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Liver Disease in Aboriginal and Torres Strait Islander People

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Abstract

Aboriginal and Torres Strait Islander people have a substantially higher prevalence of liver disease than non-Indigenous Australians. Cirrhosis and its complications were the sixth leading cause of mortality for Aboriginal and Torres Strait Islander people in 2020. Liver disease has been estimated to be the third leading cause of the mortality gap between Aboriginal and Torres Strait Islander and non-Indigenous people due to chronic disease, accounting for 11% of this gap. While current trends show reducing mortality rates for Aboriginal and Torres Strait Islander people for conditions including circulatory disease, diabetes and kidney disease, there are no data to suggest a similar decline for liver disease. This review highlights the common causes of liver disease affecting Aboriginal and Torres Strait Islander people, which include hepatitis B, hepatitis C, alcohol related liver disease, metabolic dysfunction-associated fatty liver disease, and cirrhosis and its complications including hepatocellular carcinoma. Current treatments including liver transplantation as well as suggestions for improving detection, treatment and access to liver care will also be discussed. Recent revolutions in the detection and treatment of liver disease make efforts to improve access to treatment and outcomes an urgent priority for Aboriginal and Torres Strait Islander people.

Keywords

Liver Disease, Aboriginal and Torres Strait Islander people

Aboriginal and Torres Strait Islander people are disproportionately affected by liver disease. Cirrhosis and its complications such as liver cancer was the sixth leading cause of mortality for Aboriginal and Torres Strait Islander people in 2020 (Australian Bureau of Statistics [ABS], 2021). Only ischaemic heart disease, diabetes, chronic lower respiratory diseases, respiratory malignancy and suicide accounted for a greater number of deaths. In addition, mortality rates from cirrhosis and liver disease were 3.2-fold higher in Aboriginal and Torres Strait Islander people compared to non-Indigenous people, the highest rate ratio for any disease other than diabetes and chronic lower respiratory diseases (4.9 and 3.4, respectively). Moreover, liver disease has been estimated to be the third leading cause of the mortality gap between Aboriginal and Torres Strait Islander and non-Indigenous people due to chronic disease, accounting for 11% of this mortality gap, following ischaemic heart disease (22%) and diabetes (12%) (Australian Institute of Health and Welfare [AIHW], 2010). While current trends show reducing mortality rates for Aboriginal and Torres Strait Islander people for many important diseases including circulatory disease, diabetes and kidney disease, there are no data to suggest a similar decline for liver disease. Indeed, the current obesity epidemic is likely to be a major driver into the future of liver disease morbidity and mortality.

Despite the significant morbidity and mortality from liver disease among Aboriginal and Torres Strait Islander people, the problem has received a low priority from a health education, planning and research perspective. This review will therefore discuss the common causes of liver disease affecting Aboriginal and Torres Strait Islander people which include hepatitis B, hepatitis C, alcohol related liver disease, and metabolic dysfunction-associated fatty liver disease and their current treatments including liver transplantation. It will also discuss cirrhosis and its complications including hepatocellular carcinoma (HCC). Suggestions for how to improve the detection and treatment and access to liver care will also be discussed.

Hepatitis B

Historically, Aboriginal and Torres Strait Islander people have played a vital part in the discovery of hepatitis B (HBV) with the hepatitis B surface antigen first discovered from the serum of Aboriginal and Torres Strait Islander people (Blumberg & Alter, 1965). Hepatitis B is an ancient infection which has likely existed among this population for thousands of years (Davies et al., 2013). The overall HBV prevalence in the Aboriginal and Torres Strait Islander population is more than two-fold that of the non-Indigenous population (2.5% versus 0.95%) with an even higher estimated prevalence of 5.5% in remote/very remotely living Aboriginal and Torres Strait Islander people (AIHW, 2017). Aboriginal and Torres Strait Islander people have evolved a unique HBV genotype (genotype C4) (Littlejohn et al., 2014) which appears to be associated with a greater risk of chronic liver disease, hepatocellular carcinoma and potential for vaccine failure.

