Hepatology

Nationwide survey of specialist knowledge on current standard of care (Peg-IFN/RBV) and barriers of care in chronic hepatitis C patients in China

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barriers to care, China, direct-acting antivirals, hepatitis C virus.

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Abstract

Background and Aim: Chronic hepatitis C virus (HCV) infection is the leading cause of liver diseases including cirrhosis and hepatocellular carcinoma. In China, it is a major national health problem that demands nationwide coordinated emphasis on prevention and treatment. To inform these initiatives, a nationwide survey was conducted from January to April 2015 to evaluate the knowledge, awareness, and perceived obstacles to HCV care.

Methods: A sample of 1000 HCV specialists across mainland China were recruited. Respondents were asked a series of 30 open-ended single or multiple response and Likert-scale questions about their HCV treatment knowledge, experience, assessment of HCV care status in China, and perceptions about treatment barriers.

Results: Sixty percent of the respondents answered incorrectly to more than half of the questions on basic HCV treatment principles. Over half of them incorrectly believed that maintenance therapy should be prescribed for non-responders (72%) and longer treatment duration improved sustained viral response rates (62%), regardless of HCV RNA level changes. Sixty-six percent of them believed that HCV treatment would still be interferon-based therapy in the next 5 years in China. Patient-related barriers, in particular lack of disease awareness, were considered to be the most significant barriers to HCV care. payer and medical-provider barriers included affordability issues, lack of reimbursement coverage for testing and treatments, and lack of referral to HCV specialists.

Conclusions: Focused and intense patient and provider education should be carried out to increase awareness. More effective direct-acting antivirals should be made available and affordable in China.

Introduction

Chronic hepatitis C virus (HCV) attacks the liver and leads to inflammation, which is the progressive cause of chronic hepatitis, cirrhosis, and/or hepatocellular carcinoma over time. It is estimated that up to 150 million people worldwide are chronically infected with HCV,1 and 500 000 deaths each year are attributed to HCV-related causes.2 In China, HCV seroprevalence was estimated to be 1%, representing 10 million chronic hepatitis C individuals.3–5 Moreover, data from the Chinese Center for Disease Control and Prevention report that cases of chronic hepatitis C have been increasing steadily in recent years, with more than 200 000 new cases in 2013.6

The primary goal of HCV therapy is to achieve sustained viral response (SVR) and cure, which can substantially reduce risk of downstream advanced-liver complications. In the past 2 years, treatment patterns for HCV infection around the world have undergone profound changes, with the launch of interferon-free oral direct-acting antivirals (DAAs) with greater treatment efficacy, fewer side effects and shorter treatment duration.7,8 However, in China, peg-interferon/ribavirin (Peg-IFN/RBV) is still used as the current standard treatment for HCV, which requires a longer duration of treatment (DoT), frequent monitoring, and the inconvenience associated with injections. Despite the high percentage of favorable host genotype IL-28B CC among Chinese patients,9 reported SVR rates of peg-IFN/RBV were still suboptimal, ranging from 44% to 83%.10 In addition, interferon-based therapy has a narrow window of opportunity for treatment efficacy.10 Consequently, there are many patients who
are peg-IFN/RBV intolerant, or ineligible, and they urgently need an alternative treatment option.

In addition to the limitation of the currently available HCV medications, there are many other factors that are impeding the delivery of anti-HCV therapy in China. With the growing disease burden, HCV has been recognized gradually as an urgent health problem, demanding nationwide coordinated emphasis on promotion, treatment, and prevention of HCV.

Therefore, a nationwide survey of HCV treatment providers was conducted from January to April 2015, with an aim of evaluating the physician’s knowledge and awareness of HCV treatment and perceived obstacles to care.

