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Publication details:
Internal Medicine Journal
v. 54
Chapter No. 4
Medium: Print-Electronic
1444-0903 (ISSN); 1445-5994 (ISSN)

Publication Date:
2023-01-01

Publisher DOI:
https://doi.org/10.1111/imj.16181

INTERNAL MEDICINE JOURNAL

RACP Specialists. Together

doi:10.1111/imj.16181

ORIGINAL ARTICLE

Hepatitis B genotypes in Aboriginal and Torres Strait Islander Australians: correlation with clinical course and implications for management

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Key words
hepatitis B virus, genotype, Indigenous health, Australia, epidemiology.

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Received 15 December 2022; accepted 9 July 2023.

Abstract

Background: The prevalence of chronic hepatitis B (CHB) in Aboriginal and Torres Strait Islander Australians in Far North Queensland (FNQ) is greater than twice that of the general Australian population. CHB is common in Torres Strait Islanders diagnosed with hepatocellular carcinoma (HCC) – and in Aboriginals with HCC living in the Northern Territory – however, Aboriginals diagnosed with HCC in FNQ very rarely have CHB. The explanation for this apparent disparity is uncertain.
Aims: To determine the HBV genotypes in the FNQ Aboriginal and Torres Strait Islander population and their correlation with clinical phenotype.
Methods: We determined the HBV genotype of Aboriginal and Torres Strait Islander Australians living with CHB in FNQ and correlated this with demographic and clinical findings.
Results: 134/197 (68%) enrolled individuals had a sufficient viral load for genotyping. All 40 people with HBV/D genotype had Aboriginal heritage, whereas 85/93 (91%) with HBV/C had Torres Strait Islander heritage ($P < 0.0001$). Individuals with HBV/D were younger than those with HBV/C (median (interquartile range) age: 43 (39–48) vs 53 (42–66) years, $P = 0.0002$). However, they were less likely to be HBeAg positive (1/40 (3%) vs 23/93 (25%), $P = 0.001$). All three HCCs developed in Torres Strait Islanders; two-thirds were infected with HBV/C14; genotyping was not possible in the other individual. All 10 diagnoses of cirrhosis occurred in Torres Strait Islanders, 6/10 were infected with HBV/C14, genotyping was not possible in the other four individuals.
Conclusions: HBV genotypes in Aboriginal and Torres Strait Islander Australians in FNQ differ markedly, which could explain the significant differences in the clinical phenotype in the two populations and might be used to inform cost-effective CHB care in the region.

Introduction

In Australia, the burden of chronic hepatitis B (CHB) and its complications is disproportionately borne by Indigenous Aboriginal and Torres Strait Islander peoples. The prevalence of CHB among Aboriginal and Torres Strait Islander Australians is over twice that of the general Australian population, and this contributes to a four to six times greater incidence of hepatocellular carcinoma (HCC) among Aboriginal and Torres Strait Islander Australians.[1–4]

To reduce HCC-related mortality, Australian guidelines recommend 6-monthly ultrasound surveillance for HCC in all Aboriginal and Torres Strait Islander

Conflict of interest: None.

Australians living with CHB aged ≥50 years.[5] These recommendations are based, predominantly, on Northern Territory linkage data collected between 1990 and 2011, which demonstrated a steep increase in HCC incidence once Aboriginal Australians passed the age of 50.[6] However, the generalisability of these findings to other regions of Australia has not been established.

Far North Queensland (FNQ) is the only part of Australia which includes the homelands of both Aboriginal and Torres Strait Islander Australians. Although Aboriginals and Torres Strait Islanders face many similar challenges, Torres Strait Islanders are an anthropologically distinct Melanesian population with genetic and sociocultural connections to Papuan and Austronesian peoples.[7–9] Although CHB-related HCC in the local Torres Strait Islander population is reported regularly to the Queensland Cancer Registry, no Aboriginal with CHB was diagnosed with HCC in FNQ between 1999 and 2016.[10] This has led to FNQ clinicians querying the local cost-effectiveness of the routine HCC surveillance of non-cirrhotic Aboriginals with CHB aged ≥50 years that is recommended in national guidelines.[11] It has also led to speculation about the explanation for the apparent rarity of CHB-related HCC in the FNQ Aboriginal population.

