Prospective Study

Prevalence and knowledge of hepatitis C in a middle-aged population, Dunedin, New Zealand

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Abstract

AIM: To determine the prevalence of infection with hepatitis C virus (HCV) in those most at risk of advanced liver disease and to identify gaps in knowledge of HCV.

METHODS: Questionnaires were mailed to randomly selected residents aged 40-59 to assess the extent of their general knowledge about HCV. The questionnaire assessed demographics, the extent of general knowledge about viral hepatitis, potential risks for infection and the prevalence of risk factors associated with increased progression of liver fibrosis. Anonymised residual laboratory blood samples from 40-59 year olds taken in hospital or in the community, were tested for HCV antibodies and alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transpeptidase (GGT). Linear regression was performed to examine whether the demographics sex, age, socio-economic status, qualification level and occupation sector (categorical variables) were predictors of level of general knowledge about hepatitis. For the demographics that were
found to be significant predictors of score outcome, multiple regression analysis was used to determine independent effects. \( \chi^2 \) tests were used to compare our selected sample and our responder population demographics, to the demographics of the entire 40-59 years old population in Dunedin using the 2006 NZ census data. Exact confidence intervals for the proportion positive for HCV and HBV were calculated using the binomial distribution.

RESULTS: The response rate to the mailed questionnaire was 431/1400 (30.8%). On average 59.4% questions were answered correctly. Predictors for higher scores, indicating greater knowledge about symptoms and transmission included sex (female, \( P < 0.01 \)), higher level of qualification (\( P < 0.001 \)) and occupation sector (\( P < 0.000 \)). Sharing intravenous drug utensils was a known risk factor for disease transmission (94.4%), but the sharing of common household items such as a toothbrush was not. 93% of the population were unaware that HCV infection can be asymptomatic. 25% did not know that treatment was available in New Zealand and of those who did know, only 40% assumed it was funded. Six hundred and eighty-two residual anonymised blood samples were tested for HCV antibodies, ALT, AST and GGT. The prevalence for HCV was 4.01%, 95%CI: 2.6%-5.8%. Liver function tests were not useful for identifying likelihood of HCV infection.

CONCLUSION: Prevalence of HCV in our population is high, and the majority have limited knowledge of HCV and its treatment.

Key words: Hepatitis C; Prevalence; Knowledge; Treatment; Transmission; Infection; New Zealand; Direct acting antiviral agents

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Core tip: It is projected that the public health burden due to hepatitis C virus (HCV) will increase substantially over the next 2 decades and that the mortality related to HCV will triple by 2030. We thus require a marked increase in the identification of patients infected with HCV. Safe and successful treatment of those infected is now imminently possible due to the advent of direct acting antiviral agents (DAAs). The number of diagnosed cases must increase substantially to allow DAAs to become cost effective. Our study estimated that 4.01% of asymptomatic 40-59 years old adults living in Dunedin city are infected with HCV. Most have limited knowledge of HCV and its treatment, therefore if educational and health promotion efforts are to produce maximum results for expenditure, they should be designed and targeted at audiences with lower education levels and low socio-economic status, especially immigrants and unemployed persons.

INTRODUCTION
Hepatitis C is a major global health problem affecting all countries, including New Zealand (NZ)\(^1,2\). It is estimated that approximately 80 million people worldwide or 2% of the world population are viremic\(^3\). However, as most acute hepatitis C virus (HCV) infections are asymptomatic data on the incidence of new cases is difficult to obtain\(^4\).

It is assumed that the epidemiology in NZ follows that of Australia, where chronic HCV is a notifiable disease. However the epidemiologic data on HCV in NZ is poor because only acute infection is notifiable. A significant mode of HCV transmission used to be blood transfusion but this is now mainly non-contributory since the introduction of routine screening of donated blood in 1992. It is intravenous drug use that now accounts for approximately 90% of incident cases\(^5\). A recent report estimated that the peak incidence in New Zealand occurred during the 1980s and has been declining since. However, despite the decline approximately 1000 new cases still occur each year leading to an estimated prevalence of approximately 50000-54000 infected individuals of which almost 2000 have cirrhosis\(^6,7\).

There is concern that less than half of those infected have been diagnosed and less than 10% have accessed treatment of whom only half have had a sustained virological response (SVR)\(^8\). There are several reasons for this. Initial infection is often asymptomatic and can progress insidiously without any discernible symptoms. Approximately 75% of infected individuals are unaware of the infection and of these, approximately 70% to 85% will not clear the virus and remain chronically infected\(^8,9\). Of those chronically infected a proportion will slowly progress to advanced liver disease and remain largely asymptomatic until liver cirrhosis and hepatocellular carcinoma develop\(^9\).

