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# Hepatitis B prevalence in women giving birth in the Northern Territory, Australia, 2005–2015

Amalie Dyda, Skye McGregor, Paula Binks, Jane Davies, Steven YC Tong, Vicki Krause, Peter Markey, Shu Li Qin Li, Joshua S Davis, John M Kaldor, Bette Liu

## Abstract

### Background

Hepatitis B virus (HBV) vaccination in the Northern Territory (NT) was funded for all Aboriginal and Torres Strait Islander newborns in 1988 and for all newborns in 1990. The prevalence of HBV in the Northern Territory was found to be higher in Aboriginal and Torres Strait Islander women than in non-Indigenous women across 2005–2010. We examined more recent data to assess whether the gap remains.

### Methods

We linked data from two routinely collected registries, the NT Perinatal Register and the NT Notifiable Diseases System, to investigate the prevalence of HBV infection, according to eligibility for infant HBV vaccination, in women giving birth during 2005–2015.

### Results

There were 22,781 women recorded as giving birth in public hospitals in the Northern Territory during 2005–2015. Hepatitis B virus prevalence was highest in Aboriginal and Torres Strait Islander (1.8%) and overseas-born women (1.8%). Among Aboriginal and Torres Strait Islander women, estimated hepatitis B virus prevalence was significantly higher in those born before the implementation of the vaccination program than in those born afterwards (2.4% versus 0.3%). Prevalence was highest amongst those living in very remote areas, both overall (2.2%) and within the birth cohort eligible for HBV vaccination.

### Conclusions

Hepatitis B virus prevalence in Northern Territory Aboriginal and Torres Strait Islander women appears to be declining as more individuals vaccinated as part of infant vaccination programs reach adulthood. Prevalence remains highest in remote areas, highlighting the importance of ongoing monitoring and of promoting vaccination in these regions.

Keywords: Hepatitis B; prevalence; Australia; epidemiology; data linkage

## Introduction

Infection with the hepatitis B virus (HBV) contributes significantly to global morbidity and mortality, with an estimated 257 million people living with chronic infection in 2015.<sup>1</sup> It is transmitted through contact with blood and some bodily fluids, including through sexual transmission and from mother to infant at the time of birth.<sup>2</sup> The majority of chronic infections are caused by infection acquired at birth or in early childhood, with infections acquired in adolescence or adulthood most often being cleared after an acute illness.<sup>3</sup>

In Australia, Aboriginal and Torres Strait Islander people experience a disproportionate burden of many vaccine preventable diseases, including HBV infection.<sup>4</sup> In 2017, the rate of HBV notifications across the Australian Capital Territory, Northern Territory, South Australia, Tasmania and Western Australia was 45.1 per 100 000 in Aboriginal and Torres Strait Islander Australians compared to 19.2 per 100 000 in the non-Indigenous population.<sup>5</sup>

A three-dose HBV vaccine schedule, which includes a dose at birth, is known to be effective in preventing HBV infection,<sup>2</sup> and first became available in Australia in the 1980s. This was replaced with a four-dose schedule in 2000.<sup>6</sup> The Northern Territory (NT), a jurisdiction of Australia in which 30% of the population is Aboriginal and Torres Strait Islander, funded neonatal HBV vaccinations as part of a three-dose schedule for all Aboriginal and Torres Strait Islander newborns in 1988 and for all newborns in 1990. A 'catch-up' program was implemented in NT schools in 1998 for children aged 6 to 16 years.<sup>6</sup>

A study of women giving birth between 2005 and 2010 in the NT, linked to HBV notifications, found significantly lower prevalence of chronic HBV infection among Aboriginal and Torres Strait Islander women eligible for funded HBV vaccination programs than in those not eligible (based on year of birth).<sup>7</sup> Prevalence across this study period was 40% lower in those

eligible for the catch-up program and 80% lower among those eligible for the newborn program, compared to non-eligible cohorts. However, among women eligible for the universal HBV vaccine program, prevalence was still estimated at 0.8%,<sup>7</sup> a prevalence substantially higher than that for non-Indigenous Australians in the NT. We hypothesised that vaccination coverage may have increased over time. The previous analysis, including data until 2010, was unlikely to capture women born from 1994 onwards as they would have been at most 16 years of age. Therefore, we aimed to update this earlier analysis of HBV prevalence with data from 2005 to 2015, as this most recent cohort enters the childbearing period, to determine whether HBV prevalence has continued to fall in the NT.