One hypothesis is that different HBV genotypes may explain the apparent differences in clinical course. Using phylogenetic analyses, HBV can be classified into at least 10 genotypes (A–J), with genotypes A, B, C, D and F further divided into sub-genotypes.[12] Compared to those infected with other HBV genotypes, individuals with HBV/C genotype generally have longer periods of high HBV DNA replication, delayed hepatitis B e antigen (HBeAg) seroconversion, a longer immune clearance phase and, thus, a longer phase of hepatic inflammation.[13] Patients with HBV/C infection are therefore more likely to develop cirrhosis than individuals with other HBV genotypes, and they have an up to 10-fold increase in the risk of HCC.[14,15] Aboriginals with CHB in the Northern Territory universally have an HBV/C4 infection, which is believed to contribute to their high rate of CHB-related complications.[16] Much less is known about prevailing HBV genotypes in FNQ, although in one small series, three out of five cases of Aboriginals born in southern Queensland had an HBV/D genotype infection.[17]

This study was performed to determine the HBV genotypes in the FNQ Aboriginal and Torres Strait Islander population and their correlation with clinical phenotype. We hypothesised that differences in HBV genotype might explain the striking differences in HCC incidence between Aboriginals living in FNQ and those in the Northern Territory. If a difference were identified, this might inform cost-effective HBV care and HCC surveillance strategies in the FNQ Aboriginal and Torres Strait Islander population.

Methods

This prospective, observational study was performed in FNQ, a 380 000 km^2 region of tropical Australia with a population of approximately 290 000 people, of whom 9.1% identify as Aboriginal, 4.7% identify as Torres Strait Islander and 3.0% identify as both.[18]

HBV is a notifiable disease in Queensland, and we identified potential participants using Queensland's Notifiable Conditions System. Individuals were eligible for the study if they had a diagnosis of CHB (two positive hepatitis B surface antigen (HBsAg) tests >6 months apart) and if they identified as an Aboriginal, a Torres Strait Islander or both. Eligible individuals provided written informed consent to participate in the study. The first participant was enrolled in April 2019, and all participants were followed until 1 June 2023. Demographic, clinical, laboratory and radiological data were correlated with clinical outcomes. Participants were defined as being engaged in care if they were receiving anti-HBV therapy or had a quantitative HBV viral load requested in 2022. Participants were categorised as having cirrhosis if they had a diagnosis of cirrhosis on imaging that had been reported by a specialist radiologist, their most recent AST to Platelet Ratio Index (APRI) score was >2, or their transient elastography score was >12.5 kPa without another, more likely, explanation.[5,19] Although transient elastography was performed in most patients, the remote residence of many precluded this testing in all. Metabolic-associated fatty liver disease (MAFLD) was said to be present if a specialist radiologist reported its presence on imaging.

National guidelines were used to define the phase of disease and to determine patients' eligibility for antiviral treatment.[5] Patients were considered to meet national criteria for HCC surveillance if they had cirrhosis or were ≥50 years of age. HCC was defined using Australian guidelines.[1]

Patients were asked about smoking and hazardous alcohol use (regular consumption of >10 units of alcohol per week or regular binges of >4 units per day).[20] Smoking or hazardous alcohol use was considered current if it had taken place in the 6 months prior to enrolment. Obesity was defined as a body mass index (BMI) of ≥30 kg/m^2. Patients were defined as having diabetes mellitus if there was a recorded glycosylated haemoglobin of ≥6.5%.

To determine HBV genotype, HBV DNA was extracted from 200 μL serum using the QIAamp DNA Minikit (QIAGEN, Venlo, Limburg, The Netherlands) according to the manufacturer's instructions. Sequence data and analysis for genotyping were obtained as described

previously, amplifying the reverse transcriptase region of the HBV polymerase gene (and corresponding overlapping region of the surface gene).[21] Specimens with a viral load below 400 IU/mL generally cannot be genotyped as there is insufficient DNA for a reliable result.

Notification of a cancer diagnosis to the Queensland Cancer Registry is a statutory requirement for all public and private hospitals, nursing homes and pathology services throughout Queensland. The Queensland Cancer Registry provided the individual details of all Aboriginal and Torres Strait Islander Australians diagnosed with HCC in the FNQ region between 1 January 2000 and 31 December 2020. Hepatitis B serology results of these individuals – both at the time of HCC diagnosis and historically – were determined by interrogating AUSLAB, Queensland's electronic laboratory database.

Data were de-identified, entered into an electronic database (REDcap) and analysed using statistical software (Stata version 14.2). Groups were analysed using the Kruskal–Wallis, chi-squared and Fisher's exact tests, where appropriate.

The study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (HREC-09/105) and the FNQ Human Research Ethics Committee (HREC/16/QCH/109).

Results

There were 197 individuals enrolled in the study; their median (interquartile range (IQR)) age at enrolment was 45 (38–57) years; 99/197 (50%) were male. Of the 197 individuals, 112 (57%) identified as a Torres Strait Islander, 66 (34%) identified as an Aboriginal and 19 (10%) identified as both.