Unfortunately, with current treatment regimes, SVR is achieved in only about 50% of individuals, and is complicated by clinically significant adverse events\(^10\). This scenario is likely to change with the advent of the new direct acting antiviral agents (DAAs), which have SVR rates approaching 95% across genotypes and a negligible side effect profile\(^10\).

Between 30-40 years can pass from the peak incidence years of HCV infection until the peak prevalence of cirrhosis and other complications. Based
on peak incidence occurring in the early 1980s in New Zealand it is projected that the public health burden due to HCV will increase substantially over the next 2 decades and the HCV-related mortality to triple again by 2030[1,11-13]. Already, most chronic infections have been identified in the 40-60-year group[4], Davis et al[12] found that patients older than 60 years of age will be mostly affected, and that it is this patient group that needs our urgent attention if we are to prevent complications. Unfortunately, age is a significant factor negatively associated with SVR following treatment[14]. These patients are not only at risk of developing complications of the infection but they are also at risk of transmitting the disease unknowingly. In order to minimise transmission and to increase diagnosis and treatment numbers, population-wide education is essential so that individuals recognise risk factors and symptoms of infection and eventually come forward for treatment. In this context, the United States Preventive Services Task Force has recently updated their 2004 statement and now recommends screening of persons at high risk and 1-time testing in adults born between 1945 and 1965[15].

If HCV prevention, screening, care, and treatment programs are to be successful they must take into account country-specific epidemiology, which varies by setting and level of economic development[16]. Treatment using Direct Antiviral Agents is highly effective but expensive. For them to be cost effective there must be a higher uptake of treatment. This in turn requires an increase in the number of patients being diagnosed. A recent assessment for New Zealand by Gane et al[4], shows that if the country maintains the current treatment capacity (e.g., number of specialist nurses, etc.) it will be possible to treat more patients in the same timeframe quickly exhausting the number of currently diagnosed cases. It is therefore warranted and urgent to increase awareness and knowledge of HCV and its prevalence.

This project hence set out to answer two questions. Firstly, we wanted to determine the prevalence of HCV infections amongst those 40-59 years old. The middle-aged population was targeted for testing since they are in greatest need of identification and treatment. They lived through the peak incidence years of HCV infection and would now be entering peak prevalence for cirrhosis and other complications. Our hypothesis was that a better understanding of prevalence among this cohort would allow for more accurate predictions of the imminent future burden and therefore planning of resources to manage this.

Secondly, we wanted to assess the level of knowledge in this age group regarding Hepatitis C with a view to exposure, risk factors and signs of infection. Assessment of HCV knowledge among this cohort was thought to be important in order to better understand barriers to identification, diagnosis and treatment while concurrently raising awareness of the issue.

MATERIALS AND METHODS

Study population
The study was conducted in Dunedin the 5th largest city in New Zealand, located in the South Island with a population of 120249[17]. In order to address our study questions, two separate sample groups were identified and studied.

Knowledge group: A questionnaire was mailed to randomly selected 40-59 years old people on an electronic version of the Dunedin North and South electoral roll to assess the extent of general knowledge about hepatitis C.

Prevalence group: Anonymised laboratory samples were collected from 40-59 years old Dunedin residents. Samples had been originally taken in either hospital or community settings between January and February 2013, and were subsequently tested for HCV antibodies and liver function tests (LFTs).

Questionnaire
A questionnaire assessing risk developed by Zuure et al[18] was used as a guide for content development alongside a review of literature for risk factors. The questionnaire aimed to assess the extent of general knowledge about viral hepatitis, potential risks for infection and the prevalence of risk factors associated with increased progression of liver fibrosis. The questionnaire was piloted on 50 individuals, representative of the sample population. It consisted of 3 sections with a total of 41 questions. There were 5 questions pertaining to demographic information, 9 general hepatitis knowledge questions and 27 questions profiling risk for transmission/infection.

Of the 30095 eligible adults on the electoral roll, 1400 individuals were randomly selected as our sample population and mailed a questionnaire. Non-responders were sent reminder letters after 3 wk and a repeat questionnaire to complete. Letters that were returned due to incorrect addresses and other technicalities were sent to additional people.

