Increasing prevalence of cirrhosis among U.S. adults aware or unaware of their chronic hepatitis C virus infection

Prowpanga Udompap1, Ajitha Mannalithara1, Nae-Yun Heo1,2, Donghee Kim1, W. Ray Kim1,⇑

1Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA, USA; 2Department of Internal Medicine, Haeundae Paik Hospital, Inje University, College of Medicine, Busan, Republic of Korea

Background & Aims: Cirrhosis from hepatitis C virus (HCV) infection is a major cause of end-stage liver disease and hepatocellular carcinoma worldwide. We determine the prevalence of cirrhosis among HCV-infected American adults including those unaware of their infection.

Methods: Using the National Health and Nutrition Examination Survey (NHANES) data, we identified participants aged ≥20 years with detectable serum HCV RNA. The prevalence of advanced fibrosis and cirrhosis was determined for eras 1 (1988–94), 2 (1999–2006) and 3 (2007–2012) by using FIB-4 >3.25 and APRI >2.0, respectively.

Results: Out of 52,644 NHANES examinees, 49,429 were tested for HCV, of whom 725 met the inclusion criteria (positive HCV RNA with available data for FIB-4 and APRI). Based on APRI, 6.6% (95% confidence interval [CI]: 2.2–11.0) of HCV-infected adults in era 1, 7.6% (95% CI: 3.4–11.8) in era 2 and 17.0% (95% CI: 8.0–26.0) in era 3 had cirrhosis. In the multivariable regression analysis, this era effect was attributable to increasing age (odds ratio [OR]:1.04, 95% CI: 1.02–1.07), diabetes (OR: 2.33, 95% CI: 1.01–5.40) and obesity (OR: 2.96, 95% CI: 1.15–7.57). Cirrhosis was as common among respondents who were unaware of their infection as those who were aware (both 11%). Results were identical when FIB-4 was used.

Conclusions: Among HCV-infected American adults, the proportion with cirrhosis has increased rapidly. Cirrhosis prevalence remains high in individuals unaware of their HCV infection. These data highlight the urgency for HCV screening regardless of symptoms, systematic assessment for liver fibrosis in those with HCV infection and institution of antivirals to prevent advanced liver disease.

Lay summary: Chronic hepatitis C virus (HCV) infection is a major cause of cirrhosis, creating a large public health burden. Based on the U.S. National Health and Nutrition Examination Survey sample, we found the proportion of patients with cirrhosis among Americans with HCV infection increased from 6.6% to 17.0% over the past two decades. Patients who were unaware of their infection were just as likely to have cirrhosis as those who knew about their infection, which highlights the need for screening and treatment for HCV at the population level.

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Introduction

Chronic hepatitis C virus (HCV) infection, the most common chronic blood-borne infection in the United States (U.S.), affects at least 3 million Americans [1]. As the leading cause of end-stage liver disease and hepatocellular carcinoma (HCC), it claims more lives annually than HIV infection [2]. Until its late sequelae develop, however, most patients with HCV infection remain asymptomatic, making its timely diagnosis difficult without purposeful screening. Approximately one half of U.S. adults with HCV infection are yet to be diagnosed [3].

Cirrhosis, the end result of progressive fibrosis, underlies most of the disease burden associated with HCV infection including hepatic decompensation and HCC. Evaluation of liver fibrosis is an essential element in the care of patients with chronic HCV infection, as the severity of liver fibrosis informs prognosis and treatment decisions. For example, responses to therapy available today are reduced in patients with decompensated cirrhosis, although they gain the largest benefit from successful antiviral therapy, which may halt the progression of liver fibrosis [4]. Many healthcare systems direct antiviral therapy to patients with advanced fibrosis and cirrhosis, as they attempt to prioritize utilization of the highly costly medications.

On the public health level, despite the importance of liver fibrosis in determining the current and future burden of HCV infection, reliable and generalizable data about the prevalence of HCV cirrhosis in the U.S. are unavailable [5]. The prevalence of cirrhosis among people whose HCV infection is yet to be diagnosed remains even more uncertain. We address these questions by determining the prevalence of cirrhosis and advanced fibrosis in U.S. residents with HCV infection, and comparing the prevalence between individuals who are aware and unaware of their HCV infection based on population-based data generalizable to the entire U.S. households.