After a median (IQR) of 2.4 (2.1–3.4) years, there had been seven (4%) deaths, three were due to HCC, two were due to end-stage renal disease, one was due to oesophageal cancer and one was due to pneumonia. Of the remaining 190 patients, 133 (70%) remained engaged in care (Fig. 1).

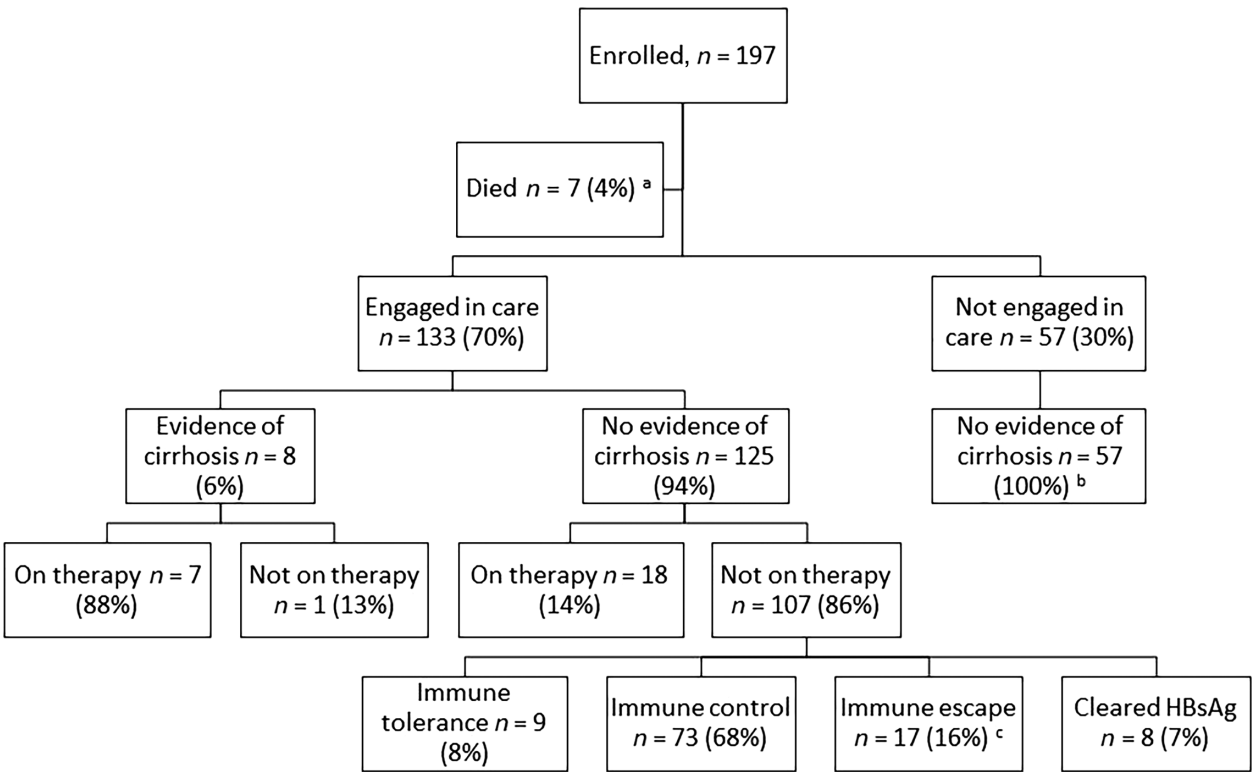

Figure 1 Consort diagram showing clinical course of patients during study. [a]Two of the seven individuals that died had confirmed cirrhosis. [b]Of these 57 patients, 56 were engaged in care in 2021; 36 (63%) were in the immune control phase, 12 (21%) were in the immune escape phase, 7 (12%) were in the immune tolerance phase and 1 (2%) was in the immune clearance phase. The final individual had insufficient blood collected to determine his HBV DNA level, so it was not possible to determine his phase.[c]7/17 met Australian criteria for therapy; all seven had shared in decision-making with their primary provider elected not to commence therapy.

Comorbidity

The median (IQR) BMI of the 186 individuals with sufficient data for its calculation was 31.7 (26.8–37.2) kg/m^2; 107/186 (58%) had a BMI ≥30 kg/m^2. Diabetes mellitus was present in 98/197 (50%), and 103/197 (52%) had imaging suggesting MAFLD. There were 106/197 (54%) who acknowledged current hazardous alcohol use, whereas 74/197 (38%) were current smokers.