## Methods

### Data sources

This study used a retrospective cohort design, based on linking data from two routinely collected registries, and based on the assumption that, as per NT clinical policy, all women who undergo antenatal care are tested for HBV infection during the course of their care.<sup>8,9</sup>

The Northern Territory Perinatal Register collects data pertaining to every birth in a hospital in the NT, reported by the health professional responsible for the birth. The reporting captures information about pregnancy, labour and birth and health conditions, as well as demographic data about the mother, including date of birth, usual area of residence, country of birth and Indigenous status.<sup>10</sup>

The Northern Territory Notifiable Diseases System, managed by the Centre for Disease Control Top End Health Service NT Health, records laboratory-confirmed diagnoses of HBV surface antigen (HBsAg) or nucleic acid positivity in the NT. A case is classified as newly acquired if there is evidence of recent infection (positive immunoglobulin M [IgM] antibody test for HBsAg or previous negative test for HBV within 2 years) and as 'unspecified' if

there is not. The information collected for each case includes type of infection (newly acquired or unspecified), date of diagnosis, date of birth, postcode and Indigenous status.<sup>11</sup>

## Data linkage

Data from the Perinatal Register and the Notifiable Diseases System were linked by NT Health, initially using a hospital record number (HRN). The HRN is a unique number allocated to individuals in the NT who access government funded health services. Where an HRN was not available, records were linked deterministically using other identifiable information including name, date of birth and sex, with any close matches manually reviewed.

We only included public hospital births as these records from public hospitals include more complete unique identifiers that enable linkage to other data. This is described in an earlier publication that used similar methods.<sup>7</sup>

## Statistical analysis

The analysis population comprised women giving birth in public hospitals in the NT between January 2005 and December 2015. Individuals were excluded if they were not recorded as residents of the NT. As previously,<sup>7</sup> women were categorised as having a chronic HBV infection if they linked to a non-acute (unspecified) HBV notification dated prior to their most recent birth recorded during the study period.

The prevalence of HBV was calculated by dividing the number of HBV notifications by the total number of women. Prevalence was compared between women who were Aboriginal and Torres Strait Islander Australians, Australian-born non-Indigenous, and overseas born, as reported in their perinatal record. Analyses were then confined to Aboriginal and Torres Strait Islander women to explore trends specific to this population given the higher prevalence. HBV prevalence was compared in four birth cohorts, based on presumed eligibility to the HBV vaccine program: pre-vaccine program

(born prior to 1982), vaccine catch-up program (1982–1988), post-vaccine program group 1 (1989–1994), and post-vaccine program group 2 (1995 onwards). HBV prevalence was also analysed by seven geographic locations corresponding to NT Health district classifications and grouped into three regions based on the Accessibility and Remoteness Index of Australia (ARIA) (outer regional, remote and very remote).<sup>12</sup>

Differences in HBV prevalence across the birth cohorts were investigated using multivariate logistic regression. The model was adjusted by ARIA categories (outer regional, remote and very remote) and Socio-Economic Indexes for Areas (SEIFA), in deciles. ARIA, calculated using residential postcodes, is an objective way in which the remoteness of a location is measured based on access to road networks, and service centres, and population.<sup>12</sup> SEIFA is a ranking system of socio-economic advantage and disadvantage by geographic location in Australia, also calculated in this analysis using postcodes.<sup>12,13</sup>

All analyses were undertaken using Stata 12.0.