Methods

Sample size and allocation. The survey was designed and conducted to cover physicians in the eastern, central, and western regions of mainland China (excluding Hong Kong, Macao, and Taiwan). A total of 1000 physicians, including 50 for the pilot survey and 950 for the final survey, were targeted to produce a nationwide margin of error less than 10%. Three categories of province/municipality were selected: (i) National Medical Resource Centers in Beijing, Shanghai and Guangzhou; (ii) the seven provinces with the highest prevalence of HCV (greater than 20/100000 according to the 2010–2012 China CDC report: Xinjiang, Henan, Gansu, Jilin, Qinghai, Inner Mongolia, and Guangxi); and (iii) randomly selected two to three provinces or municipalities from each of the three geographical regions—eastern, central, and western China, as defined by the Health Statistics Year Book of China 2013. In each selected province, a capital city and two to three non-capital cities were randomly selected. Within these selected cities, three to eight hospitals were then randomly selected to meet the qualified sample size allocated in each province/municipality. Sample size allocation in each province considered four factors: total population size, number of reported HCV cases, number of total outpatient and inpatient visits, and the number of Peg-IFN plus IFN utilization.

Physician eligibility. Physicians were considered eligible for the survey if they worked in a Tier 3/2 hospital and had at least five HCV patient visits per week. In addition, the physician had to work in an outpatient department at least once per week and be an attending physician or above. Hepatology and Infectious Disease (ID) Departments were preferred, while Gastroenterology and Internal Medicine Departments were also considered in their absence. Physicians who worked in the traditional Chinese medicine department or the surgical department were excluded.

Questionnaire design. The survey questions were based on a previous international survey of barriers to HCV treatment, customized to the local clinical practice setting in China. The survey questions were reviewed and finalized by an expert committee. Eligible respondents were asked a series of open-ended single or multiple response and Likert-scale questions. A pilot study was conducted to validate the questionnaire. The stability of the questions was tested by answering the questionnaire by the same physician twice at an interval of 1–2 weeks and measured by calculating inter class correlation values, with an inter class correlation of greater than 0.75 indicating excellent stability. Questions with poor quality or poor stability were revised and re-tested. All physicians were interviewed for 30 min in a face-to-face format by a professional survey company (IMS Health).

Survey questions. The first section of the survey assessed physician’s knowledge of HCV treatment. Physician’s knowledge was assessed according to the level of agreement with the following statements: (i) the addition of RBV to Peg-IFN treatment improves the likelihood of SVR; (ii) in peg-IFN/RBV treatment, maintaining an optimal dose of RBV is necessary to achieve SVR; (iii) for different viral genotypes, the DoT is the same; (iv) treatment should be discontinued for patients who have detectable HCV RNA at treatment week 4; (v) treatment should be discontinued for patients who fail to achieve a 2-log decrease in HCV RNA by treatment week 12; (vi) maintenance therapy should be prescribed for treatment non-responders (HCV RNA is still detectable after 24-week treatment); (vii) the longer the treatment duration is, the better the efficacy will be (regardless of the virological response during the treatment); (viii) patients with stage 1 fibrosis have worse treatment outcomes than patients with stage 4 fibrosis; and (ix) level of HCV RNA has no correlation with severity of liver disease. Another question tested what the physician defined as cure for HCV.

The respondents were also asked questions on their opinions toward the current status of HCV diagnosis and treatment in China. Each response was rated on a 10-point Likert scale, with 0 representing “strongly disagree,” 5 “neither agree nor disagree,” and 10 “strongly agree.”

Another goal of this study was to assess perceived barriers to HCV care in China. Each physician was presented with a list of 31 barriers to care, grouped into three categories; patient-provider, medical-provider, and payer-related barriers. Respondents were asked to indicate their agreement to the statements, on a scale of 0 (no obstacle) to 10 (very obvious obstacle), with a score of greater than 6 considered a high barrier to care.

Statistical analysis. Mean, range, and standard deviation were examined for each continuous variable for current standard of HCV care and barriers to HCV care, with frequencies tabulated for each categorical variable. Bivariate analysis was used to examine the relationship between physician and practice characteristics using Pearson’s correlation analysis for continuous independent variables and one-way ANOVA for each categorical independent variable.

