Review Paper

Prevalence of hepatitis C virus exposure and infection among Indigenous and tribal populations: a global systematic review and meta-analysis

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A R T I C L E   I N F O

Article history:
Received 9 December 2023
Received in revised form 23 April 2024
Accepted 25 April 2024

Keywords:
Indigenous
Tribal
Hepatitis C
Hepatitis C virus
Prevalence
Epidemiology

A B S T R A C T

Objectives: The objective of this study was to estimate prevalence of hepatitis C virus (HCV) exposure and infection among Indigenous and tribal populations globally.

Study design: Systematic review and meta-analysis.

Methods: We systematically searched bibliographic databases and grey literature (1/01/2000–16/06/2022). Prevalence estimates were synthesised overall, by World Health Organization region and HCV-risk group. For studies with comparator populations, prevalence ratios were estimated and pooled.

Results: Ninety-two studies were included. Globally, among general Indigenous and tribal populations, the median prevalence of HCV antibody (HCV Ab) was 1.3% (interquartile range [IQR]: 0.3–3.8%, I2 = 98.5%) and HCV RNA was 0.4% (IQR: 0–1.3%, I2 = 96.1%). The Western Pacific Region had the highest prevalence (HCV Ab: median: 3.0% [IQR: 0.4–11.9%], HCV RNA: median: 5.6% [IQR: 2.0–8.8%]). Prevalence was highest in people who injected drugs (HCV Ab: median: 59.5%, IQR: 51.5–67.6%, I2 = 96.6%; and HCV RNA: median: 29.4%, IQR: 21.8–35.2%, I2 = 97.2%). There was no association between HCV Ab prevalence and Indigenous/tribal status for general populations (prevalence ratio = 0.91; 95% CI: 0.56, 1.49) or key risk groups.

Conclusions: Indigenous and tribal peoples from the Western Pacific Region and recognised at-risk sub-populations had higher HCV prevalence. HCV prevalence showed no association with Indigenous/tribal status. However, this review was limited by heterogeneity and poor quality of constituent studies, varying definitions of Indigenous/tribal status, regional data gaps, and limited studies on chronic infection (HCV RNA). Comprehensive quality evidence on HCV epidemiology in Indigenous and tribal peoples is needed to tailor preventive and treatment interventions so these populations are not left behind in elimination efforts.

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Introduction

Viral hepatitis, including hepatitis C virus (HCV) infection, is one of the leading causes of death and disability worldwide. In 2020, an estimated 56.8 million people globally were living with HCV infection, and 290,000 people died from HCV-related causes in 2019. Populations at risk of HCV infection include people who inject drugs (PWID), people involved in the justice system, people receiving unscreened blood or blood products, and people exposed to unsafe healthcare practices. Mother-to-child transmission and sexual transmission among men who have sex with men (MSM) may occur but is less common. Chronic HCV infection can lead to life-threatening complications, including cirrhosis and hepatocellular carcinoma. There is no vaccine, but curative treatment (direct-acting antiviral therapy) has been available since 2014, transforming HCV management. However, in 2021, it was estimated that only 21% of people living with HCV had been diagnosed, and...
fewer had initiated treatment. In 2016, the World Health Assembly adopted the Global Health Sector Strategy on viral hepatitis, which aims to eliminate viral hepatitis by 2030.3

There are an estimated 476 million Indigenous and tribal people globally, representing over 6% of the world population.2 Despite their geographic dispersal and cultural diversity, most Indigenous and tribal peoples experience significant social and health disadvantages compared to the rest of the population in the countries where they live.2 It is important to understand the burden of HCV amongst Indigenous and tribal populations to guide the development of focussed public health initiatives as part of wider strategies to eliminate this preventable and treatable infection. The aim of this systematic review and meta-analysis was to estimate prevalence of HCV exposure (HCV antibody [HCV Ab]) and infection (HCV RNA) amongst Indigenous and tribal populations globally. This review forms part of a broader review on the prevalence of blood-borne viral hepatitis B, C, and D among Indigenous and tribal populations globally. A preliminary search of PubMed, PROSPERO, and the Cochrane library identified no pre-existing reviews on this topic.