Cirrhosis and HCC

Cirrhosis was diagnosed in 10/197 (5%). Patients with cirrhosis were older than those without cirrhosis (median (IQR): 63 (55–72) vs 46 (41–59) years, $P = 0.001$); 2/10 (20%) with cirrhosis reported current – and an additional 5/10 had a history of – hazardous alcohol consumption; 4/10 (40%) were obese. Three patients developed HCC; two were cirrhotic, developing HCC at the ages of 49 and 56 respectively. The third patient – without confirmed cirrhosis – developed HCC at the age of 75. All three had a history of hazardous alcohol consumption, and all three patients died from their HCC during the study.

Antiviral therapy and HCC surveillance

At the end of the study, there were 33/133 (25%) patients engaged in care who satisfied Australian criteria for initiating antiviral therapy, of whom 25/33 (76%) were receiving it. There were 64/133 (48%) who satisfied Australian criteria for HCC surveillance, of whom 28/64 (44%) had a least one ultrasound during 2022.

Table 1 Characteristics of Aboriginal and Torres Strait Islander Australian participants at end of study period

	Aboriginal Australian, $n = 66$	Torres Strait Islander heritage,† $n = 131$	*P*
Age (years)	44 (39–52)	52 (42–64)	0.0003
Male sex	39 (59%)	60 (46%)	0.08
Follow-up time (years)	2.2 (1.9–2.6)	2.6 (2.3–3.5)	0.0001
Cirrhosis	0	10 (8%)	0.03
HCC	0	3 (2.4%)	0.55
HCC or cirrhosis	0	11 (8%)	0.02
APRI score	0.30 (0.20–0.42)	0.37 (0.25–0.49)	0.004
Transient elastography (kPa)‡	6.6 (4.8–8.1)	6.3 (5.0–9.1)	0.50
Most recent ALT	25 (19–43)	32 (20–52)	0.10
HBeAg positive	3 (5%)	21 (16%)	0.02
HBV DNA (IU/mL)§	123 (19–2118)	297 (23–2338)	0.58
Engaged in care¶	45 (68%)	95 (73%)	0.53
HCC surveillance ultrasound in 2022††	6/20 (30%)	36/71 (51%)	0.13
On treatment	4 (6%)	22 (17%)	0.04
Cleared HbsAg	2 (3%)	7 (5%)	0.72
Died during the study	0	7 (5%)	0.10
Body mass index (BMI) (kg/m^2)	27.8 (22.5–35.1)	33.1 (28.7–37.7)	0.0002
BMI >30 kg/m^2,‡‡	23/58 (40%)	84/128 (66%)	0.001
Diabetes mellitus	24 (36%)	74 (56%)	0.008
MAFLD	20 (30%)	83 (63%)	<0.0001
Other prescribed medications	1 (0–3)	3 (1–6)	0.0004
Current hazardous alcohol	51 (77%)	55 (42%)	<0.0001
Ever hazardous alcohol	64 (97%)	90 (69%)	<0.0001
Current cigarette smoker	37 (56%)	37 (28%)	<0.0001
Ever cigarette smoker	40 (61%)	73 (56%)	0.51

†Includes 19 individuals who identified as both Aboriginal and Torres Strait Islander Australian.

‡Only 162 patients were able to receive transient elastography.

§Only includes those individuals not receiving antiviral therapy.

¶Currently receiving antiviral therapy or had a HBV DNA performed during 2022.

††Of the individuals in whom HCC surveillance is suggested in national guidelines.[5]

‡‡Only 186 patients had sufficient data to calculate a BMI.

All numbers are the absolute number (%) or median (IQR). APRI, AST to Platelet Ratio Index; ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; HbsAg, hepatitis B surface antigen; HBV DNA, hepatitis B virus deoxyribose nucleic acid; HCC, hepatocellular carcinoma; IQR, interquartile range; MAFLD, metabolic-associated fatty liver disease.