Hepatitis B vaccination is a cornerstone for the prevention of the virus, resulting in reduced rates of infection and its associated complications in vaccinated populations (Chang, 2011). The universal HBV vaccination program was introduced in the year 2000 for infants in Australia and current recommendations are for HBV screening for all Aboriginal and Torres Strait Islander people and vaccination of all Aboriginal and Torres Strait Islander people who are non-immune (National Aboriginal Community Controlled Health Organisation & The Royal Australian College of General Practitioners, 2018). Nationally, full immunisation of infants by 12 months of age has reached the 95% target (MacLachlan et al., 2019), yet vaccination rates in Aboriginal and Torres Strait Islander children younger than 12 months of age is lower at 93% (Kirby Institute, 2018). However, by 24 months of age, the vaccination rate among Aboriginal and Torres Strait Islander children was found to be higher at 98% compared to 96% among non-Indigenous children between 2013-2017. Nevertheless, the rate of new infections remains higher in Aboriginal and Torres Strait Islander people compared to non-Indigenous people with the notification rate 2.3 times that of non-Indigenous people in 2017 (45.1 per 100 000 vs 19.2 per 100 000) (Kirby Institute, 2018).

Furthermore, this does not factor in under-reporting of cases with only approximately 50% of notifications including Aboriginal and Torres Strait Islander status at the time.

The difficulties of delivering HBV care in remote Aboriginal and Torres Strait Islander communities has been highlighted in a recent study of patients attending a remote Aboriginal and Torres Strait Islander health service (Narayana et al., 2021). The study found high rates of both chronic HBV infection (12%) and resolved infection (20%). Only 52% of patients had been screened for HBV infection and 48% had completed a full HBV vaccination course.

A further concern is possible suboptimal response to the vaccine in Aboriginal and Torres Strait Islander people, with high rates of breakthrough HBV infection noted (Dent et al. 2010; Hanna et al., 1997). In the study by Narayana et al. (2021), 24% of patients had sub-therapeutic levels of hepatitis B surface antibody (HBsAb) (<10 IU/mL) and 6% had breakthrough HBV infection despite being fully vaccinated. It has been suggested that primary vaccine failure may be the reason behind the subtherapeutic HBsAb levels with 22% of participants in the study failing to seroconvert despite prospective vaccination. These findings are consistent with previous reports (Dent et al., 2010; Griffiths et al., Hanna et al., 1997; 2014). The reasons for possible lower seroconversion and protection following HBV vaccination in Aboriginal and Torres Strait Islander people are unknown. Immunosuppression related to a higher comorbidity burden seen in Aboriginal and Torres Strait Islander people as well as a mismatch between the serotype used in the HBV vaccine (A2 subgenotype) and the main serotype affecting Aboriginal and Torres Strait Islander people (C4 subgenotype) are potential causes contributing to vaccine failure (Cheah et al., 2018; Davies et al., 2013; Littlejohn et al., 2014). Overall, further research into HBV in Aboriginal and Torres Strait Islander people is needed, including exploring the need for an alternative to the current vaccine available.

Once HBV infection has been detected, long-term six-monthly monitoring of chronic infection is vital. Chronic infection (characterised by positive hepatitis B surface antigen) can transition from inactive infection to active hepatitis and requires regular monitoring with six-monthly liver function tests and viral load. Active hepatitis is asymptomatic and without

treatment can lead to liver fibrosis, cirrhosis, liver failure and HCC. For patients with active hepatitis, highly effective antiviral agents (entecavir, tenofovir) are available, and treatment can substantially reduce complications including cirrhosis and HCC. Aboriginal and Torres Strait Islander people with chronic HBV infection who are over 50 years old, have an increased risk of HCC and should be offered six-monthly liver ultrasound surveillance. Ultrasound surveillance in HBV has been shown to reduce mortality in the surveillance group due to early detection of smaller, curable tumours (Zhang et al., 2004).

Improving engagement in HBV care via increased uptake of monitoring and treatment should be a major goal in Aboriginal and Torres Strait Islander health. Promising models have been described in remote settings involving co-designed, culturally appropriate mobile liver clinics (Hla et al., 2020) aimed at improving uptake of monitoring, treatment and HCC surveillance.

Hepatitis C

Hepatitis C (HCV) is another blood-borne virus that disproportionally affects Aboriginal and Torres Strait Islander people, with a prevalence of 4.4% and 0.94% between Aboriginal and Torres Strait Islander and non-Indigenous populations, respectively (Hepatitis C Estimates and Projections Working Group, 2006). While Aboriginal and Torres Strait Islander people comprise 2.8% of the population, they account for 9% of the patients diagnosed with HCV (Kirby Institute, 2016). Between 2013 to 2017, notification of hepatitis C infection in Aboriginal and Torres Strait Islander people increased by approximately 15%, whereas it decreased in non-Indigenous people by 12%. In Aboriginal and Torres Strait Islander males, the rate of infection increased by 28.5% whilst in Aboriginal and Torres Strait Islander females, the rate decreased by 6%. The higher prevalence of HCV in Aboriginal and Torres Strait Islander people can be attributed in part to their over representation in high-risk groups such as people in custody and people who use intravenous drugs (Brener et al., 2016).