Results

Respondent’s profile. A total of 950 physicians were surveyed across 236 hospitals among 41 cities in 18 provinces/municipalities (Fig. 1). Physician and practice characteristics are summarized in Table 1. Overall, 33% of the physicians were from ID hospital, and 67% of the physicians were from general hospitals. Physicians were in specialty practice for a mean of 17.4 years, 75% of the physicians who had been practicing for ≥10 years and had an average of 9.7 HCV patient-visits each week (range, 5–38). Physicians were largely from Tier 3 hospitals (75%), which are recognized as the highest level in China.
Physicians were mainly specialized in ID or Hepatology (79%), followed by GI (13%) and general internal medicine (6%).

**Knowledge.** Overall, 60% of respondents answered incorrectly to half or more questions, indicating poor knowledge with current standard of care. The percentage varied significantly by region (75% in the Western Region) and by category (41% in highly prevalent provinces). Overall, the majority of physicians (97%) understood that addition of RBV to peg-IFN improved the likelihood of SVR and additionally that the optimal dose was an important consideration. Many physicians (73%) did not follow recommendations about genotype-guided treatment duration in guidelines (Table 2). Over half of physicians incorrectly believed that maintenance therapy should be prescribed for non-responders (72%) and longer treatment duration improved SVR rates (62%), regardless of change in HCV RNA level during treatment. Moreover, only 25% of respondents indicated that SVR12 or SVR24 were cured as indicated by in-HCV RNA level during treatment. Additionally, only 25% of respondents believed that awareness of HCV by the general public was low, and few patients knew that HCV is curable. Specialists around them understood HCV very well and adhered to diagnosis and treatment guidelines (mean score at 8.4 on a scale of 0 to 10). Over 60% of the physicians agreed to the questions “public awareness about HCV is high” and “most patients know that HCV is curable.” Physicians in high prevalence provinces were more likely to report that awareness of HCV by the general public was low, and few patients knew that HCV is curable. An interesting finding was that 90% of the physicians with poor knowledge tended to agree more on the statement that specialists around them had good awareness of HCV. Further, over 90% of the physicians expected a new treatment regimen to become available in the next 5 years, with shorter duration, higher SVR, a better safety profile, and more clinical convenience. Despite DAAs being widely available outside of China, the majority of respondents believed that treatment of HCV will still be IFN-based therapy in the next 5 years in China.

**Opinions toward current HCV care.** Physician opinions regarding the current status of HCV care are shown in Table 3. Overall, physicians felt satisfied with current HCV care and management. In particular, 95% of the physicians agreed that the physicians around them understood HCV very well and adhered to diagnosis and treatment guidelines (mean score at 8.4 on a scale of 0 to 10). Over 60% of the physicians agreed to the questions “public awareness about HCV is high” and “most patients know that HCV is curable.” Physicians in high prevalence provinces were more likely to report that awareness of HCV by the general public was low, and few patients knew that HCV is curable. An interesting finding was that 90% of the physicians with poor knowledge tended to agree more on the statement that specialists around them had good awareness of HCV. Further, over 90% of the physicians expected a new treatment regimen to become available in the next 5 years, with shorter duration, higher SVR, a better safety profile, and more clinical convenience. Despite DAAs being widely available outside of China, the majority of respondents believed that treatment of HCV will still be IFN-based therapy in the next 5 years in China.

**Barriers to care.** Overall, perceived barriers to care in this study were in the mid-range, with the greatest barriers reported in western provinces. Patient-related barriers to care (5.8 on scale of 0 to 10) were viewed as most significant, followed by payer-related barriers to care (5.4), while medical provider-related barriers were considered the least burdensome (4.5) (Fig. 2). In regards to patient-related barriers to care, patient awareness was considered to be the most significant barrier to HCV care (average