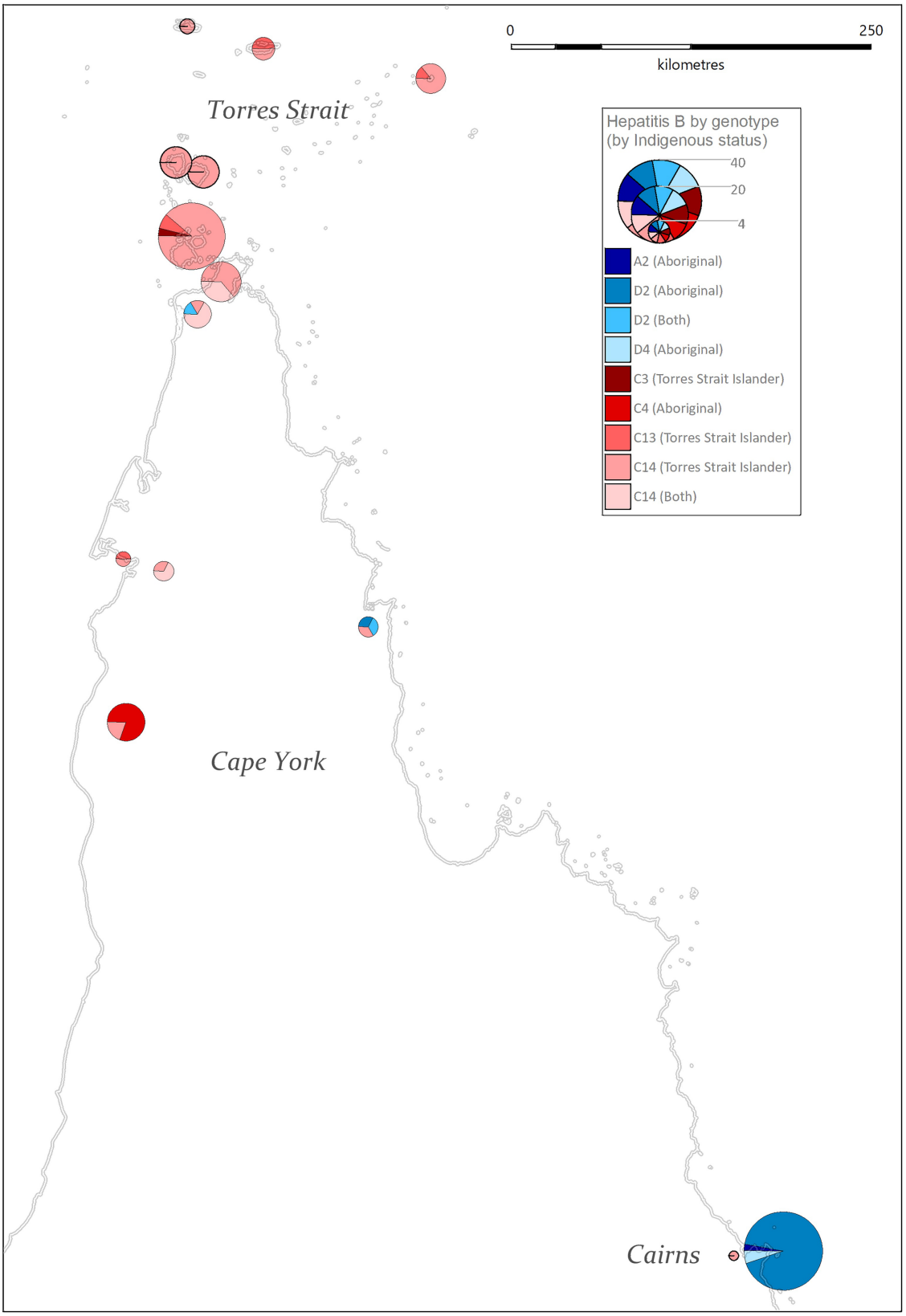

Figure 2 Geographic distribution of sub-genotypes stratified by Aboriginal and Torres Strait Islander status.

Comparison of Aboriginal and Torres Strait Islander Australians

The Aboriginals in the cohort were younger than those with Torres Strait Islander heritage; however, they were more likely to be HBeAg negative. No Aboriginal had cirrhosis or was diagnosed with a HCC during the study; instead, all 10 diagnoses of cirrhosis and all three diagnoses of HCC occurred in Torres Strait Islanders (Table 1).

Genotype

A genotype could be determined in 134/197 (68%); in 61 (31%), the viral load was too low and two had insufficient blood for testing. There were 93 individuals with HBV/C (HBV/C14 in 78 (84%), HBV/C4 in eight (9%), HBV/C13 in six (6%) and HBV/C3 in one (1%)), 40 with HBV/D genotype (HBV/D2 in 37 (93%), HBV/D4 in two (5%) and HBV/D3 in two (3%)) and one with a HBV/A2 genotype.

The individuals' genotypes correlated with their ethnicity and region of residence: 38/47 (81%) Aboriginals with a confirmed genotype had a HBV/D genotype, compared with 0/75 of Torres Strait Islanders ($P < 0.0001$). Among the 12 individuals identifying as both Aboriginal and Torres Strait Islander, two (17%) had a HBV/D genotype. All but two (37/39 (95%)) of the individuals living in the region's south had a HBV/D genotype; one Aboriginal, born in New South Wales, had a HBV/A2 genotype. The sole individual with an HBV/C genotype living in the south of the region was a Torres Strait Islander who had relocated there. In contrast, all 55 individuals with a confirmed genotype living in the Torres Strait Islands had a HBV/C genotype. All eight Aboriginals with a HBV/C genotype lived in a single remote community on the Cape York Peninsula and had HBV/C4. HBV/C4 was not identified in any other study participant (Fig. 2).