Screening and detection of HCV has become increasingly important following the recent revolution in HCV therapy and the availability of direct acting antivirals (DAAs)

(Pawlotsky et al., 2015). Unlike prior ineffective and highly toxic interferon-based therapies, DAA medications can ‘cure’ HCV infection in 95% of individuals without a significant side effect profile. Commonly prescribed regimens include Sofosbuvir/Velpatasvir (Epclusa®, one tablet taken daily for 12 weeks) and Glecaprevir/Pibrentasvir (Maviret®, three tablets daily for eight weeks) and are now commonly prescribed in primary care (Hepatitis C Virus Infection Consensus Statement Working Group, 2020).

However, uptake of these medications by Aboriginal and Torres Strait Islander people remains low compared to the general population. In the 2016 Australian Needle and Syringe Program Survey, 18% of Aboriginal and Torres Strait Islander respondents who have HCV and inject drugs had been treated for HCV over the past year in contrast to 23% of non-Indigenous respondents (Kirby Institute, 2017). Aboriginal and Torres Strait Islander participants in the REACH-C study of HCV treatment had a higher rate of loss to follow up (24% compared to 15% for non-Indigenous people) (Yee et al., 2022). However, overall, Aboriginal and Torres Strait Islander status was not associated with loss to follow-up following adjusted analysis (OR=1.21 [1.00-1.46] p=0.05). Increasing HCV screening and treatment uptake for Aboriginal and Torres Strait Islander people should now be an important priority. Part of this challenge involves reducing barriers to treatment including the stigma and shame associated with HCV which prevents Aboriginal and Torres Strait Islander people openly discussing HCV with healthcare providers, family and friends as well as the wider community (Brener et al., 2016). Programs such as dedicated liver clinics which include support from Aboriginal and Torres Strait Islander Health Workers, specialist nurses, general practitioners and oversight from physicians have been effective in improving access to HCV treatment in Aboriginal and Torres Strait Islander communities (Wallace et al., 2018). However, more programs are needed to improve access to HCV treatment among Aboriginal and Torres Strait Islander people in order to prevent progression towards cirrhosis and its complications and to reduce ongoing HCV transmission by infected individuals.

Alcohol Related Liver Disease

Similar to other diseases affecting the liver, Aboriginal and Torres Strait Islander people are affected by alcohol-related liver disease more than non-Indigenous people. Aboriginal and Torres Strait Islander people are 1.2 times more likely to ingest alcohol at harmful levels compared to non-Indigenous people, according to recent data (Gray et al., 2018). The issue affects Aboriginal and Torres Strait Islander males more than females, with males more than twice as likely to consume harmful amounts of alcohol. During the period 2014 to 2018, mortality from alcohol related causes was higher among Aboriginal and Torres Strait Islander people, with 31 per 100,000 Aboriginal and Torres Strait Islander males dying from alcohol related causes compared to 7.2 per 100,000 non-Indigenous males (AIHW, 2020). Amongst females, 11 per 100,000 Aboriginal and Torres Strait Islander females died from alcohol related causes compared to 2.3 per 100,000 non-Indigenous females (AIHW, 2020). Alcohol related liver disease was the most common cause of alcohol related deaths and accounts for the majority of liver disease related mortality in Aboriginal and Torres Strait Islander people.

Harmful alcohol use among Aboriginal and Torres Strait Islander people is a complex issue which relates to broader social factors and historical events including colonisation, segregation and dispossession of culture and land (Gray et al., 2018). Recent data demonstrate a number of encouraging trends concerning alcohol use in Aboriginal and Torres Strait Islander people, including a 1.3-fold higher rate of alcohol abstinence in Aboriginal and Torres Strait Islander versus non-Indigenous people. Of note, in 2018-2019, 26% of Aboriginal and Torres Strait Islander people had never consumed alcohol or were abstinent from alcohol in the past year in comparison to 21% of the general Australian population (AIHW, 2020). A further encouraging trend is the reduction in alcohol related deaths in Aboriginal and Torres Strait Islander people by 40% over 20 years, with 31 deaths per 100,000 in 1998 compared with 18 deaths per 100,000 in 2018 (Figure 1). Single occasion risky alcohol intake is also declining in Aboriginal and Torres Strait Islander people,

with 54% drinking more than four standard alcoholic drinks during one sitting in the past twelve months in 2018-2019 compared to 57% in 2012-2013.