Keywords: Hepatitis C virus; Liver fibrosis; Cirrhosis.

Received 20 October 2015; received in revised form 10 January 2016; accepted 12 January 2016; available online 22 January 2016

⇑ Corresponding author. Address: Division of Gastroenterology and Hepatology, Stanford University School of Medicine, 300 Pasteur Dr. Always Bldg, Room M211, Stanford, CA 94305, USA. Tel.: +1 650 725 6511; fax: +1 650 723 5488.
E-mail address: wrkim@stanford.edu (W.R. Kim).

Abbreviations: HCV, hepatitis C virus; HCC, hepatocellular carcinoma; APRI, AST to platelet ratio index; FIB-4, Fibrosis-4; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index.
Materials and methods

Data source

The National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics, is a program to assess the health and nutritional status of adults and children in the U.S. over time. Hepatitis C testing began in the NHANES sample collected between 1988 and 1994. Subsequent NHANES data sets encompassing years 1999−2012 included hepatitis C testing as well. In this analysis, we divided the data sets into three periods: era 1 (1988–94), era 2 (1999–2006), and era 3 (2007–2012).

Details on the survey design for the NHANES is available on line (http://www.cdc.gov/nchs/data/series/sr_02/sr02_155.pdf). From the wide array of information included in the NHANES data file, demographic (age, sex, race/ethnicity) and laboratory data (anti-HCV, HCV RNA, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and platelet count) were extracted. Detailed description of laboratory methods used in the NHANES is publicly available [6–8]. Since 2001, an additional survey was included in patients with positive anti-HCV in order to assess what proportion of the participants already knew of their infection status, what they knew about HCV, and what actions were taken after their infection status was discovered. This survey was conducted by phone approximately 6 months after the original examination. The HCV Follow-Up Questionnaire is available on line (http://www.cdc.gov/nchs/data/nhanes/pf_hcq_03_08.pdf).

Study participants

Of the NHANES participants, we selected subjects aged 20 years or older, with detectable HCV RNA in the serum and available laboratory values consisting of AST, ALT and platelet count. In the process, survey respondents who did not undergo laboratory testing or did not have available serum sample for HCV testing were excluded.

For the comparison of the prevalence of advanced fibrosis and cirrhosis between those who were aware and unaware of their infection, only those participants who responded to the question HOQ:030: “Was the test result in our laboratory the first time you were told you have hepatitis C?” in the Hepatitis C Follow-up Questionnaire were included.

The way in which race and ethnicity were defined in the NHANES data changed over time. To compare information for the three eras, race/ethnicity data were formatted following the classification used in era 1, which included non-Hispanic white, non-Hispanic black, Mexican American and other. Body mass indices (BMI) were used to group subjects into three categories: obese (BMI >30), overweight (BMI: 25−29.9) and lean (BMI <25). Of several variables on alcohol use, the most complete one that includes categories of current or previous drinker or non-drinker was included.

Main study outcomes

Assessment of liver fibrosis is essential for chronic HCV management, namely to determine the prognosis and to make therapeutic decisions. Thus, our main outcome measures were the proportions of HCV-infected individuals with advanced fibrosis and cirrhosis.

Severity of liver fibrosis has traditionally been gauged by liver histology, based on the location and amount of collagenous deposits in the hepatic parenchyma. More recently, non-invasive markers of liver fibrosis have been developed [9]. In this study, we employed APRI [10] and FIB-4 [11] scores to evaluate the severity of liver fibrosis. These markers were developed among patients with chronic HCV infection and have been validated in patients with HCV and other liver disease [12,13]. The scores were calculated for participants with available AST, ALT and platelet count data based on the following formulas:

APRI = (AST, upper limit of normal)/platelet count × 100

FIB-4 = (age × AST)/(platelet count × √ALT)