## Ethical approval

This study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research, reference HREC-2014-2152.

## Results

A total of 22,781 NT resident women were recorded on the Perinatal Register as giving birth in public hospitals in the NT from 2005 to 2015. Of those, 8,753 (38.4%) were Aboriginal and Torres Strait Islander Australians, 9,228 (40.5%) were Australian-born non-Indigenous women and 4,800 women (21.1%) were born overseas. Among these 22,781 women, 253 linked to an unspecified (presumed chronic) HBV notification before or during their last pregnancy (Table 1). HBV prevalence across this study period was highest in Aboriginal and

**Table 1: Demographic characteristics of women giving birth in public hospitals and resident in the Northern Territory, 2005 to 2015**

	All	Australian-born Aboriginal and Torres Strait Islander	Australian-born non-Indigenous	Overseas born
<b>Total (%)</b>	<b>22,781</b>	<b>8,753 (38.4)</b>	<b>9,228 (40.5)</b>	<b>4,800 (21.1)</b>
% maternal birth year > 1988 (N)	20.9 (4,758)	34.9 (3,052)	13.9 (1,279)	8.9 (427)
% link to HBV notification before or during most recent pregnancy (N)	1.1 (253)	1.8 (161)	0.1 (7)	1.8 (85)

Torres Strait Islander and overseas-born women at 1.8% in both groups, compared to 0.1% in Australian-born non-Indigenous women.

The proportion of Aboriginal and Torres Strait Islander women linking to an HBV record was significantly higher for those born prior to 1989 than for those born in 1989 or later (2.4% versus 0.3%,  $p < 0.001$ ). By region of residence, prevalence was highest in East Arnhem (4.0%; 95% confidence interval [95% CI]: 3.0–5.3%), rural

Alice Springs (2.4%; 95% CI: 1.6–3.4%) and rural Darwin (2.0%; 95% CI: 1.4–2.8%). This was also reflected with an increase in prevalence with remoteness, ranging from 0.4% (95% CI: 0.1–0.9%) in outer regional areas to 2.2% (95% CI: 1.7–2.9%) in very remote areas (Table 2).

Table 3 shows the prevalence of HBV in Aboriginal and Torres Strait Islander birthing mothers by birth cohorts, categorised according to their likely exposure to vaccination programs.

**Table 2: Hepatitis B prevalence in Aboriginal and Torres Strait Islander birthing mothers according to maternal birth cohort and area of residence, Northern Territory Australia, 2005–2015**

	Mean age at most recent birth record (years)	Number of birthing mothers	Chronic HBV record linked	HBV prevalence %	95% CI
<b>By birth cohort</b>					
< 1989 (pre-newborn program)	29.4	5,701	139	2.4%	2.0–3.0
1989+ (newborn program)	20.2	3,052	10	0.3%	0.2–0.6
<b>By NT area of residence</b>					
Darwin urban	27.3	1,498	6	0.4%	0.2–1.0
Darwin rural	25.9	1,609	32	2.0%	1.4–2.9
Katherine	26.1	1,506	20	1.3%	0.8–2.0
East Arnhem	25.8	1,240	50	4.0%	3.0–5.3
Barkly	25.8	577	< 5	< 2.0%	0.2–1.9
Alice Springs urban	26.9	849	7	0.8%	0.3–1.7
Alice Springs rural	25.6	1,270	30	2.4%	1.6–3.4
<b>By ARIA</b>					
Outer regional	27.2	1,492	6	0.4%	0.2–1.0
Remote	26.1	4,812	90	1.9%	1.5–2.3
Very remote	25.6	2,441	54	2.2%	1.6–2.8

HBV prevalence was highest in those born prior to availability of the vaccine in 1982, at 3.1% (95% CI: 2.5–3.8%). Prevalence decreased over time to 1.8% (95% CI: 1.4–2.4%) for those born in 1982–1988 (adjusted odds ratio [aOR]: 0.54; 95% CI: 0.38–0.76) and fell to a prevalence of 0.1% (95% CI: 0.0–0.8%) in those born after 1994 (aOR: 0.04; 95% CI: 0.01–0.27) (Table 3).