It was possible to genotype the HBV in 2/3 individuals who developed HCC; in both, this was HBV/C14. The incidence of HCC among patients with a HBV/C infection was 12.8/1000 patient-years; it was 0/1000 patient-years among patients with a HBV/D infection. It was possible to genotype the HBV in 6/10 individuals with cirrhosis; in all six, it was HBV/C14.

Despite their greater burden of HCC and cirrhosis, individuals with a HBV/C genotype were less likely to be male

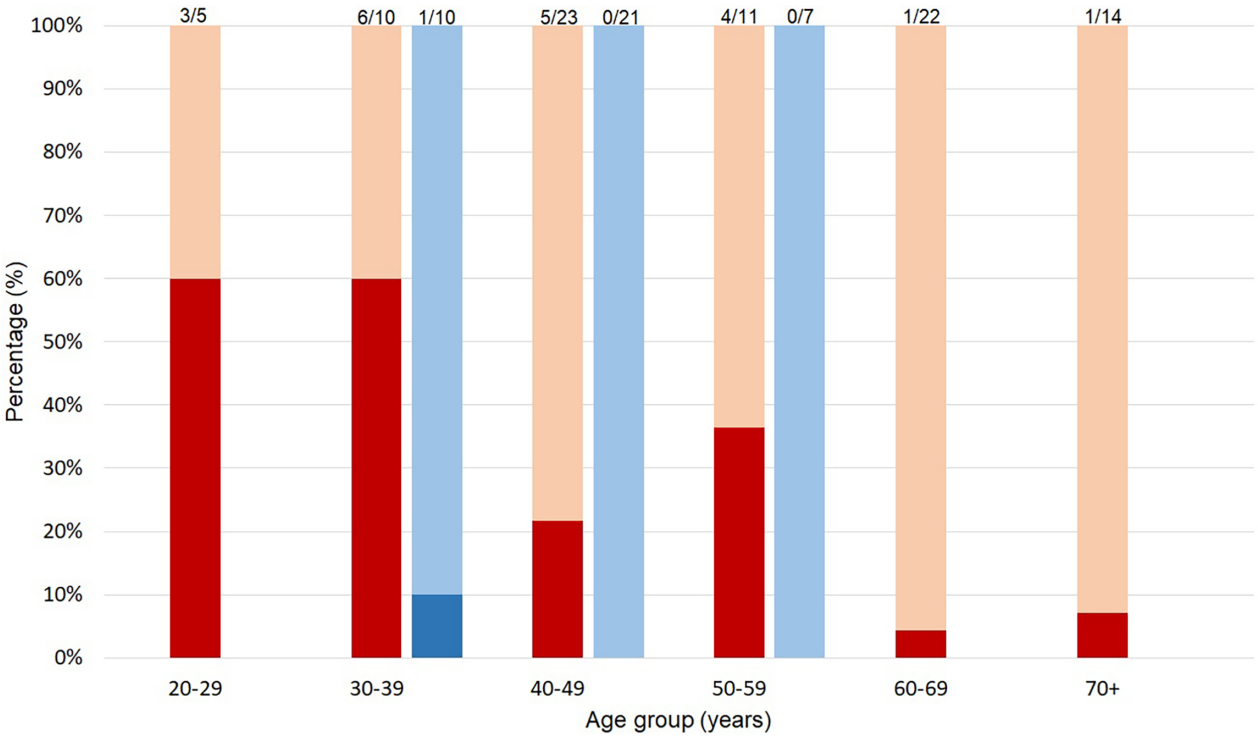

Figure 3 Proportion of patients with a HBV/C and HBV/D genotype who remained HBeAg positive over time. HBeAg, hepatitis B e antigen. (■) C genotype eAg positive; (■) C genotype eAg negative; (■) D genotype eAg positive; (■) D genotype eAg negative.

Table 2 Comparison of characteristics of individuals infected with HBV/D genotype compared with those with HBV/C genotype