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Table 1  Physician and practice characteristics by category and region

| Characteristic                          | Total (n = 950) | National medical center (n = 230) | High reported province (n = 126) | Random selected province (n = 594) | East (n = 523) | Middle (n = 193) | West (n = 234) |
|----------------------------------------|----------------|----------------------------------|---------------------------------|----------------------------------|----------------|-----------------|----------------|
| Years in specialty practice, mean      | 17.4           | 18.2                             | 16.8                            | 17.3                             | 17.9           | 17.7            | 16.2           |
| >10 years above, mean (%)              | 686 (75%)      | 187 (82%)                        | 84 (67%)                        | 415 (74%)                        | 413 (79%)      | 120 (74%)        | 153 (66%)      |
| HCV patient visit per week†, mean     | 9.7            | 9.9                              | 10.8                            | 9.4                              | 8.4            | 13              | 10.0           |
| Ratio of HBV to HCV patients, mean    | 7.6            | 8.1                              | 6.7                             | 7.6                              | 8.7            | 7.3             | 5.5            |
| Hospital distribution, mean (%)        |                |                                  |                                 |                                  |                |                 |                |
| Tier 3 hospital                        | 712 (75%)      | 202 (88%)                        | 91 (72%)                        | 419 (71%)                        | 406 (78%)      | 135 (70%)        | 171 (73%)      |
| Tier 2 hospital                        | 238 (25%)      | 28 (12%)                         | 35 (28%)                        | 175 (30%)                        | 117 (22%)      | 58 (30%)         | 63 (27%)       |
| ID hospital                            | 313 (33%)      | 108 (47%)                        | 60 (47%)                        | 145 (25%)                        | 223 (43%)      | 34 (17%)         | 56 (24%)       |
| General hospital                       | 637 (67%)      | 122 (53%)                        | 66 (53%)                        | 449 (76%)                        | 300 (57%)      | 159 (83%)        | 178 (76%)      |
| Tier 3 ID hospital                     | 193 (20%)      | 98 (43%)                         | 31 (24%)                        | 64 (11%)                         | 143 (28%)      | 10 (5%)          | 40 (17%)       |
| Tier 2 ID hospital                     | 120 (13%)      | 10 (4%)                          | 29 (23%)                        | 81 (14%)                         | 80 (15%)       | 24 (12%)         | 16 (7%)        |
| Tier 3 general hospital                | 519 (55%)      | 104 (45%)                        | 60 (48%)                        | 355 (60%)                        | 263 (50%)      | 125 (65%)        | 131 (56%)      |
| Tier 2 general hospital                | 118 (12%)      | 18 (8%)                          | 6 (5%)                          | 94 (16%)                         | 37 (7%)        | 34 (18%)         | 47 (20%)       |
| Specialty, mean (%)                    |                |                                  |                                 |                                  |                |                 |                |
| Hepatology                             | 328 (35%)      | 115 (50%)                        | 61 (48%)                        | 152 (26%)                        | 223 (43%)      | 43 (22%)         | 62 (26%)       |
| Infectious disease                     | 421 (44%)      | 87 (38%)                         | 38 (30%)                        | 296 (50%)                        | 218 (42%)      | 104 (54%)        | 99 (42%)       |
| Gastroenterology                       | 122 (13%)      | 26 (11%)                         | 25 (20%)                        | 71 (12%)                         | 63 (12%)       | 23 (12%)         | 36 (15%)       |
| Internal medicine                      | 58 (6%)        | 1 (0%)                           | 2 (2%)                          | 55 (9%)                          | 6 (1%)         | 23 (12%)         | 29 (12%)       |
| Others                                 | 21 (2%)        | 1 (0%)                           | 0 (0%)                          | 20 (3%)                          | 13 (2%)        | 0 (0%)           | 8 (3%)         |
| Professional title, mean (%)           |                |                                  |                                 |                                  |                |                 |                |
| Chief physician                        | 262 (28%)      | 55 (24%)                         | 31 (25%)                        | 176 (30%)                        | 147 (28%)      | 42 (22%)         | 73 (31%)       |
| Associate chief physician              | 370 (39%)      | 100 (43%)                        | 51 (40%)                        | 219 (37%)                        | 205 (39%)      | 78 (40%)         | 87 (37%)       |
| Attending physician                    | 318 (33%)      | 75 (33%)                         | 44 (35%)                        | 199 (33%)                        | 171 (18%)      | 73 (38%)         | 74 (32%)       |

†Sampled physician with at least five HCV patient visits per week.
6.8 on scale of 0 to 10). The DoT, concern about the side effects of the drugs, and low SVR rate of current treatments were also considered as deterring factors for patients. Another major barrier to care was considered to be lack of affordability (6.6) (Table 4).