Both APRI and FIB-4 scores incorporate two cut-off values to correlate with Ishak fibrosis stages. For detection of cirrhosis, an APRI score >2.0 is indicative of a high probability of cirrhosis (Ishak stages 5−6), whereas a score <1.0 correlates with a low probability. A FIB-4 score >3.25 correlates with a high probability of advanced fibrosis (Ishak stages 4−6) and a score <1.45 with a low probability [14]. Of the two scores, APRI was used for the primary analysis and FIB-4 for a confirmatory analysis, since the latter includes age as a variable, which could potentially confound the trend in the prevalence of advanced fibrosis over time. Hence, advanced fibrosis/cirrhosis was defined by FIB-4 score >3.25 and cirrhosis was defined by APRI >2.0.

Results

In the NHANES data set, there were 52,644 adults 20 years or older who participated in the examination component and underwent laboratory testing (Fig. 1). Of those, 49,429 (93.9%) had available serum samples for HCV testing, of whom 1047 (2.1%) were positive for anti-HCV. Among anti-HCV-positive subjects there were 736 (70.3%) who were positive for HCV RNA, whereas in 122 (11.6%) their HCV RNA status could not be ascertained, mostly for lack of available samples. Out of the 736 HCV RNA-positive patients, a vast majority (n = 725, 98.3%) had complete laboratory values for calculating APRI and FIB-4 scores and they constituted the final data set for this analysis.

Table 1 depicts the characteristics of participants with regard to HCV results. Overall, there was a trend for decreasing prevalence of HCV infection. The prevalence of U.S. adults with chronic HCV infection decreased from 1.5% (95% confidence interval [CI]: 1.0–2.0) in era 1, to 1.2%, (95% CI: 1.0–1.4) in era 2, and then to 1.0% (95% CI: 0.8–1.3) in era 3, which project to 2.7 million (95% CI: 1.8–3.5 million), 2.5 million (95% CI, 2.1–2.9 million), and 2.2 million (95% CI, 1.7–2.8 million) Americans with HCV infection for eras 1, 2, and 3, respectively.

The mean age of survey participants with HCV infection increased from the early 40s to the 50s over time. The proportion of women did not change. The proportion of non-Hispanic whites increased, whereas those of Mexican Americans and of other race decreased. The proportion of overweight or obese subjects increased as well as those with diabetes, whereas the proportion of non-drinkers decreased. The mean serum activities of aminotransferases were higher than the upper limit of normal and tended to increase in each era. The mean platelet counts decrease from 251 × 10^3/μl in eras 1 (95% CI: 235–266) and 2 (95% CI: 238–264) to 221 × 10^3/μl (95% CI: 207–235) in era 3. The mean APRI and FIB-4 scores increased in era 3 compared to previous eras, suggesting higher prevalence of advanced fibrosis in the last era.