	HBV/D,† $n = 40$	HBV/C,‡ $n = 93$	P
Age	43 (39–48)	53 (42–66)	0.0002
Male sex	26 (65%)	40 (43%)	0.02
Aboriginal	38 (95%)	8 (9%)	<0.0001
Torres Strait Islander	2 (5%)	85 (91%)	<0.0001
Follow-up time (years)	2.3 (2.1–2.6)	2.6 (1.6–3.5)	0.38
Cirrhosis	0	6 (6%)	0.18
HCC	0	2 (2%)	1.0
APRI score	0.30 (0.19–0.40)	0.37 (0.25–0.49)	0.007
FibroScan score	6.6 (4.4–10.1)	6.3 (5.1–9.1)	0.63
Engaged in care	29 (73%)	59 (67%)	0.54
Most recent ALT	30 (19–43)	32 (20–51)	0.25
HBeAg positive	1 (3%)	23 (25%)	0.001
HBV DNA (IU/mL)§	437 (50–2800)	620 (137–234 975)	0.05
On treatment	1 (3%)	14 (15%)	0.04
Cleared	1 (3%)	2 (2%)	1.0
Died	0	5 (5%)	0.32
Body mass index (kg/m^2)	26.9 (21.6–34.2)	32.4 (27.5–36.3)	0.001
Diabetes mellitus	15 (38%)	50 (54%)	0.09
Current hazardous alcohol	35 (88%)	42 (93%)	<0.0001
Ever hazardous alcohol	37 (93%)	64 (69%)	0.004
Current cigarette smoker	22 (55%)	30 (32%)	0.01
Ever cigarette smoker	22 (55%)	54 (58%)	0.74

†Includes individuals with genotypes D2 (37), D3 (1) and D4 (2).

‡Includes individuals with genotypes C3 (1), C4 (8), C13 (6) and C14 (78).

§Only includes those individuals not receiving antiviral therapy.

All numbers are the absolute number (%) or median (IQR). APRI, AST to Platelet Ratio Index; ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; HbsAg, hepatitis B surface antigen; HBV DNA, hepatitis B virus deoxyribose nucleic acid; HCC, hepatocellular carcinoma; IQR, interquartile range; MAFLD, metabolic-associated fatty liver disease.

and less likely to be currently smoking or drinking alcohol hazardously. Individuals with a HBV/C genotype were older than those with a HBV/D genotype, but despite this, they were more likely to be HBeAg positive (Fig. 3, Table 2). The sole HBeAg-positive patient with a HBV/D genotype was 38 – and the test was weakly positive – whereas the oldest patient HBeAg-positive with a HBV/C genotype was 78 (Fig. 3). Among the eight Aboriginals with a C4 genotype, 2/8 (25%) remained HBeAg positive at the ages of 51 and 54 respectively.

HCC in Aboriginal and Torres Strait Islander Australians in FNQ, 2000–2020

Between 1 January 2000 and 31 December 2020, there were a total of 34 Aboriginals and 30 Torres Strait Islanders diagnosed with HCC in FNQ; of these 64 individuals, 58 (91%) had an accessible HBsAg result. Aboriginals were less likely to be HBsAg positive at HCC diagnosis than Torres Strait Islanders (1/29 (3%) vs 20/29 (69%), $P < 0.0001$) (Fig. S1). The sole Aboriginal who was HBsAg positive at HCC diagnosis lived in the community where the HBV genotype among Aboriginals was universally HBV/C4. There were 39/64 (61%) who had an accessible hepatitis B core antibody (HBcAb) result. Aboriginals were less likely to be HBcAb positive at HCC diagnosis than Torres Strait Islanders (3/13 (23%) vs 24/26 (89%), $P < 0.0001$). One of these three Aboriginals was the HbsAg-positive individual highlighted above; the other two had been HBsAg-negative for 20 and 5 years respectively. All three HBcAb-positive Aboriginals with HCC were cirrhotic and had ongoing hazardous alcohol use at the time of their HCC diagnosis.

Discussion

In a region of Australia where there has only been a single case of HCC in an HBsAg-positive Aboriginal this century, it was notable that over 80% of Aboriginals in this cohort had a HBV/D genotype and that all individuals with a HBV/D genotype >38 years of age had cleared HBeAg. Indeed, despite a significant burden of comorbidities that would be expected to increase the risk of liver disease, no Aboriginals in this cohort had cirrhosis or developed HCC during the study. In contrast, over 97% of Torres Strait

Islanders in the cohort had a HBV/C genotype, with one individual remaining HBeAg positive into their eighth decade. All three HCCs and all 10 diagnoses of cirrhosis in the cohort occurred in Torres Strait Islanders.

Indeed, since 2000, two-thirds of the Torres Strait Islanders diagnosed with HCC in the region were HBsAg positive. In contrast, only one Aboriginal diagnosed with HCC was HBsAg positive, and this individual lived in the community where all Aboriginals with a confirmed HBV genotype had the HBV/C4 genotype.