Methods

This study is registered with the International Prospective Register of Systematic Reviews (PROSPERO (CRD42018092833)) and adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.8,9

Search strategy and selection criteria

We systematically searched PubMed, EMBASE, Web of Science, Scopus, Informit databases, and Google Scholar. Regional and Indigenous-specific databases were searched, including VIH Regional Portal, SciELO, Arctic Health, Circumpolar Health Bibliographic Database, Australian Indigenous HealthInfoNet, African Journals Online, Native Health Database, and NZresearch.org. Reference lists of relevant editorials, letters, literature reviews, and systematic reviews retrieved were hand-searched for additional studies. The search was last updated on 16 June 2022. The strategy was developed in collaboration with a health librarian (Supplementary Material), and inclusion/exclusion criteria considered the participant population, condition and context as described in the following.

Population

Studies reporting Indigenous or tribal people according to the International Labour Organization (ILO) Convention No. 169,8 and characteristics outlined by the UN Permanent Forum on Indigenous issues in their country or region of origin were included. Decision-making was also guided by reference to the International Work Group for Indigenous Affairs website and the Lancet–Lowitja Institute Global Collaboration.10 Studies not defining ethnicity of the participants were excluded. There were no restrictions on age or gender. Studies that included comparative analysis with a reference population were included where available.

Condition

Studies reporting the prevalence of HCV exposure (HCV Ab positivity, indicating current or past infection) and/or HCV viraemia (HCV RNA detected on nucleic-acid testing, indicating current infection) were included. Studies describing self-reported HCV status, hospital coding data, and mathematical modelling and notification data without testing data were excluded.

Context

Studies were eligible if published after 1st January 2000 and data collection occurred after 1st January 1990. Relevant studies reported in languages other than English were included. Data from outbreak settings were excluded.

Data screening and extraction

References were managed with Endnote 20 (Clarivate Analytics, Boston, USA) and Covidence 2020 (Veritas Health Innovation Ltd, Melbourne, Australia). Two reviewers carried out independent title, abstract, and full-text screening, with conflicts resolved via discussion or a third reviewer. Data extraction was completed using Stata 17 (StataCorp., College Station, Texas). The strategy was last updated on 16 June 2022. The strategy was developed in collaboration with a health librarian (Supplementary Material), and inclusion/exclusion criteria considered the participant population, condition and context as described in the following.

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Results

A combined search for hepatitis B, C, and D prevalence studies in Indigenous and tribal populations retrieved 3934 studies (Supplementary Figure 1). Of the final selection of studies (n = 185), 92 included data on HCV exposure and/or infection and were included in this review.

Prevalence of HCV Ab among general populations

Forty-two studies provided HCV Ab prevalence estimates for general populations across 19 countries (including 72,287 Indigenous or tribal participants; Supplementary Table 1, Figs. 1 and 2). WHO regions were not equally represented, with most studies from the Western Pacific (13 studies, 31%), Americas (12 studies, 29%), and South-East Asia (11 studies, 26%) (Fig. 1). Within each WHO region, a small number of countries accounted for most studies. Study design, diagnostic assay, population age, and timing of data collection varied. There were 37 sero-surveys conducted in community settings, most of which used convenience sampling. Three studies included blood donors, one included national-service recruits, and one included national-service recruits, and one study reported data from an outreach screening program. Three Western Pacific studies included only children (age: 1–13 years). Heterogeneity was high overall ($I^2 = 98.5$%), within regions, countries, and even between communities or tribal groups within the same study ($I^2 = 98.5$%). Globally, the median prevalence of HCV Ab in general populations was 1.3% (IQR: 0.3–3.8%) (Supplementary Table 2). Sensitivity analysis was conducted to assess the influence of studies conducted only in children. When the three studies of children aged <18 years were excluded, the median prevalence for the Western Pacific region (where all studies of children originated) was 6.7% (IQR: 2.7–14.8%), and the median prevalence overall was 1.7% (IQR: 0.3–4.6%).