The greatest medical provider-related barrier to care was lack of referral to HCV specialists by other physicians (5.3) and lack of awareness of HCV screening among non-specialized medical providers (5.0) limited early treatment.

Physicians highlighted several payer-related barriers to care, such as laboratory tests not being reimbursed (6.2), lack of reimbursement for outpatient treatment (5.7), and a low percentage of reimbursement by medical insurance (5.7).

**Bivariate analysis.** Along with geographic region, perceived barriers were significantly associated with category, hospital distribution, hepatology specialty, and physician knowledge (Table 5). Subspecialists (hepatology and IDs) reported fewer perceived barriers than GIs and internists. Likewise, physicians from Tier 3 ID hospitals and national medical centers, and ones with higher knowledge scores, reported fewer barriers to care on average (Table 5).

**Discussion**

This nationwide multidisciplinary survey provided insight into the current status of hepatitis C care, as viewed by 950 liver specialists in China. The key findings of this study were deficits in provider knowledge in China, perceived barriers to care for HCV treatment were shared between regions, the importance of patient-level obstacles to treatment, and the shared expectation for better treatment options for HCV patients.

**HCV is a public health issue with underestimated importance.** It is estimated that 1% (10 million people) in China are infected with HCV, which ranks China as the highest population of HCV patients in the world. Moreover, the number of new cases reported in China has been increasing in recent years—between 1997 and 2012, the reported incidence of HCV infection per 100,000 population rose from 0.7 to 15.0 cases, with the majority reported in the over-35 population. Therefore, the prevention and treatment of hepatitis C is a major public health issue. Only until recent years; however, due to the decrease in the prevalence of hepatitis B as a result of widespread use of the hepatitis B vaccine, hepatitis C has attracted increasing attention. A previous survey in 2011 showed non-specialists have little understanding of hepatitis C. In this article, the authors called for these non-specialists to learn from HCV specialists in order to have a greater understanding of the prevention and treatment of hepatitis C. However, there is no study conducted on understanding the knowledge and treatment status of hepatitis specialists in China. The findings in this comprehensive questionnaire, developed and piloted by a panel of nationally recognized HCV experts further indicate that there is an urgent need to improve the current status of hepatitis C care.

**The knowledge deficit about HCV treatment is likely due to the complexity of IFN-based therapy.** In the first place, HCV-treated physicians showed deficits in knowledge of IFN-based treatment. This was likely due to the complexity of IFN-based therapy and in general hectic work load among the physicians in China. Specialists in our survey...
Table 2  Physician’s knowledge by global region and medical specialty, % correct rate