In Fig. 2, the proportion of survey participants with abnormal AST and platelet results increased over time. Consequently,
was 11.2% among subjects unaware of their HCV infection, com-
cirrhosis, as determined by APRI. The proportion of cirrhosis
respondents with a high, indeterminate, and low probability of
between the two groups. Fig. 3 compares the proportions of
There was no difference in the mean APRI and FIB-4 scores
2.96-fold, 95% CI: 1.15–7.57), the effect of era became smaller
2.33-fold, 95% CI: 1.01–5.40), and obesity (increased odds by
by 4% (95% CI: 2–7%) per year), diabetes (increased odds by
of advanced fibrosis and cirrhosis for eras 1, 2, and 3, re-
Table 2 summarizes results of a series of logistic regression
analyses for potential variables that may explain the higher
prevalence of cirrhosis in the recent era. In univariate analyses,
age, diabetes and BMI categories of overweight/obesity were
associated with cirrhosis, in addition to the most recent era.
These variables remained significant in bivariate models in which
they were considered individually in conjunction with the eras. In
the final model which included age (increased odds of cirrhosis
by 4% (95% CI: 2–7%) per year), diabetes (increased odds by
2.33-fold, 95% CI: 1.01–5.40), and obesity (increased odds by
2.96-fold, 95% CI: 1.15–7.57), the effect of era became smaller
and insignificant. When the analysis was repeated with FIB-4
score, the results were similar (Supplementary Table 1).
In NHANES 2001–2012, 163 participants who tested positive
for HCV RNA had available data for APRI and FIB-4 scores and
responded to the Hepatitis C Follow-up Survey with regard to
awareness of their HCV infection. In Table 3, those respondents
were mostly male (67.5%, 110/163) and non-Hispanic white
(44.8%, 73/163). The mean age was 52.5 ± 11.7, AST 55.5 ± 36.7
(U/L), ALT 57.6 ± 40.5 (U/L), and platelets 225.2 ± 83.3 (× 10³/µL).
There was no difference in the mean APRI and FIB-4 scores
between the two groups. Fig. 3 compares the proportions of
respondents with a high, indeterminate, and low probability of
cirrhosis, as determined by APRI. The proportion of cirrhosis
was 11.2% among subjects unaware of their HCV infection,
compared to 10.8% in those who were aware (p = 0.99). A similar
pattern was seen with the FIB-4: the proportion of a high, inde-
terminate and low probability for advanced fibrosis was 15%,
36% and 49% among respondents aware of their HCV infection,
respectively, compared to 22%, 30% and 48% among those who
were unaware, respectively (p = 0.48).

Discussion
With the advent of highly effective, yet highly costly antiviral
agents against HCV, there has been much debate about how
patients with HCV infection should be diagnosed, evaluated and
treated [17]. The most contentious element in this debate is
whether antiviral therapy should be offered to all with HCV infec-
tion or be prioritized to patients with evidence of significant liver
fibrosis. There is little debate, however, that HCV patients with
cirrhosis must be treated [18]. In this context, accurate data
about the prevalence of cirrhosis are of critical importance in
determining healthcare strategies regarding antiviral therapy
and resource allocation for optimal management of HCV infection
on the population level.
We report in this work that while the overall prevalence of
HCV infection has decreased over time [2,5,19], the proportion
of HCV patients with cirrhosis more than doubled during the
study period, reaching 17% (with the upper end of 95% confidence
interval being 26%) in the latest era. Importantly, the prevalence
of cirrhosis in patients who were unaware of their HCV infection
was at least as high as that in those who had been diagnosed.
Patients with HCV infection who have not been diagnosed should
be urgently sought, so that appropriate hepatological care is pro-
vided, including modification of risk factors such as alcohol con-
sumption and controlling body weight and disease monitoring,
in addition to choosing and administering the most appropriate
antiviral therapy.
Since only one half of HCV infection in the U.S. is believed to
have been diagnosed so far, our data suggest that at least 200,000
Americans with HCV cirrhosis remain undiagnosed. As NHANES
excludes population with the highest HCV prevalence, such as
homeless or incarcerated individuals, these figures likely under-
estimate the true number of those with HCV infection at risk of
experiencing complications [20,21]. To date, accurate
population-based data about the prevalence of HCV cirrhosis in
the U.S. have been scarce. Several estimates, obtained with
Markovian models derived from presumed duration of infection
and projected rates of fibrosis progression, varied widely from
261,000 [22] to 600,000 [23] and to nearly 800,000 [5]. The only
actual population-denominated, although not necessarily gener-
lizable, data about advanced fibrosis are derived from the Veter-
ans Administration system, which reported that the prevalence
of HCV-related cirrhosis increased from 9% in 1996 to 18.5% in 2006
[24].
This rising trend is in part attributable to the aging of Ameri-
cans with HCV infection, as shown in the demographic charac-
teristics in Table 1 and the regression analysis in Table 2. It is well
described that the majority of Americans with chronic HCV infec-
tion belong in the birth cohort between 1945 and 1965. As the
generation with HCV infection becomes older, the duration of
infection also increases, allowing liver fibrosis to progress
[25,26]. The significant increase in the proportion of participants
with elevated AST level is consistent with increasing prevalence
of advanced fibrosis and cirrhosis. On the other hand, ALT activ-
ities are commonly thought to decline as fibrosis progresses. The
rising trend in ALT level in our data may be in part due to con-
comitant non-alcoholic fatty liver disease (NAFLD), which may
accelerate fibrosis progression. As some of these patients have
two different disease processes in the liver, the extent to which
the presence of NAFLD may have influenced our assessment of
fibrosis is uncertain; as for example, FIB-4 score which has ALT
in the presence of NAFLD may have influenced our assessment of
fibrosis.