Aboriginal and Torres Strait Islander people are acutely aware of the harmful effects of alcohol on their health and that of the broader community and in many instances have implemented their own interventions to address the problem over the years (Wilson et al., 2010). It is important to note that most Aboriginal and Torres Strait Islander people either abstain from alcohol or do not drink alcohol at levels harmful to their overall health (Gray et al., 2018). However, ongoing efforts and resources are needed to reduce alcohol related morbidity and mortality in Aboriginal and Torres Strait Islander people. Solutions will also involve public health measures that understand and address the underlying complex social inequalities that contribute to the vicious cycle of ongoing misuse.

Figure 1.

Age Standardised Mortality Rate Related to Alcohol Use from 1998 to 2018 in NSW, Qld, WA, NT and SA Among Aboriginal and Torres Strait Islander People and Non-Indigenous People.

Note. From *Aboriginal and Torres Strait Islander Health Performance Framework 2020 summary report*, by AIHW. Copyright AIHW 2020.

Metabolic Dysfunction-Associated Fatty Liver Disease

Non-alcoholic fatty liver disease is a leading cause of chronic liver disease worldwide (Loomba & Sanyal, 2013). It is defined by an excessive amount of fat in the liver, steatosis, unaccounted for by other factors such as alcohol use (Wong et al., 2018). More recently it has been renamed metabolic dysfunction-associated fatty liver disease (MAFLD) to more accurately represent the disease, its subphenotypes and its close association with obesity and metabolic syndrome (Eslam et al., 2020). By 2030 it is estimated that the prevalence of MAFLD in Australia will rise by 25% with over seven million cases projected (Adams et al., 2020). Furthermore, incident MAFLD related mortality in Australia is estimated to increase by 85% between 2019 and 2030. The prevalence amongst Aboriginal and Torres Strait Islander people is less well known. In a study of patients with chronic liver disease, 3% were noted to have MAFLD or non-alcoholic steatohepatitis (NASH) (Valery et al., 2020). Another study of HCC found that 6.1% had MAFLD/NASH (Wigg et al., 2021). However, this is likely an underrepresentation given the recognised poor coding for this condition. The prevalence of MAFLD is often underestimated in healthcare databases that use International Classification of Diseases (ICD) codes, with a recent study finding the prevalence of MAFLD underestimated by 42.9% (Hayward et al., 2021). Diabetes, a surrogate for MAFLD, is also significantly more prevalent in Aboriginal and Torres Strait Islander people with rates ranging between 3.5% and 33.1% (Nguyen et al., 2016). Obesity (BMI ≥30 kg/m), another risk factor for MALFD, is also more prevalent among Aboriginal and Torres Strait Islander people (Thurber et al., 2018). A study in New South Wales, Australia found that 39% of Aboriginal and Torres Strait Islander people were obese compared to 22% of non-Indigenous participants (Thurber et al., 2018). This worrying trend indicates we will see more cases of MAFLD amongst Aboriginal and Torres Strait Islander people in the future, adding to the overall burden of liver disease.

Currently, despite intensive research in the area, the only available treatment for MAFLD is weight loss. A 10% reduction in weight has been shown to improve liver fat and fibrosis and is the recommended weight loss goal for patients (Vilar-Gomez et al., 2015).

MAFLD is important to recognise as it can be one of the first manifestations of metabolic syndrome. Addressing MAFLD/obesity with weight loss can prevent future metabolic complications including hypertension, dyslipidaemia and diabetes and subsequent cardiovascular morbidity (Abdelaal et al., 2017).

Cirrhosis

All chronic liver diseases predispose individuals to the development of advanced fibrosis/cirrhosis (Powell et al., 2019). Cirrhosis is often asymptomatic but with ongoing injury, decompensation may occur. Decompensation is heralded by the complications of cirrhosis which include the development of ascites, variceal bleeding and hepatic encephalopathy, jaundice, renal dysfunction and HCC. Decompensation is an important clinical event as it indicates a significantly reduced survival. Decompensation is associated with an average two-year survival ranging from 38% to 70%, depending on severity (D'Amico et al., 2006).

Unfortunately, Australian data suggests that hospitalisations related to cirrhosis and decompensation are increasing. A study in Queensland, Australia found that hospital admissions due to cirrhosis increased 1.6-fold over the past eight years (Powell et al., 2019). Aboriginal and Torres Strait Islander people were overrepresented among admitted patients with the number increasing by 8.8% from 201 admissions in 2008 to 341 in 2016. Another study in Queensland found that 7% of patients admitted with chronic liver disease (CLD) between 2008 to 2017 identified as an Aboriginal and/or Torres Strait Islander person (Valery et al., 2020). Compared to non-Indigenous patients, more Aboriginal and Torres Strait Islander patients were younger than 50 years of age (44% versus 19% of non-Indigenous patients), had CLD due to alcohol related liver disease (70% versus 47%), resided in the most disadvantaged areas (51% versus 26%), presented via the Emergency Department (68% versus 47%), had a higher rate of readmission and a lower overall survival.