| Number | Statement and physician’s knowledge overall | Total (n = 950) | Respondents percentage with correct answer (%) |
|--------|--------------------------------------------|----------------|-----------------------------------------------|
|        |                                            | National medical center (n = 230) | High reported province (n = 126) | Random selected province (n = 594) | East (n = 523) | Middle (n = 193) | West (n = 234) |
| 1      | Addition of RBV to Peg-IFN treatment improve the likelihood SVR. | 97             | 98                                           | 96                                   | 97             | 98             | 97             | 96             |
| 2      | In Peg-IFN + RBV treatment, maintaining an optimal dose of RBV is necessary to achieve SVR. | 96             | 98                                           | 93                                   | 96             | 98             | 94             | 94             |
| 3      | For different viral genotypes, the treatment duration is the same. | 37             | 39                                           | 53                                   | 32             | 39             | 42             | 26             |
| 4      | Treatment should be discontinued for patients who have detectable HCV RNA at treatment week four. | 51             | 52                                           | 68                                   | 47             | 59             | 51             | 32             |
| 5      | Treatment should be discontinued for patients who fail to achieve a 2-log decrease in HCV RNA by treatment week 12. | 47             | 51                                           | 22                                   | 51             | 44             | 48             | 54             |
| 6      | Maintenance therapy should be prescribed for treatment non-responders (HCV RNA is still detectable after 24 weeks treatment). | 28             | 28                                           | 33                                   | 27             | 30             | 26             | 25             |
| 7      | The longer the treatment duration is, the better the efficacy will be (regardless of the virological response during the treatment). | 38             | 30                                           | 54                                   | 37             | 39             | 48             | 28             |
| 8      | Patients with stage one fibrosis have worse treatment outcomes than patients with stage four fibrosis. | 41             | 44                                           | 63                                   | 35             | 45             | 48             | 27             |
| 9      | Level of HCV RNA has no correlation with severity of liver disease. | 57             | 67                                           | 53                                   | 55             | 60             | 47             | 60             |
| 10     | For anti-HCV treatment, which standard do you use to define a patient as “being cured”? | 25             | 32                                           | 24                                   | 23             | 29             | 26             | 18             |
|        | Respondents with ≥5 correct answers among 10 questions | 60             | 59                                           | 41                                   | 63             | 56             | 55             | 75             |

Correct answer is defined as (1) agreement level, ≥6 for questions 1, 2, 5, and 9; and (2) disagreement level, <5 for questions 3, 4, 6, 7, 8, and 10.

Chronic hepatitis C virus (HCV) RNA remains undetectable during 3 or 6 months after cessation of treatment were considered as sustained viral response (SVR) by physicians in this study. Peg-IFN, peg-interferon; RBV, ribavirin.
| Number | Statement                                                                 | Total (n = 950) | Mean score (respondents percentage who agree with statement ≥6) |
|--------|---------------------------------------------------------------------------|-----------------|---------------------------------------------------------------|
|        |                                                                           | Category         | Region                                                        |
|        |                                                                           | National medical center (n = 230) | High reported province (n = 126) | Random selected province (n = 594) | East (n = 523) | Middle (n = 193) | West (n = 234) |
| 1      | The specialists around me understand HCV very well, the diagnosis and treatment are normalized. | 8.4 (95%)        | 8.6 (97%)          | 8.5 (94%)          | 8.3 (94%) | 8.7 (97%) | 8.1 (93%) | 7.9 (93%) |
| 2      | The doctors around me have a strong sense of HCV screening.               | 7.8 (87%)        | 7.9 (90%)          | 7.7 (79%)          | 7.8 (88%) | 8.3 (93%) | 7.1 (75%) | 7.3 (85%) |
| 3      | The public has a high awareness of HCV.                                  | 6.2 (65%)        | 6.4 (61%)          | 4.7 (34%)          | 6.5 (73%) | 6.6 (71%) | 5.2 (45%) | 6.1 (68%) |
| 4      | HCV patients I encountered can accurately understand the consequence of non-treatment. | 6.5 (70%)        | 6.6 (67%)          | 5.6 (53%)          | 6.7 (75%) | 7.0 (78%) | 5.5 (54%) | 6.2 (66%) |
| 5      | Most patients know that HCV is curable.                                  | 6.2 (63%)        | 6.3 (64%)          | 5.1 (41%)          | 6.3 (67%) | 6.5 (72%) | 5.4 (45%) | 6.0 (58%) |
| 6      | Most patients who receiving anti-HCV treatment could pay a regular return visit as required. | 7.0 (83%)        | 7.5 (87%)          | 7.5 (87%)          | 6.8 (80%) | 7.3 (87%) | 7.2 (86%) | 6.3 (71%) |
| 7      | Patients with HCV can get appropriate treatment or management in local hospitals. | 6.9 (79%)        | 7.0 (78%)          | 6.9 (79%)          | 6.9 (79%) | 7.1 (80%) | 6.9 (81%) | 6.5 (77%) |
| 8      | I think the policy makers (including those who make HCV-related policies, e.g., medical insurance) understand the guideline of hepatitis C well. | 7.3 (84%)        | 7.7 (89%)          | 7.0 (74%)          | 7.2 (84%) | 7.6 (90%) | 7.2 (79%) | 6.7 (74%) |
| 9      | I think treatment for CHC will not change much in the next 5 years.       | 6.2 (66%)        | 6.4 (67%)          | 6.1 (56%)          | 6.2 (68%) | 6.7 (78%) | 5.3 (49%) | 5.7 (55%) |