Blood testing
Anonymised left-over lab samples of 40-59 years old people from Dunedin taken in hospital or in the community were used to test for the prevalence of HCV and LFTs. We used the “SD Bioline One Step anti-HCV” test (Standard Diagnostics Incorporated, South Korea) to test for Hepatitis C anti-bodies. Testing of blood from a known hepatitis C positive individual was undertaken to validate the test kits since these are not the current NZ lab approved tests for HCV identification. All positive test strips were confirmed by electrochemiluminescent immunoassay (ECLIA) by Southern Community Laboratories, Dunedin (Modular analyser, E unit, Roche Diagnostics, GmbH, Mannheim, Germany).
Germany). Liver function tests including aspartate transaminase (AST), alanine transaminase (ALT) and gamma-glutamyl transpeptidase (GGT) were also completed in all patients (standardised against IFCC, Modular analysers, P unit, Roche Diagnostics, GmbH, Mannheim, Germany).

Statistical analysis

Questionnaire: Linear regression was performed to examine whether the demographics sex, age, socio-economic status (SES), qualification level and occupation sector (categorical variables) were predictors of level of general knowledge about hepatitis. For the demographics that were found to be significant predictors of score outcome, multiple regression analysis was used to determine independent effects. Cases with missing answers (n = 52) were excluded. When analysing individual questions, response rates for each individual question were calculated regardless of the questionnaire being completed in full. \( \chi^2 \) tests were used to compare our selected sample and our responder population demographics to the demographics of the entire 40-59 years old population in Dunedin using the 2006 NZ census data\(^\text{[19]}\).

Blood tests: Exact confidence intervals for the proportion positive for HCV and HBV were calculated using the binomial distribution. Logistic regression was used to compare liver function test values between HCV positive and negative groups. Stata 12 (StataCorp LP, College Station, TX, United States) was used for our statistical analysis.

RESULTS

At 3 wk 1059/1400 individuals had not responded and were sent reminder letters. At week 12 the total response rate was 431/1400 (30.8%). Over the same period, 682 anonymised, residual laboratory blood samples were tested for HCV infection of which 518 were taken outside the hospital (community samples).

Knowledge group

There was no statistical difference between responders and non-responders regarding socio-economic status (SES), occupation or sex (data not shown).

Level of general knowledge: The average percentage of educational questions answered correctly was 59.4% (95%CI: 57.4%-61.4%) with a minimum score of 3.2% and a maximum score of 93.5% (Figure 1).

Statistically significant predictors for an individual’s questionnaire score included sex (\( p < 0.01 \)), level of qualification (\( P < 0.0005 \)) and occupation sector (\( P < 0.0005 \)). The number of correct answers by females tends to be 5.4% higher (95%CI: 1.4-9.4), on average compared with males after taking account of possible differences in qualification and occupation sector, age and SES (Table 1).

Furthermore, with every increasing level of qualification, the percentage of correct answers increased by, on average, 5.0% (95%CI: 3.1%-6.9%) (Figure 2). This was mirrored by an average score increase of 4.8% (95%CI: 2.4-7.3) with each change in occupation sector. Health workers were the most
knowledgeable compared to white collar workers, blue collar workers and those unemployed who scored on average 15.7%, 23.4% and 21.7% less respectively (Figure 3).

Specific questions regarding risk factors, symptoms and treatment: The most widely known risk factor for viral hepatitis transmission was the sharing of intravenous drug utensils (94.4%) and the most unrecognised was the sharing of common household items (toothbrush or razor blade) with an infected individual (64.7%). Most knew about symptoms of fatigue, nausea and lack of appetite as symptoms, but 93.0% did not know that HCV infection can be asymptomatic (Table 2). Eleven percent of people did not know about any of the long-term consequences of untreated disease. Over a quarter of the study population did not know that treatment is available and only 40.0% assumed that it was funded in New Zealand.

Specific questions regarding factors associated with accelerated fibrosis: We also asked about risky behavior that is commonly associated with an accelerated progression of fibrosis. The number of standard drinks consumed per sitting increases by 0.5 as level of qualification decreases, with males drinking 1.6 standard drinks more per sitting and more often than females. 43.4% of the study population reported themselves as overweight and of those, 7.2% as excessively overweight.

Prevalence group
From a total of 682 anonymised blood samples, 34 samples were removed; two because they were out of the age range and 32 because they had the same date of birth, sex and potentially could have been repeat samples from the same patient bringing the total to 648 blood samples.