These data suggest that, given the significant challenges associated with delivering care to remote Australia, an approach that incorporates HBV genotype into HCC screening strategies may assist with the delivery of cost-effective care.[22] It is notable that the incidence of HCC in HBV/D genotype infections in this cohort was below the incident threshold of >2/1000 patient-years recommended by the American Association for the Study of Liver Diseases as cost-effective for HCC surveillance.[23]

Current Australian guidelines – which make no distinction between Aboriginal and Torres Strait Islander Australians and which do not consider genotype in the screening algorithm – recommend that all Aboriginal and Torres Strait Islander Australians with CHB receive biannual ultrasound HCC surveillance after the age of 50. However, these recommendations are based predominantly on linkage data collected in Aboriginals living in the Northern Territory, a population which universally has the HBV/C4 genotype, a genotype which was identified in only a single community in this FNQ cohort.[24] The absence of HCC in an HBsAg-positive Aboriginal living outside of this community this century suggests that routine HCC surveillance in Aboriginals infected with HBV/D in the region is likely to be a low-value investigation in the absence of cirrhosis or a strong family history of HCC.[25]

HBV/C infection is associated with an increased risk of HCC, independent of the presence of liver cirrhosis, patient age, sex, HBeAg positivity and ALT level.[14] HBV/F and HBV/A infections are also associated with increased HCC risk.[26,27] In contrast, there was only a single case of cirrhosis and no cases of HCC among 114 Canadian Inuits with an HBV/B6 infection during a median follow-up of 23 years.[28] In an Alaskan study that has many similarities with this FNQ cohort's findings, individuals with HBV/C infection had HBeAg seroconversion almost 30 years later than individuals with genotype HBV/A, HBV/B and HBV/D and had a higher incidence of HCC.[26] The incidence of HCC in this Alaskan cohort was 4.77 per 1000 patient-years among individuals with HBV/C infection, approximately 10 times the rate of 0.47 per 1000 patient-years for individuals with HBV/D infection.[15]

Obesity, hazardous alcohol consumption and cigarette smoking were common in this FNQ cohort. Not only do all three increase the risk of HCC, but they are also important risk factors for the five most common causes of death in Aboriginal and Torres Strait Islander Australians in the region: coronary artery disease, diabetes mellitus, lung cancer, cerebrovascular disease and chronic obstructive pulmonary disease.[29–32] They are also risk factors for seven of the eight cancers (lung, breast, colorectal, uterine, cervical, oesophageal and stomach cancer, several of which require invasive testing for diagnosis) that occur more commonly than HCC in the region's remote north, where over 90% of the population report Torres Strait Islander heritage.[33] They are also significant risk factors for sepsis in Aboriginal and Torres Strait Islander Australians in the region.[34] Indeed, it was notable that a minority of the deaths in this cohort of individuals living with CHB was due to liver disease and that all three individuals with HCC also had a history of hazardous alcohol consumption. The management of comorbidity is not strongly emphasised in current national guidelines – receiving only a C1 GRADE recommendation – however, it is essential to integrate the management of these comorbidities into CHB care to reduce liver complications and improve long-term general health outcomes.[4,35]

The study had several limitations. The follow-up period was short. The Aboriginals enrolled in the study were – as a population – younger than the Torres Strait Islanders, and this is likely to have contributed to their lower rate of cirrhosis and HCC. However, the reported association between genotype and clinical phenotype accords with the observation that only one HBsAg-positive Aboriginal has been diagnosed with HCC in FNQ this century and that individual was resident in a community where Aboriginals with CHB in this cohort universally had the HBV/C4 genotype. The earlier clearance of HBeAg in the Aboriginals with an HBV/D infection also provides a plausible mechanism for our hypothesis and replicates observations from other parts of the world.[15] Only a third of the patients meeting criteria for HCC surveillance had an ultrasound in 2022, highlighting the real-world challenges of delivering this surveillance in remote Australia. Underdiagnosis of HCC in the cohort is therefore possible, although the absence of cirrhosis in all Aboriginal individuals in the cohort suggests that it is unlikely to be a major issue.[22]

Conclusions

Geographical differences in prevailing HBV genotypes – that correlate strongly with Aboriginal and Torres Strait Islander

status – provide a plausible biological mechanism to support local clinicians' observations that the clinical phenotype of Aboriginals with CHB in FNQ is different to that seen in Torres Strait Islanders in the region and in Aboriginal Australians in the Northern Territory. HBV genotype might be employed to stratify HCC risk in the FNQ region – and potentially nationally – to inform more cost-effective HBV care.

Acknowledgements

The authors would like to acknowledge Mr Peter Horne who assisted with the production of Figure 2. The research was funded by the Australian National Health and Medical Research Council (grant 1156722). Open access publishing facilitated by University of New South Wales, as part of the Wiley - University of New South Wales agreement via the Council of Australian University Librarians.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Figure S1. Hepatitis B status of Aboriginal and Torres Strait Islander Australians with a diagnosis of hepatocellular carcinoma reported to Queensland Cancer Registry between January 2000 and December 2020.