HCV, Chronic hepatitis C virus.
Table 4 Perceived barriers to HCV treatment

| Patient-related Barrier                                                                 | Score |
|----------------------------------------------------------------------------------------|-------|
| 1. Patient’s awareness/knowledge of HCV is not enough or wrong.                       | 6.8   |
| 2. The patient worries about low SVR rate.                                              | 6.6   |
| 3. Unaffordability                                                                      | 6.6   |
| 4. Patient thinks that the DoT is too long.                                             | 6.5   |
| 5. The patient is too busy to pay needed follow-up visits (e.g., traveling frequently, or unable to get injection regularly). | 6.0   |
| 6. Patient is afraid of excessive blood tests.                                         | 5.3   |
| 7. Patient is afraid of injection.                                                     | 4.8   |
| 8. Patient is afraid of the side effects of the drugs.                                 | 6.5   |
| 9. Patient is afraid of the effects of drugs on the fertility and offspring.           | 6.3   |
| 10. Patient prefers to receive traditional therapies (traditional Chinese medicine or other alternative therapies). | 5.7   |
| 11. Patient cannot find good doctors/medical resources at local.                       | 5.4   |
| 12. Contraindicated or intolerant to the interferons.                                  | 5.6   |
| 13. Contraindicated or intolerant to RBV.                                               | 5.5   |
| 14. Unwilling to be treated with current medications, waiting for new drugs.           | 4.7   |
| 15. Patients cannot inject themselves or cannot get helps for injection.                | 5.0   |
| 16. No conditions (low temperature) to preserve (peg) interferons.                     | 4.7   |

Provider-related Barrier

| Provider-related Barrier                                                                 | Score |
|----------------------------------------------------------------------------------------|-------|
| 1. The number of hospitals/doctors that is capable of treating HCV is not enough.      | 4.4   |
| 2. Awareness of HCV screening is generally low, which limits early diagnosis.         | 5.0   |
| 3. Lack of referral to HCV providers by other physicians, which limits early treatment.| 5.3   |
| 4. Lack of tests for the diagnosis and treatment of HCV.                               | 4.4   |
| 5. Insufficient training for HCV management.                                          | 4.7   |
| 6. Medication for HCV treatment cannot be regularly supplied.                         | 4.0   |
| 7. Lack of proper storage for medications.                                            | 3.4   |
| 8. The hospital cannot provide sufficient diagnosis and treatment due to the medical insurance quota. | 4.6   |

Payer-related Barrier

| Payer-related Barrier                                                                 | Score |
|----------------------------------------------------------------------------------------|-------|
| 1. Many patients do not have medical insurance.                                        | 4.5   |
| 2. Medical insurance partially covers CHC treatment.                                    | 5.0   |
| 3. HCV medication cannot be reimbursed at outpatient clinic and can only be reimbursed at inpatient. | 4.7   |
| 4. Medical insurance limits the choice of HCV medication.                               | 5.4   |
| 5. Medical insurance limits the ToD of HCV treatment.                                   | 5.3   |
| 6. Low percentage of reimbursement by medical insurance.                                | 5.7   |
| 7. Several important lab tests cannot be reimbursed, such as HCV RNA quantitation with high sensitivity and virus genotype, etc. | 6.2   |

Figure 2 Overall, perceived barriers to care in this study were in the mid-range, with the greatest barriers reported in western provinces. Patient-related barriers to care were viewed as most significant, followed by payer-related barriers to care, while medical provider-related barriers were considered the least burdensome. Patients, ■; Medical Provider, ■; Payer, ■; Mean, ■.
understood that the addition of RBV to interferon treatment improved the likelihood of SVR and also agreed that dosing strongly affects SVR. However, treatment duration based on genotype was not well adopted, and only one quarter of physicians indicated that SVR12/24 was considered a cure, which is recommended by international guidelines. Many concepts for treating hepatitis B patients were incorrectly adopted by physicians when treating hepatitis C patients. For example, more than half of physicians believed that longer treatment duration more improved treatment efficacy. Therefore, physicians often treated non-responders with maintenance therapy, despite the lack of efficacy in clinical practice. These findings indicate that there are some serious deficits in basic HCV treatment principles, even among experienced HCV-treating physicians.