Management of cirrhosis and decompensated cirrhosis is complex and challenging and requires high quality coordinated care approaches that integrate the patient with both

primary and tertiary care. Coordinated care models based on chronic disease management principles have been described and have shown promise in a small randomised controlled pilot trial (Wigg et al., 2013). Such models aim to create improved relationships between patients and the healthcare system using nurse coordinators and better implement the many evidenced based treatments for cirrhosis and decompensation. Treatment of primary liver disease (antiviral therapy, weight loss, alcohol abstinence), management of complications (diuretics and large volume paracentesis for ascites, lactulose and rifaximin for hepatic encephalopathy, beta blocker and endoscopic therapy to prevent variceal haemorrhage, dietetic input for malnutrition), regular monitoring, improved education and self-management are all goals of this model. Designing chronic disease models for cirrhosis that are relevant and appropriate for Aboriginal and Torres Strait Islander people is an important clinical priority, given the overrepresentation of this group in cirrhosis-related admissions.

Hepatocellular Carcinoma (HCC)

Aboriginal and Torres Strait Islander people with cirrhosis (and with non-cirrhotic HBV over 50 years of age) are at an increased risk of developing HCC, the most common primary liver cancer (Villanueva, 2019). Between 2009 and 2013 the incidence rates for HCC in Aboriginal and Torres Strait Islander people was 2.4-fold higher compared to non-Indigenous people (AIHW, 2018). Indeed, HCC is one of the most common causes of cancer-related mortality in Aboriginal and Torres Strait Islander people. The age standardised mortality rate from HCC was also 2.4-fold higher in Aboriginal and Torres Strait Islander people compared to non-Indigenous people. This difference in HCC survival between Aboriginal and Torres Strait Islander and non-Indigenous people is higher than for any other cancer.

Epidemiologically, HCC has many significant differences in Aboriginal and Torres Strait Islander people compared with HCC in non-Indigenous people. Differences in Aboriginal and Torres Strait Islander HCC patients include a higher comorbidity burden, younger age at diagnosis (60 versus 65 years), lower socioeconomic status, higher rurality (52% versus 3% remote/very remotely living) and a greater proportion affected are female

(31% versus 18%) (Wigg et al., 2021). Aboriginal and Torres Strait Islander HCC patients also tend to have multiple HCC cofactors (i.e., viral hepatitis, alcohol misuse, diabetes and obesity) with 51% of cases having two or more cofactors, the most common being viral hepatitis and alcohol. Aboriginal and Torres Strait Islander patients also tend to receive curative treatment less often than non-Indigenous patients (6.6% versus 14.5%, p=0.001) which contributes to the higher mortality rate seen in Aboriginal and Torres Strait Islander people as well as the lower five-year survival (10.0% versus 17.3%, p=0.001).

As per other liver diseases, the higher prevalence and poorer outcomes of HCC for Aboriginal and Torres Strait Islander people suggest the urgent need to understand and address the factors contributing to these differences including improved detection of cirrhosis and increased uptake of liver ultrasound surveillance in those at risk (Villanueva, 2019; Wigg et al., 2021). Detection of HCC at early stages is critical as early-stage HCC has curative treatment options including liver resection, liver transplantation, percutaneous ablation and radiotherapy. Intermediate stage HCC also has treatment options including trans arterial chemotherapy and systemic therapy, that although not curative, have been shown to improve survival in randomised controlled trials (Finn et al., 2020; Llovet et al., 2002; Lo et al., 2002).

Liver Transplantation

Liver transplantation is one of the treatment options in decompensated cirrhosis and early-stage HCC. Despite Aboriginal and Torres Strait Islander people being disproportionately affected by liver disease, less Aboriginal and Torres Strait Islander patients proceed to liver transplantation and are underrepresented in the Australian liver transplant population overall (Chinnaratha et al., 2014). Between 1985 and 2012, out of 3493 liver transplants only 45 (1.3%) were Aboriginal and Torres Strait Islander people. The reasons for this are unknown, however may relate to less early detection and referral of liver disease in primary care, cultural barriers leading to lack of referral, or higher rates of contraindication/comorbidities of referred patients.