![Fig. 1. Global map showing distribution of studies on hepatitis C antibody prevalence in Indigenous and tribal populations by risk category.](image)

Among 14 studies of general populations that included comparator populations, there was no association between HCV Ab prevalence and Indigenous or tribal status (PR = 0.91; 95% CI: 0.56, 1.49; $I^2 = 88.5$%) (Supplementary Table 3, Fig. 3).

Prevalence of HCV Ab among specific sub-populations

There were 47 eligible studies of HCV Ab prevalence in sub-populations at risk of HCV (138,807 Indigenous or tribal participants) (Fig. 4, Supplementary Table 4). Studies in high-risk populations were predominantly from Canada (21 studies), Australia (11 studies), and United States (10 studies) (Fig. 1).

People who inject drugs

Eleven eligible studies of HCV Ab prevalence among PWID were conducted in Australia, the United States, and Canada (2890 Indigenous or tribal participants) (Fig. 1). All studies used convenience sampling in community settings or services for PWID. Definitions of injecting drug use varied (Supplementary Table 4). The median HCV Ab prevalence was 59.5% (IQR: 51.5–67.5%); the highest of all risk groups, but heterogeneity was high ($I^2 = 96.6$%) (Supplementary Table 2).

Among nine studies in PWID that included comparator populations, the prevalence of HCV Ab positivity was not associated with Indigenous or tribal status (PR = 1.1, 95% CI: 1.0, 1.2; $I^2 = 60.9$%) (Supplementary Table 5, Fig. 5).

Justice-involved people

There were six studies of HCV Ab prevalence of people involved with the justice system, five from Australia, and one from Canada (3834 Indigenous or tribal participants, Supplementary Table 4, Fig. 4). Two studies included only adolescents (mean age: 16 years) (27,28). Most participants were male (range: 74–94%). There were four sero-surveys and two studies based on prison health records. The range of HCV Ab prevalence estimates (1.5%–56.8%) reflected variation in prevalence of self-reported injecting drug use.
The median prevalence for justice-involved people was 15.5% (IQR: 2.5–42.4%) (Supplementary Table 4).

All studies of justice involved people included comparator populations (Supplementary Table 5). HCV Ab–antibody positivity was not associated with Indigenous or tribal identity (pooled PR: 0.9, 95% CI: 0.4–1.9) but heterogeneity was high ($I^2 = 97.8\%$) (Fig. 5).

**People accessing healthcare and emergency departments**

Studies in healthcare settings (ten studies excluding emergency departments (EDs), including 77,546 Indigenous or tribal
participants) included diagnostic data from laboratory or medical records (six studies) and clinic-based sero-surveys (four studies) (Supplementary Table 4, Fig. 4). Most studies were from the Americas (eight studies) (Fig. 1). Prevalence ranged from 0% to 10.1%. There was selection bias in all studies, due either to risk-based testing or participant self-selection; no studies undertook universal screening. Prevalence estimates were higher than that for the general population, with a median prevalence 3.9% (IQR: 4.3–4.9%) (Supplementary Table 2).

Three studies conducted among people attending EDs in Australia29,30 and Canada31 (567 Indigenous or tribal participants) estimated higher HCV Ab prevalence than studies in the general population or other healthcare settings. Two studies that screened all ED patients with blood drawn30,31 yielded similar HCV Ab prevalence estimates (24.3% and 24.9%), whereas risk-based testing produced a higher prevalence estimate (41.7%).29 The median prevalence was 24.9% (IQR: 24.3–41.7%) (Supplementary Table 2).

The single study of healthcare patients with a comparator population, found lower prevalence of HCV exposure in Indigenous than in non-Indigenous people in Canada (PR = 0.85; 95% CI: 0.78, 0.9212) (Supplementary Table 5). Two studies of ED patients showed higher prevalence of HCV exposure in Indigenous people than in non-Indigenous people26,31 (PR = 3.5; 95% CI: 2.9, 4.4; I² = 0%) (Supplementary Table 5).