The overall trend of HBV prevalence decreasing with recency of birth cohorts was consistent across each of the different geographical locations examined. Among women living in the Darwin and Katherine regions of the Top End, prevalence fell from 2.5% among women born prior to 1982 to 0.0% in the 357 women born from 1995 onwards. Similarly, prevalence in the Central NT (Alice Springs and Barkly) fell from 2.1% among women born prior to 1982 to 0.0% in the 251 women born from 1995 onwards. In each birth cohort, the prevalence of HBV infection was highest in East Arnhem compared to Darwin and Katherine and Central NT and while small numbers meant statistical comparisons were not made, East Arnhem appears to be the location with the highest prevalence in the most recent time period available for analysis. When adjusting for ARIA and SEIFA, the trend remained the same in all geographical areas.

## Discussion

This study builds on the earlier research conducted in Aboriginal and Torres Strait Islander women giving birth from 2005–2010,<sup>7</sup> to show that chronic HBV prevalence in cohorts of women vaccinated as part of an infant program may be continuing to decrease, with prevalence the lowest at 0.1% in those born from 1995 onwards. Similar to other studies, we also showed that prevalence is higher in Aboriginal and Torres Strait Islander women and in women born overseas than in non-Indigenous Australian-born women.<sup>11</sup> The prevalence of HBV was also found to be highest in more remote areas in earlier cohorts, however this was less apparent due to small numbers in the most recent cohort. The overall decrease in HBV prevalence over time was shown in all geographical locations examined, with the highest prevalence remaining in East Arnhem.

A number of our findings are consistent with earlier reports in the NT and in other Australian jurisdictions. These include: the higher HBV prevalence in Aboriginal and Torres Strait Islander women than in non-Indigenous women; reductions in HBV prevalence among Aboriginal and Torres Strait Islander women that began prior to vaccine introduction but that accelerated following newborn vaccination; and, in older cohorts, large differences in HBV prevalence between Aboriginal and Torres Strait Islander women living in remote regions compared to those living in more urban

**Table 3: Hepatitis B prevalence and odds ratio (OR) for HBV in Aboriginal and Torres Strait Islander birthing mothers according to birth cohorts, Northern Territory Australia, 2005–2015**

Year of birth (vaccine program)	Mean age at most recent birth	HBV prevalence %	OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)
< 1982 (pre-vaccine)	32.8	3.1%	1	1
1982–1988 (catch-up)	25.3	1.8%	0.58 (0.41–0.82)	0.54 (0.38–0.76)
1989–1994	20.5	0.4%	0.12 (0.06–0.24)	0.11 (0.05–0.22)
1995+	17.0	0.1%	0.04 (0.01–0.32)	0.04 (0.01–0.27)

a adjusted for ARIA and SEIFA, see methods.

regions.<sup>7,11,14–16</sup> Of importance, we were able to show that in the NT, the HBV prevalence in Aboriginal and Torres Strait Islander women has continued to fall from an estimate in the earlier study of 0.8% in the cohort of mothers born after 1988 to 0.1% in the cohort of mothers born from 1995 onwards in this study.<sup>7</sup> This is reassuringly much closer in absolute terms, and not significantly different, to the prevalence reported among non-Indigenous Australian-born women in the NT.

Notably, the higher prevalence in Aboriginal and Torres Strait Islander women, compared to non-Indigenous women, appears to be driven by higher prevalence among Aboriginal and Torres Strait Islander women living in remote areas. The highest prevalence in this study was identified in East Arnhem Land (4.0%; 95% CI: 3.0–5.3%), which is comprised of remote and very remote areas. It is unclear why this differential exists, but it is recognised that access to health services in remote and very remote locations is poorer than in regional areas and cities.<sup>17</sup> We hypothesise it is also possible, given that most transmission is vertical, that this difference may result from difficulties in administration of hepatitis B immunoglobulin at birth if more women in remote areas give birth out of hospital.