A total of 26 patients tested positive for Hepatitis C (4.0%, 95%CI: 2.6%-5.8%, 19 male). In samples from outside the hospital, 17 patients tested positive (community samples - 3.3%, 95%CI: 1.9%-5.2%, 13

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**Table 1** Relationship between general hepatitis knowledge scores and population demographics

| Demographic      | Unadjusted | Adjusted \(^a\) |
|------------------|------------|-----------------|
| Sex              | 8.5 (4.6-12.4) \(^a\) | 5.4 (1.4-9.4) \(^a\) |
| Qualification level | 6.5 (4.6-8.4) \(^a\) | 5.0 (3.1-6.9) \(^a\) |
| Occupation sector | 7.1 (4.9-9.3) \(^a\) | 4.8 (2.4-7.3) \(^a\) |
| Age              | -0.6 (-2.5-1.2) | -0.1 (-2.1-1.8) |
| SES              | -0.9 (-1.5-1.4) | 0.2 (-1.3-1.7) |

\(^a\)Adjusted for the other four demographic variables. \(^b\)P < 0.0005, unadjusted vs adjusted.

**Table 2** Recognition of acute or chronic hepatitis symptoms n = 427

| Symptoms of an acute/chronic hepatitis infection | Recognised | %     | 95%CI |
|------------------------------------------------|------------|-------|-------|
| Fatigue                                        | 82.4       | 78.5-85.7 |
| Nausea                                         | 67.9       | 63.3-72.2 |
| Loss of appetite                               | 66.3       | 61.7-70.6 |
| Jaundice                                       | 63.7       | 59.0-68.1 |
| Abdominal pain                                 | 57.1       | 52.4-61.8 |
| Skin irritations                               | 56.0       | 51.2-60.6 |
| Vomiting                                       | 33.3       | 28.7-37.6 |
| Fever                                          | 32.3       | 28.1-36.9 |
| Don’t Know                                     | 14.0       | 11.1-17.1 |
| Asymptomatic                                   | 7.0        | 4.9-9.9  |

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**Figure 2** Relationship between general hepatitis knowledge scores and qualification levels.

![Graph showing relationship between general hepatitis knowledge scores and qualification levels.](https://example.com/graph.png)

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The average liver function test (AST, ALT, GGT) was increased in patients infected with HCV but logistic regression showed that the odds of having an elevated ALT, AST or GGT were the same for both the HCV positive and negative groups (Table 3).

DISCUSSION

Even though the incidence of Hepatitis C cases seems to have declined, it is estimated that the economic burden of HCV related treatment and complications will continue to increase over the next two decades. Currently in NZ, the majority of HCV infections are not diagnosed and only about 2% of diagnosed patients are treated. For the new DAAs to have a significant impact, treatment numbers need to be increased at least four-fold [4,20].

While it can be expected that more patients with known HCV infection will come forward voluntarily for treatment, this study revealed an alarmingly low knowledge about viral hepatitis, and a higher than expected prevalence of hepatitis C in the 40-59 years old.

The lack of general knowledge about HCV and high prevalence as indicated in our study is of concern as our population sample (40-59 years old) was selected for its high risk of developing complications related to undiagnosed or untreated chronic infection. Worldwide, HCV-related end-stage liver disease already accounts for more than 40% of adult elective liver transplants, and the number of referrals for transplantation is projected to double within the next decade[21]. In NZ, complications due to HCV infection such as cirrhosis and hepatocellular carcinoma are the leading indication for assessment for liver transplantation, next to HBV related complications and alcohol. A recent 12-year audit by Hsiang et al.[22] of cirrhotic patients showed that HCV was the third most common cause for cirrhosis (22.3%) of which 69.7% were previously unsuccessfully treated with interferon-based regimes. Patients were usually male and in their mid-50s [22].

These projections emphasize how critical it is for any Health System to identify infected persons and treat their disease before advanced liver disease develops. The only strategy for those already infected is prevention of disease progression through suppression or eradication of HCV. Disconcertingly the rate of treatment with pegylated interferon and ribavirin is declining and has almost reached 2007 levels (data from the NZ Ministry of Health)[23]. In part, this can be explained by the fact that patients are aware of the newer and safer treatment options and are deciding to wait. However, the majority of patients are unaware of their infection.
Raising awareness of Hepatitis C will aid the identification of patients in need of treatment. Formal patient education can be successful but needs to target the right population group[24]. Our findings are important to the success of the government funded national hepatitis C action plans recently initiated in several countries[25,26]. From our results, it is clear that the majority of this population is unaware of the potential asymptomatic nature of HCV and when the nonspecific symptoms of an infection are likely to manifest. 93.0% of participants did not recognise that HCV infection can be asymptomatic and 53.1% of participants did not know how long it would take for symptoms of a chronic infection to manifest. In addition 11.0% of people did not know about any long-term consequences of untreated disease. These findings have critical repercussions for HCV education and management. Furthermore, over one quarter of the population did not know that treatment is available and only 40.0% assumed that it was funded. Along with the unpopularity of interferon-based treatments, these factors could be a barrier to people coming forward for testing.