### People living with HIV

There were three Canadian studies and one Nigerian study in people living with HIV (763 Indigenous or tribal participants; Supplementary Table 4, Fig. 4). Canadian people living with HIV (PLHIV) studies included PWID and MSM and found higher HCV Ab prevalence. The median prevalence was 31.1% (IQR: 19.1–50.8) (Supplementary Table 2). Among three studies that included comparator populations, the prevalence of HCV exposure was higher in Indigenous than in non-Indigenous PLHIV (PR = 1.8, 95% CI: 1.2, 2.8, I² = 91.4%, P < 0.001) (Supplementary Table 5).

### Other high risk

Fourteen studies reported prevalence for high-risk populations that could not be included in other categories (Supplementary Table 4). Many of these studies included a subgroup of PWID (range: 17–67% of participants), but Indigenous or tribal status was only provided for the total study population. Other groups with a known higher risk of HCV included MSM, veterans, and clients of drug treatment centres.24,35,36 Prevalence in Canadian Indigenous MSM was approximately 6-fold higher than in non-Indigenous MSM.13
In other high-risk studies that included a comparator population, prevalence of HCV exposure was higher in Indigenous or tribal populations in four of six studies (Supplementary Table 5).

**HCV RNA**

Thirteen studies provided HCV RNA prevalence estimates across ten countries (including 8259 Indigenous or tribal participants; Supplementary Table 6). Overall, for general populations, the HCV RNA median prevalence was 0.4% (IQR: 0.0–1.3%) and was highest in the Western Pacific (Supplementary Table 7).

The highest HCV RNA prevalence estimates were observed among Indigenous PWID (median: 29.4% [IQR: 21.8–35.2%]) (Supplementary Tables 7 and 8). Four studies of PWID included 1897 Indigenous or tribal participants. Serial cross-sectional studies among Australian PWID show recent declines in prevalence of HCV infection since government-subsidised direct-acting antiviral agents became universally available in 2016 but indicated a
persistent gap between Indigenous and non-Indigenous people.37,38

In justice-involved populations (two studies, 1186 Indigenous or tribal participants), the median HCV RNA prevalence was 15.1% (IQR: 5.4–24.9%) (Supplementary Table 7). HCV RNA prevalence of 25.0% in a study of Australian Indigenous justice-involved people was associated with a high self-reported prevalence of injecting drug use 39 (Supplementary Table 8). In three US studies of healthcare patients based on clinical records or survey results (34,106 Indigenous or tribal participants, Supplementary Table 8), median HCV RNA prevalence was 2.8% (IQR: 2.5–2.8%) (Supplementary Tables 7 and 8).

In studies that included comparator populations, the direction of the relationship between Indigenous/tribal status and prevalence of HCV infection was not consistent (Supplementary Table 9).

Discussion

To our knowledge, this is the first systematic review to present a synthesis of global prevalence data for HCV exposure and infection among Indigenous and tribal peoples. As expected, prevalence of HCV exposure (HCV Ab) and infection (HCV RNA) differed markedly between population groups with different levels of identified risk, with higher prevalence in PWID, justice-involved, MSM, ED attendees, and PLHIV. Consistent with recognised geographic variation in HCV epidemiology, this review also identified a greater prevalence of HCV in general Indigenous and tribal populations in the Western Pacific Region, notably in China, Taiwan, and Mongolia. No clear relationship between HCV prevalence and Indigenous and tribal status was identified. However, the over-representation of Indigenous and tribal people in some countries within high-risk sub-populations (e.g., PWID or justice-involved) means their relative risk of infection is higher.

Major limitations of this review related to variability, poor data quality, inconsistent identification of Indigenous or tribal status with associated regional data gaps, and limited data on HCV RNA prevalence, a marker of chronic infection. There was significant heterogeneity among studies, even within countries. While this could reflect true variations in HCV exposure, differences in participant characteristics, study design, and quality, diagnostic assay and timing of data collection are also likely to have contributed. Few high-quality studies were retrieved (Supplementary Table 11). Most studies used non-probability sampling methods. Almost no studies reported population coverage, response rate, or provided information about non-responders. Sample size was inadequate in approximately half of studies. Many studies failed to provide sufficient details of participant population, study design, and assays used.