Although transplanted less frequently, encouragingly the median overall survival was

similar between Aboriginal and Torres Strait Islander and non-Indigenous people. However, in paediatric transplant recipients there was a trend towards increased re-transplantation and mortality rates for those living in remote areas. Previous studies have also shown that rural areas are also associated with less liver transplant waitlist registration and transplantation (Axelrod et al., 2008; Chinnaratha et al., 2014). This trend is concerning given that 16% and 45% of Australians living in remote and very remote areas, respectively, are Aboriginal and Torres Strait Islander people (ABS, 2018).

Clearly, there is a need to understand and address the barriers to liver transplantation for Aboriginal and Torres Strait Islander people. A starting point may be learning from the experience of kidney disease and transplantation in Australia. A comprehensive review into the hurdles, practical challenges and service gaps faced by Aboriginal and Torres Strait Islander patients receiving treatment for kidney disease has already been performed (Garrard & McDonald, 2019). From this review, funding was established for the National Indigenous Kidney Transplantation Taskforce, involving Aboriginal and Torres Strait Islander representatives, responsible for implementing and evaluating the priority recommendations of the review. A similar approach seems now warranted for liver disease and liver transplantation.

Towards Improving Outcomes for Aboriginal and Torres Strait Islander Liver Diseases

Liver disease affects Aboriginal and Torres Strait Islander people disproportionally. Although effective and evidence-based treatments are available for all major liver diseases (hepatitis B vaccination, antiviral therapy, alcohol abstinence, weight loss, liver transplantation), improving outcomes remains a significant challenge. Potential approaches to address these challenges are outlined below.

Understanding social determinants of health

Liver diseases in Aboriginal and Torres Strait Islander people are intimately linked to social determinants of health. Poverty, poor health literacy, rurality and poor access to care are all facilitators of the key drivers for liver disease in Aboriginal and Torres Strait Islander people including viral hepatitis, alcohol misuse and obesity/metabolic syndrome. Without

political will and effective public health interventions to address these inequalities, the prospects for health care interventions alone to achieve major improvements remain guarded.

Co-design and Strengths-Based Approach

Effective health interventions for liver diseases will need to involve close collaboration with Aboriginal and Torres Strait Islander communities to co-design culturally appropriate programs that draw on the traditional strengths and beliefs of these communities and combine them with western models of care (Dillon, 2021). Such an approach is particularly relevant in remote communities where language barriers and traditional health beliefs must be considered before planning new health interventions.

Improving Health Literacy Surrounding Liver Disease

A significant challenge for improving liver disease outcomes is improving health literacy for both patients and health care workers in primary care (Dunn & Conrad, 2018; Kaps et al., 2018; Poureslami et al, 2016). Liver disease is largely an unrecognised epidemic with opportunities for early detection and treatment often missed. Avoiding a sole focus on hepatitis B, understanding the emerging importance of MAFLD and the additive effects of multiple liver cofactors are needed. The often asymptomatic nature of liver disease, the need for early detection and knowledge of the highly effective therapies now available are concepts that need greater focus in primary health care education.

Improving Detection and Screening of Liver Disease in Primary Care

The long asymptomatic phase of many liver diseases, the high prevalence of liver disease and the availability of highly effective therapies make screening for liver disease a critical part of primary care for Aboriginal and Torres Strait Islander people. Our recommendations for screening are summarised in Table 1.

Table 1.

Recommended Screening Tests for Hepatitis B, Hepatitis C, Advanced Fibrosis/Cirrhosis and Hepatocellular Carcinoma.

	Hepatitis B (HBV)	Hepatitis C (HCV)	Advanced fibrosis/ cirrhosis	Hepatocellular carcinoma
Screening test(s)	Hepatitis B surface antibody (HBsAb), Hepatitis B surface antigen (HbsAg), and Hepatitis B core total antibody (HbcAb) (Hepatitis B Virus Testing Policy Expert Reference Committee, 2020)	Hepatitis C serology (HCV antibodies) (Hepatitis C Virus Infection Consensus Statement Working Group, 2020)	Fibrosis-4 (Fib 4) score (using platelet count, ALT and AST combined with age) (Sterling et al., 2006). Or APRI score (AST to platelet ratio index) (Wai et al., 2003) and Vibration controlled elastography (Fibroscan®) or Shear wave elastography (Mueller & Sandrin, 2010)	Six-monthly abdominal ultrasound and α-fetoprotein (AFP) (Lubel et al., 2020).

