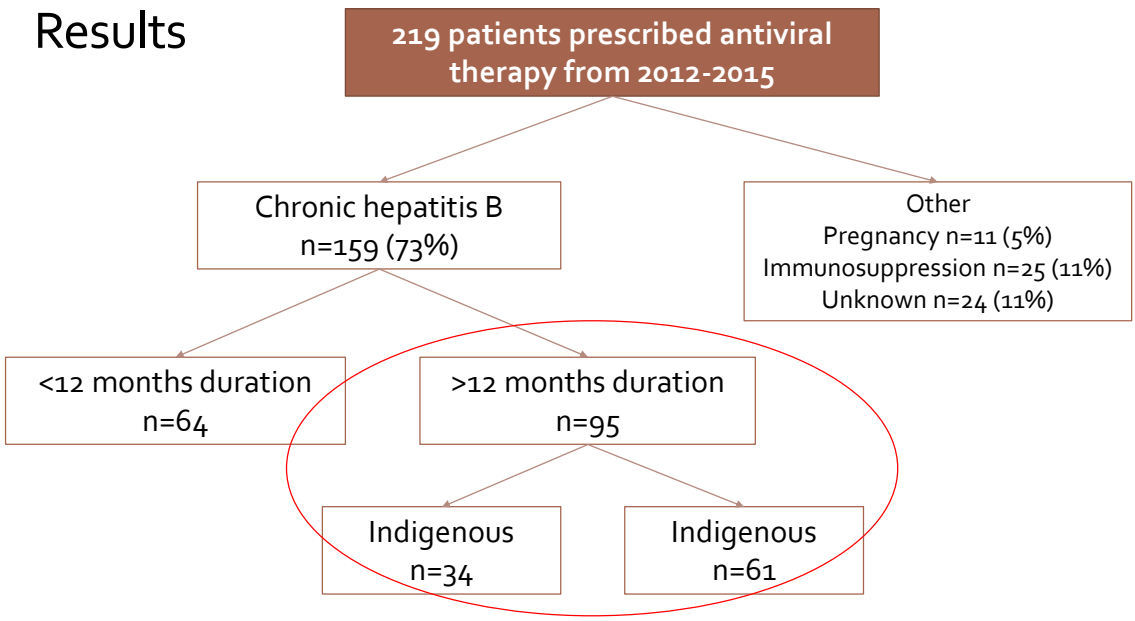
Results

219 patients prescribed antiviral therapy from 2012-2015

Antiviral agent

- Entecavir n=152 (69%)
- Tenofovir n=60 (27%)
- Lamivudine n=10 (5%)
- Adefovir n=3 (1%)
- >1 agent n=6 (3%)

Results



Results: Virological response for Indigenous & non-Indigenous patients on >12 months antiviral therapy for CHB, remote

	Remote (n=31)	
Virological response (HBV DNA, IU/mL)	**Indigenous [b] N (%)**	**Non-Indigenous N (%)**
Total	25 (100)	6 (100)
Complete response (undetectable)	14 (56)	5 (88)
Partial response (20-2000)	5 (20)	1 (17)
Failure (>2000)	5 (20)	0 (0)

Results: Virological response for Indigenous & non-Indigenous patients on >12 months antiviral therapy for CHB, Darwin

	Darwin (n=64)	
Virological response (HBV DNA, IU/mL)	**Indigenous N (%)**	**Non-Indigenous N (%)**
Total	9 (100)	55 (100)
Complete response (undetectable)	4 (44)	50 (91)
Partial response (20-2000)	2 (22)	4 (7)
Failure (>2000)	3 (33)	1 (2)

Results: Ongoing engagement with treatment

- **Overall:** 81% (77/95) of CHB patients, >12 mths therapy
  - *Dispensed medication within 2 months prior to end of study period or date of death*
- **Indigenous**: 74% (25/34)
- **Non-Indigenous:** 85% (52/61)
- **Higher for people living in Darwin vs remote:** 90% vs 61%

Reasons for treatment failure

- **Social circumstances:** "Did not take medication while an escort", "in prison"
- **Drug availability and communication/knowledge:** "Intermittent compliance due to drug availability and misunderstanding"
- **Side effects:** "Stopped taking due to nausea and vomiting"

Discussion: comparison with the literature

- Our study: complete response - 56% of remote Indigenous CHB patients
- Previous audit: 77% remote Indigenous had complete response (n=10/12)
- HBV Antiviral Rx
  - Systematic review (Lieveld, 2013): mean adherence **81-99%**
  - Sydney, Australia (Sheppard-Law, 2017): poor adherence **24%**
  - Melbourne, Australia (Allard et al, 2017): non-adherence **20%**

Discussion: comparison with the literature

- Indigenous Australians, other chronic disease medications
  - Aboriginal Medical Service Victoria (Deacon-Crouch, 2016): **85%** self-reported adherence
  - Rheumatic heart disease prophylaxis, NT (de Dassel, 2017): **67%** adherence
- Indigenous people, British Columbia, Canada: HIV treatment (Milloy et al., 2016)
  - **Two thirds** achieved non-detectable viral loads

Discussion: strengths & weaknesses

- Strengths
  - Complete capture
  - Use of clinical outcome (HBV DNA) as primary outcome
  - Inclusion of patients in remote settings
- Limitations
  - Retrospective
  - Lack of robust adherence measure
  - Relatively small numbers

Medication access a challenge

Elcho Island (Galiwinku)

Conclusion

- **First study** to describe adherence and virological outcomes to HBV antiviral Rx Indigenous Australians
- HBV antiviral Rx is **feasible** and can achieve reasonable virological response (76% complete or partial viral response) in remote Indigenous patients
- Adherence is a multi-dimensional issue and broader social and systemic factors should be addressed
- **Future research:** factors affecting / strategies to optimise HBV antiviral therapy amongst remote indigenous Australians

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Questions?