**Expectations toward the future of HCV treatment**

**Better treatment options.** Interestingly, despite the high satisfaction rate toward IFN-based therapy shown in survey, physicians were clearly aware of the unmet medical needs caused by IFN-based therapy and held a high expectation on a better treatment characterized as “shorter duration, higher SVR, better safety profile and more clinical convenience.” Unfortunately, they had low awareness and knowledge of improvements of anti-HCV treatment (DAAs) worldwide therefore believed the treatment for HCV will still be IFN-based therapy in the next 5 years in China.

In the survey, physicians highlighted several patient-related barriers to HCV care, including inadequate patient awareness, low treatment efficacy, lack of affordability of HCV treatment, long DoT, and significant side effects for patients, which subsequently reduce treatment adherence and rates of SVR. Low awareness of the disease among the general public is a reoccurring theme in China, with one survey finding that less than 1% of public respondents reporting having some knowledge about HCV transmission and prevention. DoT and side effects of drugs were also highlighted by physicians as major patient-related obstacles to care. Another study found that many patients with HCV fail therapy due to substantial side effects of interferon-based treatments as well as high treatment costs. Furthermore, in our study, 55% of physicians believed that patients with contraindications and intolerance to IFN based therapies are unlikely to seek further treatment.

Taken together, this study highlights the need for DAAs to become available in China. DAAs have fewer side effects, shorter DoT, and have been shown to increase rates of SVR for treatment-naive and treatment-experienced HCV patients.

**Better referral system.** In regards to patient-provider barriers, physicians highlighted lack of referral to specialists by other physicians as a major problem. This mirrors the results from a previous survey of 1362 non-specialists showing that only 56% of the non-specialists would advise a HCV-positive patient to consult a HCV specialist. Moreover, as few as 29% of these non-specialists believed that hepatitis C was curable or had a very low curable rate, and nearly 50% of these non-specialists thought there was no effective treatment for hepatitis C. In our study, HCV specialists confirmed that the awareness of HCV screening by medical providers was generally low, which limits early treatment, increases complications and reduces the number of patients who were eligible to receive anti-HCV treatment. A better referral system to specialists in Tier 3 ID hospitals is highly recommended and in need according to this study.

**Better medication access.** These issues are further compounded by payer-level issues. Physicians believed that lack of reimbursement for lab tests and low reimbursement levels by medical insurance were the major payer-related barriers to treatment. Moreover, HCV medication currently available in China can only be reimbursed for inpatient care. High treatment costs and limited insurance may deter patients from commencing treatment.

**Conclusions and action plan**

Overall, our survey found that there were substantial barriers that may impede prompt and appropriate treatment of HCV infection in China. Given the limitation of IFN-based therapy, prevalence...
of intolerant, and ineligible patients as well as the significant side effects associated with IFN-based therapy, a better treatment option with fewer side effects, better outcomes, and easy access is in urgent need in China for HCV patients. With a growing disease burden, the prevention and treatment of HCV demand nationwide coordinated emphasis. Now China government is negotiating on the DAA price and will accelerate DAs approval to improve the accessibility of DAs in China. We recommend that the reimbursement for DAs should be evaluated and considered in order to reduce downstream HCV-related complications, improve patient quality of life, and reduce subsequent costs to the health system. Focused and intense patient education should be carried out to increase disease awareness in order to achieve affordable and effective treatment of HCV in China and facilitate the global fight against HCV infection.

Disclosures

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