![Fig. 5. Comparison of hepatitis C antibody prevalence among Indigenous or tribal and comparator high-risk sub-populations including people who inject drugs (PWID), justice-involved, emergency department patients, and people living with HIV (PLHIV). See Supplementary Material for details of included studies.](image-url)
In addition to these fundamental data-quality issues, regional differences in standards and approaches to defining Indigenous/tribal status when reporting data for these populations probably also contributed to heterogeneity and regional data gaps. Limited or no data were available for many countries, particularly in Central and South America, Africa, and the Eastern Mediterranean Regions. Self-identification, community acceptance, legal recognition, genealogy, and blood quantum are variously used to define Indigenous and tribal populations. Lack of formal recognition and systemic oppression of Indigenous and tribal peoples is likely to be a factor in paucity of data from some regions.\(^4\) Where Indigenous or tribal peoples represented only a small proportion of the total population, their data were sometimes not reported separately but were combined with data for other ethnic minority groups. Data for ethnically and/or culturally diverse Indigenous or tribal peoples were also often reported collectively due to small numbers within individual populations or for ease of reporting, a practice which could obscure variations in prevalence.

Concerningly, only 13 studies reporting HCV RNA prevalence were identified. Without measuring HCV RNA, the burden of disease attributable to chronic HCV infection cannot be assessed, and discrepancies in access to testing, care, and treatment among Indigenous and tribal populations cannot be accurately quantified. In some Indigenous populations, there have also been reports of relatively higher proportions with self-limiting infection than in non-Indigenous populations,\(^3\) so assessing HCV RNA prevalence is needed to gain a true picture of the disease burden.

To achieve reasonable geographical coverage of global Indigenous populations, we included studies published since 2000 with data collected from 1990. However, we acknowledge that older data may be less accurate because earlier HCV Ab assays used for screening had lower sensitivity and specificity.\(^4\) Older data may not have been fully representative of the recent status due to changes in access to treatment (interferon, followed by direct-acting antivirals) and prevention (safe blood and other invasive health care practices; harm reduction for PWID including needle and syringe programs, opioid agonist therapy). However, these studies have been retained as for certain populations, no more recent data were available. Finally, we covered a wide range of data sources in our search, but we appreciate that some data may have been available but not included in this review.

As countries work towards hepatitis C elimination and direct-acting antiviral agents become more widely available, it will be important to have accurate prevalence estimates to inform planning and resource allocation for testing, treatment and prevention programs, and evaluation of national hepatitis strategies. Social determinants of health-related to ongoing impacts of colonisation, dispossession, and marginalisation experienced by many Indigenous and tribal populations are likely to be associated with over-representation in sub-populations at increased risk of HCV infection.\(^4\) This review has highlighted the need for better data on prevalence of hepatitis C infection in Indigenous and tribal populations to ensure that they are not left behind in elimination efforts.

Author statements

Acknowledgements

We thank the following people for their input: Nikki May and Daniel Difore for their contribution to the search strategy; Daniella Nolan, Nicole Allard, and Jacqueline Stephens for assisting with screening; Zachary Munn and Edoardo Aromataris, from the JBI Institute, for their expert consultation on systematic review methodology; Gregory Low, Yiming Wang, Sasha Zhang, and Janet Xiang-Yu Ho for their support with translation of articles; Kiara Minto for producing the map; Victor Oguoma for discussion on defining Indigenous status in Africa and advice on statistical analyses; and Nicole Allard and Ben Cowie for their expert consultation on hepatitis.

Ethical approval

Not applicable.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interests

We declare no competing interests.

Contributors

JW conceptualised and provided oversight to the study. SE, EF, and SM performed the searches, conducted title, abstract, and full-text screening of all articles, data extraction and quality appraisal. BH provided advice on systematic review methodology and developed the statistical analysis plan. HW conducted statistical analysis. SM performed statistical analysis and produced the figures. MM provided specialist expert advice. SE and EF wrote the manuscript with input from MM, BH, and SM. All authors reviewed and approved the final draft of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2024.04.035.

References