Despite the recent recommendation for enhanced HCV
classification [27–29], a large proportion of Americans with HCV
infection remains undiagnosed. Importantly, we found that cir-
rhosis was equally common in those unaware of their infection.
This was contrary to our initial hypothesis that individuals who
had their HCV infection diagnosed may have had a higher likeli-
hood of having advanced liver disease. An alternate hypothesis

| Table 1. Characteristics of NHANES participants, aged ≥20 (weighted). |
|-----------------------------|-----------------------------|-----------------------------|
| Study subjects             |                             |                             |                             |
| Number of US residents ≥20 years, in millions (95% CI) | 177.2 (164.9-189.5) | 203.1 (191.8-214.3) | 219.4 (204.9-233.8) |
| Proportion of HCV RNA+ (95% CI) | 1.5% (1.0-2.0)            | 1.2% (1.0-1.4)             | 1.0% (0.8-1.3)             |
| HCV RNA+, in millions (95% CI) | 2.7 (1.8-3.5)             | 2.5 (2.1-2.9)              | 2.2 (1.7-2.8)              |
| Characteristics of HCV-RNA+ subjects, age ≥20 with available APRI and FIB-4 results |                             |                             |                             |
| Number, in millions (95% CI) | 2.6 (1.7-3.4)              | 2.5 (2.1-2.9)              | 2.2 (1.6-2.7)              |
| Age* (95% CI)                           | 40.3 ± 0.9                      | 47.5 ± 0.8                            | 50.5 ± 0.8                            |
| Sex (% female, 95% CI) | 32.2 (23.8-40.6)            | 33.2 (25.2-41.2)            | 33.1 (24.2-42.0)            |
| Race/ethnicity (% female, 95% CI) | Non-Hispanic white | 55.9 (42.3-89.4) | 64.1 (56.3-72.0) | 63.2 (53.3-73.1) |
| Non-Hispanic black | 22.3 (15.7-28.9)            | 23.0 (17.0-29.0)            | 23.4 (15.1-31.7)            |
| Mexican American | 6.7 (3.7-9.7)               | 6.0 (2.3-9.7)               | 5.6 (2.5-8.8)               |
| Other | 15.1 (2.4-27.8)            | 6.9 (2.6-11.1)              | 7.8 (3.3-12.3)              |
| Body mass index (% female, 95% CI) | ≥30 (obese) 22.0 (12.3-31.8) | 19.5 (12.9-26.1) | 28.8 (19.8-37.9) |
| 25-29.9 (overweight) | 23.3 (16.6-30.1)           | 37.0 (31.3-42.7)           | 35.2 (25.7-44.4)           |
| <25 (lean) | 54.6 (44.6-64.6)          | 43.6 (35.3-51.9)           | 36.0 (26.4-45.5)           |
| Alcohol consumption (% female, 95% CI) | Non-drinker 7.3 (0.2-14.4) | 7.0 (1.9-12.2) | 2.2 (0.1-4.4) |
| Current drinker | 68.9 (60.0-77.7)           | 86.1 (80.1-92.1)           | 83.8 (75.8-91.8)           |
| Ex-drinker | 23.8 (14.8-32.9)          | 6.8 (3.5-10.2)             | 14.0 (6.3-21.6)            |
| Diabetes mellitus (% female, 95% CI) | 5.0 (2.1-7.9) | 7.5 (2.7-12.4) | 11.0 (3.8-16.3) |
| AST (U/L)* | 48.5 ± 3.1 | 51.3 ± 3.0                  | 63.4 ± 5.1                  |
| ALT (U/L) | 46.4 ± 3.1 | 57.8 ± 3.8                  | 70.0 ± 7.2                  |
| Platelets (x10³/μl)* | 250.9 ± 7.7 | 251.1 ± 6.5                  | 221.5 ± 6.9                  |
| APRI score* | 0.73 ± 0.12 | 0.76 ± 0.06                  | 1.14 ± 0.12                  |
| FIB-4 score* | 1.87 ± 0.32 | 1.63 ± 0.13                  | 2.21 ± 0.17                  |