To remain cost-effective, educational efforts should be targeted. We have shown that individuals with a tertiary qualification scored highest on the questionnaire. Our finding that a higher level of qualification positively correlates with knowledge about Hepatitis C fits with the current literature. A study by Proeschold-Bell et al[27] about HCV knowledge among HIV patients from North Carolina, United States involving 179 HIV patients, also found more accurate levels of HCV knowledge among study participants with higher education levels. Similarly a study of 201 HCV infected individuals in San Francisco that tested knowledge about Hepatitis C diagnosis, symptoms, natural history and treatment, showed patients with at least a high school education had higher baseline knowledge scores[24]. Again in New South Wales, Australia, following a mass media HCV campaign, the number of correct responses in the follow up cohort sample was independently associated with having a post-secondary education. Interestingly improvements in knowledge were equal across all demographic descriptors[28]. We know there is a strong association between health literacy and low- income/socio-economic status[29]. In accordance to our findings, the populations most vulnerable to the impact of poor health literacy knowledge are immigrants, seniors and unemployed persons[30]. Our study found that unemployed individuals are among the lowest scoring occupational sectors. Furthermore, knowledge about viral hepatitis seems to be associated with gender. Females in our study were found to be more knowledgeable about Hepatitis C compared with males. Unfortunately as of 2011, 62% of injecting drug users in New Zealand are male[31].

Thus health promotion messages need to be designed to reach and cater for audiences with lower education levels and those of low socio-economic status, especially immigrants and unemployed persons. Our mail survey had a return rate of just less than 31%. Our result is almost identical to a recent study by Zuure et al[32], which showed only 28% followed advice to be tested for HCV. The authors identified the main reasons for not being tested to be inconvenient testing facilities, a lack of commitment, along with the belief that personal risk is low, the absence of symptoms, low perceived urgency for testing and treatment and fear of the consequences of a positive test result[32]. While our study was not designed to ask these questions, anecdotally, some blank questionnaire were returned with the note that people did not think they were at risk and therefore completion of the questionnaire was not seen as appropriate.

An unexpected finding was the high prevalence rate of 3.3%-4.0% of HCV amongst the 40-59 years old population with the majority being male. This number is of particular importance as it allows targeted treatment efforts. While it is estimated that approximately 50000 New Zealanders or roughly just over 1% of the population are infected with HCV, an age-adjusted prevalence is not known. Interestingly, as shown by Hsiang et al[22], patients with HCV-related liver disease such as cirrhosis were predominantly males in their mid-50s. Although liver function tests were elevated in HCV infected patients, logistic regression showed that the odds of having an elevated ALT, AST or GGT were the same for both the HCV positive and negative groups.

In summary, the population group most knowledgeable about the risk of transmission, possible symptoms and treatment of hepatitis C, are well-educated and qualified women who are working in the health or white collar sector. Therefore public health initiatives need to prioritise other groups with a particular focus on males and persons with low levels of education. The overall level of knowledge needs to improve across the community as a whole.

There were some obvious limitations to our study. Firstly, unlike the knowledge group, blood samples were not a random sample of the Dunedin 40 to 59-year-old population as the knowledge group but were taken from hospital and community individuals who had a blood test taken for other medical reasons. This introduces the potential for selection bias, especially as it can be assumed that patients with HCV might seek more medical help compared to the healthy population. There was also no way of identifying if positive blood samples were representing a new diagnosis or were already previously diagnosed with HCV and if these people were unaware of their infective status. We did not ask for coffee and cannabis consumption, known modulators of liver disease progression.

Approximately 10% of NZ citizens are not registered on the electoral roll; therefore the response rate data cannot be considered a direct reflection of the
population living in Dunedin. Given the prevalence profiles, our study may have underestimated prevalence.

The low response rate to the questionnaire (30.8%) decreased the sample size therefore increasing standard error of estimates leading to decreased precision and study power. Consequently, caution needs to be taken when interpreting this data from the questionnaire, as the study population may not accurately represent the true population of 40-59 years old in Dunedin.

Limitations aside, we found a surprisingly high prevalence rate of 3.3%-4.0% among the 40-59 years old population in urban Dunedin, New Zealand. This is coupled with a low level of general knowledge in the population group mostly at risk of infection or transmission. Awareness campaigns need to be directed at the groups most vulnerable in order to reduce barriers that prevent their testing and diagnosis. Increasing awareness and diagnosis of HCV infection in this population, will subsequently allow for successful treatment with the new DAAs. This will decrease prevalence, and halt the increasing mortality from the Hepatitis C virus in our community.

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