Given the high prevalence of HCV and HBV in Aboriginal and Torres Strait Islander people we recommend screening for these infections in all adults as per Table 1. We also recommend screening for liver disease in all Aboriginal and Torres Strait Islander patients with the following risk factors; alcohol misuse history, obesity/diabetes, family history of HCC and abnormal liver function tests. Baseline testing should include liver function tests, complete blood count, INR and abdominal ultrasound. Liver ultrasound is useful to detect advanced cirrhosis (nodular liver edge, ascites) but lacks sensitivity for the detection of early cirrhosis/advanced fibrosis.

A key aspect of liver disease screening involves assessment of fibrosis, as progressive fibrosis is the key determinant of prognosis for all liver diseases. A number of simple fibrosis assessment tools are now readily available and accessible in primary care. All these fibrosis tests are non-invasive and liver biopsy is now rarely required to achieve a diagnosis of

advanced fibrosis/cirrhosis. All have strengths and limitations in fibrosis assessment and must be interpreted in the correct clinical context. Key fibrosis assessment tools include:

Fibrosis-4 (Fib 4)

Initially developed to non-invasively assess fibrosis in those with Hepatitis C and HIV co-infection and to avoid recurrent liver biopsy. The score uses platelet count, ALT and AST combined with age to calculate a score that correlates with the level of fibrosis (Sterling et al., 2006). Calculators are available online (University of Washington, 2022). A score less than 1.45 has a negative predicable value of 90% for advanced fibrosis whereas a score greater than 3.25 has a 97% specificity and positive predicate value of 65% for advanced fibrosis (Sterling et al., 2006). Fib4 score is a simple way to rule out cirrhosis/fibrosis.

APRI Score (AST to platelet ratio index)

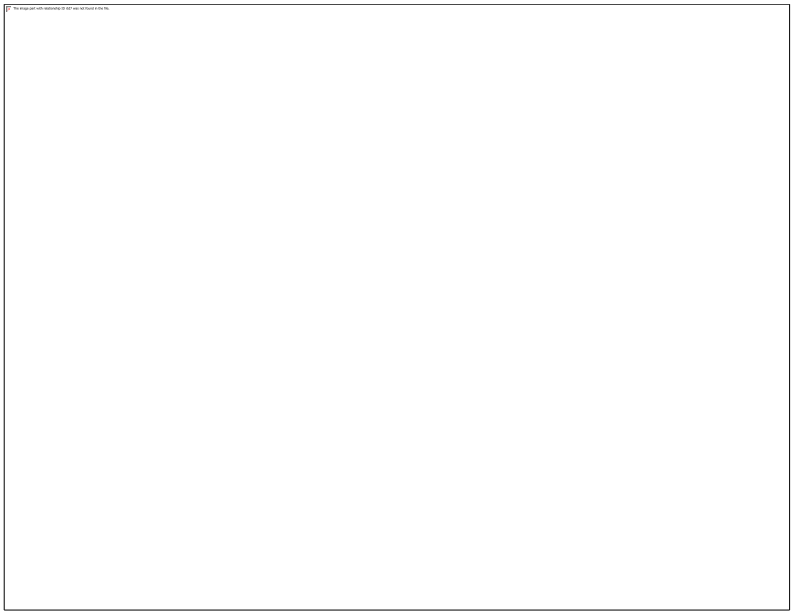
The APRI Score is another score that can be used to predict fibrosis. Calculators can be found online (University of Washington, 2022) and require only AST and platelet count. The aim of developing this score was to find a cheap, non-invasive way to estimate fibrosis. A score less than 0.5 has a high negative predictive value (Wai et al., 2003). Similarly, to Fib4 score, the APRI score's strength is ruling out cirrhosis, but it is less reliable at picking up cirrhosis (Yilmaz et al., 2011).

Vibration Controlled Elastography (Fibroscan®)

Vibration Controlled Elastography (VCE) is a non-invasive imaging modality that can be used to assess the stiffness/hardness of the liver. It uses low frequency vibration waves and measures the amount of time that the wave takes to travel from skin to the liver. It does not cause any pain to the patient. As depicted below in Figure 2, a transducer probe is placed between the ribs aimed at the right lobe of the liver. The probe sends a low amplitude wave to the liver, this produces a wave through the liver tissue which can be measured. Normal liver stiffness is in the range of 4-6 Kilopascals (kPa) and cirrhosis is found at >12.5kPa (Mueller & Sandrin, 2010). The main strength of VCE in ruling out advanced fibrosis rather than detecting it, relates to its high negative predictive value. A limitation of this technology is accessibility, with most units located at tertiary care liver centres only.

Figure 2.