*Mean ± standard deviation.
*Upper limits of normal 1,2: 40 U/L prior to 2000, 33 U/L thereafter.
SI conversion factors: To convert AST and ALT to kkat/L, multiply values by 0.0167.

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| Table 2. Factors associated with cirrhosis* in chronic HCV infection. |
|-----------------------------|-----------------------------|
| Variable                      | Odds ratio (95% CI)         |
|                             | Univariate analysis | Bivariate analysis** | Multivariable analysis |
| Era (reference = Era1)        |                             |                             |
| Era3                         | 2.91 (1.15-7.37) | n.a.                    | 1.74 (0.65-4.69) |
| Era2                         | 1.17 (0.47-2.90) | 0.84 (0.33-2.17)        |                   |
| Age                          | 1.05 (1.03-1.07) | 1.04 (1.02-1.07)         | 1.04 (1.02-1.07) |
| Sex (reference = female)     | 1.33 (0.54-3.24) |                   |                   |
| Race/ethnicity (reference = NH white) | 1.03 (0.50-2.11) |                   |                   |
| NH black                     | 1.04 (0.34-2.08) |                   |                   |
| Mexican                      | 1.62 (0.63-4.21) |                   |                   |
| Diabetes                     | 4.33 (1.94-9.70) | 3.91 (1.80-8.49)       | 2.33 (1.01-5.40) |
| BMI (reference = BMI <25)    |                             |                             |
| ≥30                          | 3.42 (1.30-9.00) | 3.05 (1.17-7.96)       | 2.96 (1.15-7.57) |
| 25-29.9                      | 2.35 (1.05-5.23) | 2.14 (0.96-4.77)       | 1.99 (0.91-4.36) |
| Drinking (reference = non-drinker) | 0.34 (0.06-1.87) |                   |                   |
| Current drinker              | 0.77 (0.12-4.79) |                   |                   |
| Previous drinker             |                             |                             |

*Mean ± standard deviation.
*Upper limits of normal 1,2: 40 U/L prior to 2000, 33 U/L thereafter.
SI conversion factors: To convert AST and ALT to kkat/L, multiply values by 0.0167.

**Each variable was individually considered in conjunction with the era.
that may associate HCV diagnosis with less severe fibrosis may be that patients aware of their HCV may be more likely to modify their life style (e.g., alcohol consumption) that could alter the trajectory of their disease progression. Unfortunately, information about whether HCV diagnosis led to behavioral changes is not available in the NHANES data. It is also possible that some of the diagnosed patients may have undergone antiviral therapy, which might have temporized progression of fibrosis.

Thus, one of the limitations in this study is the lack of data on HCV treatment, which might have affected fibrosis progression as well as overall HCV prevalence. The proportion of such patients is likely to be small as only a fraction of patients were treated in the prior antiviral era and even fewer patients responded successfully to therapy. Another limitation of this study is that while cirrhosis remains a histologic diagnosis, obtaining liver biopsies in a large epidemiological survey is impossible and, thus, we relied on surrogate indices to gauge fibrosis. Both APRI and FIB-4 scores have been developed and validated in patients with HCV and have been used to correlate with disease outcome and guide therapeutic decisions [30]. Recently, the World Health Organization adopted APRI as a tool to evaluate HCV patients in settings where more direct measures of liver fibrosis are not available. Both scores are limited by the fact that AST and ALT may be affected by factors other than fibrosis, such as liver inflammation from other causes (NAFLD) as well as demographic factors (age, sex, and BMI). However, when results produced with APRI and FIB-4 scores were taken together, the increasing trend and the approximate percentage of subjects with advanced fibrosis and cirrhosis were consistent with each other. Finally, our total sample size of 725 may appear relatively modest for a population-based study. However, a unique strength of this sample is that it is designed to be representative of the U.S. general population.