Another potential reason for the higher prevalence of HBV in Aboriginal and Torres Strait Islander women living in remote regions could be access to vaccination. HBV vaccination coverage in the NT is higher in Aboriginal and Torres Strait Islander children aged 24 months of age, at 96.2%, than in non-Indigenous children at 94.7% (birth cohort 1 January 2014 – 31 December 2014). However, the opposite is true for children at 12 months of age for the same birth cohort, with coverage in Aboriginal and Torres Strait Islander children at 92.8% compared to non-Indigenous children at 93.5%.<sup>4</sup> This suggests that timeliness of vaccination could be improved in Aboriginal and Torres Strait children in the NT, although coverage is consistently high in all groups. We were unable to obtain reports on vaccination coverage by

region that date back to the cohorts of interest for this study. However, recent data has shown a higher proportion of vaccination delays are occurring in remote and very remote areas.<sup>4</sup> Aboriginal and Torres Strait Islander children in major cities also have a higher percentage of delays of 1–≤ 2 months than do the non-Indigenous population.<sup>4</sup> Delays in providing the HBV vaccine schedule may have contributed to the increased prevalence of HBV observed in those living in more remote regions. However, we lacked comprehensive immunisation records during infancy on women included in this linked study to examine if reduced coverage, or delayed vaccination, may have been a contributing factor.

Concerns about vaccine effectiveness in NT Aboriginal and Torres Strait Islander peoples have been raised because of a mismatch between the current HBV vaccine (HBV subgenotype A2 [subtype *adw2*]) and the circulating HBV strain (HBV subgenotype C4 [subtype *ayw3*]).<sup>18</sup> An examination of a longitudinal birth cohort from the NT demonstrated that the vaccine was protective against developing chronic disease (defined as HBsAg positive) but less effective against past HBV infection (defined as HBsAg negative but anti-HB core positive), with vaccine efficacy against past infection only 67%.<sup>19</sup> However, more recent longitudinal data shows that vaccine breakthrough may be lower, with anti-HBV seroconversion following documented vaccine-derived immunity of 3.06%.<sup>16</sup> The findings in this current study of pregnant women provide further evidence that the vaccine is effective in protecting against chronic HBV.

Study limitations include the potential for missed links due to quality of the data linkage. Women classified in the vaccinated birth cohorts were born more recently, hence were younger at the time of the analysis and had lower mean age at most recent birth. It is unlikely that age is the main factor affecting the decrease in prevalence, but we were unable to adjust for this in the analysis given the nature of the analysis by birth cohort. Data regarding HBV prevalence



before routine HBV vaccination began in the NT show no consistent trend regarding any increase in prevalence of HBV with increasing age.<sup>20–22</sup> Additionally, our analysis did not capture births occurring in private hospitals, nor births outside of hospitals with no health care professional present.<sup>23</sup> Private hospital births are likely to have minimal impact on the study results due to small numbers, but births outside of hospital may impact the results, with those less likely to seek healthcare at higher risk of missing vaccinations. Finally, it is important to note that men have higher HBV prevalence than women, with data from the NT reporting male:female prevalence ratios ranging from 1.4:1 to 1.7:1,<sup>16,24</sup> and findings may not necessarily be extrapolated to men.

HBV vaccine programs are the most effective way to decrease the prevalence of HBV in the population, and our study provides further evidence that HBV prevalence in the NT may be continuing to fall in Aboriginal and Torres Strait Islander women who were eligible for vaccination at birth. Importantly, HBV prevalence remains higher in remote areas, and this highlights the need to continue to promote vaccination and to monitor vaccination coverage and timeliness in these regions, so as to address disparities in HBV between Aboriginal and Torres Strait Islander Australian and non-Indigenous women.

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