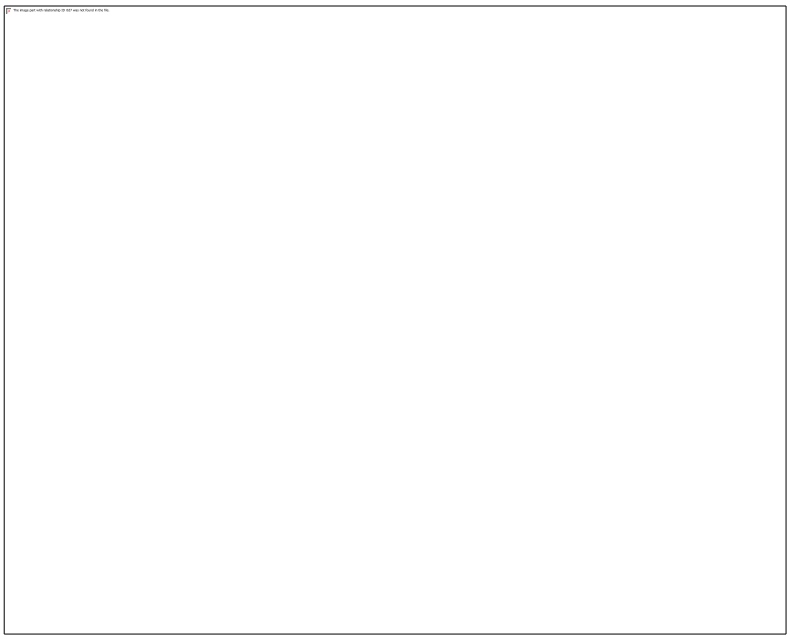
Vibration Controlled Elastography



Note. VCE probe on patient. The probe is placed between the ribs and a minimum of 10 elastography measurements are taken.

Figure 3.

Vibration Controlled Elastography Result



Note. VCE results demonstrating a median liver stiffness of 4.6 kPa, with low variability of measurements (IQR/median ratio = 24%) highly suggestive of absent or minimal fibrosis.

Shear wave elastography

This is a related ultrasound technology with similar performance characteristics to VCE but is now widely accessible to general practitioners as an “add on” to standard liver ultrasonography offered by many radiology companies.

Improving surveillance for HCC

Once advanced fibrosis/cirrhosis has been identified, affected patients should be enrolled in a six-monthly liver ultrasound surveillance program together with monitoring serum α-fetoprotein to detect early curable HCC and reduce HCC-related mortality (Lubel et al., 2020). Whilst serum α-fetoprotein can be associated with false-positive results, overall, when paired with ultrasound it improves earlier detection of HCC compared to ultrasound alone (Lubel et al., 2020). Other complications also need to be screened for including bone disease, malnutrition, and vaccination for hepatitis A and HBV, if non-immune. The reality is that HCC surveillance and cirrhosis care is challenging, and adherence is often poor, particularly in remote communities with suboptimal access to radiology facilities and specialist care (Parker et al., 2014). Robust models of care and protocols are required to achieve acceptable adherence in all practice settings.

Mobile liver clinic models

Mobile liver clinics to Aboriginal and Torres Strait Islander communities in remote areas have emerged in several Australian jurisdictions and aim to increase uptake of screening and surveillance tests and treatment in remote settings. The concept has been energised by recent advances in technology including the development of high quality mobile elastography and ultrasound devices (Figure 4). The ongoing development of point of care pathology testing for HCV and HBV also makes delivering high quality care in remote settings more feasible. These clinics have linkages with liver disease clinicians and use an on-site sonographer with portable elastography (FibroScan®), ultrasound scans and educational apps in the patient’s Aboriginal and/or Torres Strait Islander language (Davies et al., 2015). Significant community engagement by local health care workers, prior to visits, is

needed to ensure adequate attendance during mobile liver clinic visits. Such mobile clinics have reported improved HCC surveillance and monitoring and treatment uptake of hepatitis B (Hla et al., 2020). However, further evaluation of these clinics in terms of efficacy and cost effectiveness is required before translation into widespread application/national programs can be advocated.

Figure 4.

A Mobile Liver Clinic in Remote South Australia Utilising Fibroscan and Ultrasound.

Conclusions

Aboriginal and Torres Strait Islander people are disproportionally affected by liver disease resulting in significant morbidity and mortality. However, all major causes of liver disease can be prevented and significant recent advances in medical technology and treatment mean that most liver disease can now be easily detected and effectively treated. The current challenge is to raise awareness of this growing epidemic in Aboriginal and Torres Strait Islander people and to harness the strengths of Aboriginal and Torres Strait Islander people and healthcare services to improve outcomes.

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