Emerging data indicate that following eradication of HCV with antiviral therapy, cirrhotic patients may experience improvements in liver histology and long-term clinical outcome [4,31]. However, as antiviral therapy available to date has reduced efficacy in patients with cirrhosis, our data point to the urgency with which systematic screening should be implemented for HCV patients with cirrhosis who remain asymptomatic but at risk of developing hepatic decompensation and/or HCC in the foreseeable future. Moreover, cirrhosis may be even more common in people who were not captured in the NHANES study, in whom the prevalence of co-existing conditions to accelerate fibrosis such as excessive alcohol use and HIV infection may be higher [32].

In summary, data derived from the NHANES samples over a span of 14 years, generalizable to HCV-infected American adults, show that the number of adults with HCV cirrhosis is rising in an accelerated fashion. The prevalence of cirrhosis remains high even in subjects whose HCV infection has not been diagnosed. These data call for public health efforts to reduce the burden of HCV infection by ensuring adherence to the screening recommendations followed by systematic assessment for liver fibrosis and implementation of antiviral therapy in appropriate patients for primary and secondary prevention of cirrhosis and its complications.

### Financial support

The work was supported by grants from the National Institutes of Health (DK-34238 and DK-92336) attributable to WR Kim.

### Conflict of interest

Dr. Kim reports consulting and advisory board participation with Bristol-Myers-Squibb and Gilead Sciences. No other authors report potential conflicts.

### Authors’ contributions

Prowpanga Udompap: acquisition of data; analysis and interpretation of data; drafting of the manuscript; statistical analysis.
Ajitha Mannalithara: acquisition of data; analysis and interpretation of data.
Nae-Yun Heo: critical revision of the manuscript for important intellectual content.
Dong H. Kim: critical revision of the manuscript for important intellectual content.

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**Table 3. Characteristics of positive HCV RNA participants who were and were not aware of their infection.**

<table>
<thead>
<tr>
<th></th>
<th>Aware</th>
<th>Not aware</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survey participants (n)</td>
<td>80</td>
<td>83</td>
<td>0.81</td>
</tr>
<tr>
<td>Sex (% female, (n))</td>
<td>37.5 (30)</td>
<td>27.7 (23)</td>
<td>0.18</td>
</tr>
<tr>
<td>Race/ethnicity (%,(n))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>45.0 (36)</td>
<td>44.6 (37)</td>
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</tr>
<tr>
<td>Non-Hispanic black</td>
<td>31.3 (25)</td>
<td>37.4 (31)</td>
<td>0.63</td>
</tr>
<tr>
<td>Mexican American</td>
<td>12.5 (10)</td>
<td>12.1 (10)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11.3 (9)</td>
<td>6.0 (5)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.8 ± 10.6</td>
<td>52.1 ± 12.7</td>
<td>0.70</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>54.9 ± 33.3</td>
<td>56.1 ± 39.9</td>
<td>0.83</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>56.8 ± 37.7</td>
<td>58.3 ± 43.3</td>
<td>0.82</td>
</tr>
<tr>
<td>Platelets(x10^3/μl)</td>
<td>219.8 ± 78.7</td>
<td>230.4 ± 87.7</td>
<td>0.42</td>
</tr>
<tr>
<td>APRI score (n = 163)</td>
<td>1.02 ± 1.16</td>
<td>0.96 ± 1.05</td>
<td>0.76</td>
</tr>
<tr>
<td>FIB-4 score (n = 163)</td>
<td>2.24 ± 1.96</td>
<td>2.17 ± 2.06</td>
<td>0.84</td>
</tr>
</tbody>
</table>

**Fig. 3. Proportion of the respondents with high, indeterminate and low probability of cirrhosis based on APRI score.**
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W. Ray Kim: study concept and design; obtained funding; administrative, technical, or material support; study supervision.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jhep.2016.01.009.

References