Baseline Characteristics and Treatment Patterns of the Patients Recruited to the China Registry of Hepatitis B

Shan Shan¹, Hong You¹, Junqi Niu², Jia Shang³, Wen Xie⁴, Yuexin Zhang⁵, Xun Li⁶, Hong Ren⁷, Hong Tang⁸, Huiguo Ding⁹, Xihong Wang¹⁰, Yuemin Nan¹¹, Xiaoguang Dou¹², Tao Han¹³, Lingyi Zhang¹⁴, Xiaqing Liu¹⁵, Cunliang Deng¹⁶, Jilin Cheng¹⁷, Xiaozhong Wang¹⁸, Qing Xie¹⁹, Shumei Lin²⁰, Yan Huang²¹, Youqin Xu²², Yong Xiong²³, Wu Li²⁴, Xuebing Yan²⁵, Hongxin Piao²⁶, Wenxiang Huang²⁷, Qinghua Lu²⁸, Weijin Gong²⁹, Shiping Li³⁰, Xiaoxuan Hu³¹, Xiaolan Zhang³², Shourong Liu³³, Yufang Li³⁴, Dongliang Yang³⁵, Hai Li³⁶, Caixia Yang³⁷, Mingliang Cheng³⁸, Lioyun Zhang³⁹, Huanwei Zheng⁴⁰, Xinhua Luo⁴¹, Feng Lin⁴², Wei Wang⁴³, Guanghua Xu⁴⁴, Xiaoyuan Xu⁴⁵, Lai Wei⁴⁶, Jinlin Hou⁴⁷, Zhongping Duan⁴⁸, Hui Zhuang⁴⁹, Xizhong Yang⁵⁰, Yuanyuan Kong⁵¹*, and Jidong Jia¹* for the CR-HepB study group, Beijing, China

¹Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine on Liver Cirrhosis, National Clinical Research Center for Digestive Diseases, Beijing, China; ²Department of Hepatology, First Hospital of Jilin University, Changchun, Jilin, China; ³Department of Infectious Diseases, Henan Provincial People's Hospital, Zhengzhou, Henan, China; ⁴Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, Beijing, China; ⁵Department of Infectious Diseases, First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, China; ⁶Department of General Surgery, The First Hospital of Lanzhou University, Lanzhou, Gansu, China; ⁷Department of Infectious Diseases, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China; ⁸Department of Infectious Diseases, West China Hospital of Sichuan University, Chengdu, Sichuan, China; ⁹Department of Gastroenterology and Hepatology, Beijing Youan Hospital, Capital Medical University, Beijing, China; ¹⁰Center of Infectious Diseases, The Third People's Hospital of Taiyuan, Taiyuan, Shanxi, China; ¹¹Department of Traditional and Western Medical Hepatology, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, China; ¹²Department of Infectious Diseases, Shengjing Hospital of China Medical University, Shenyang, Liaoning, China; ¹³Department of Hepatology, Tianjin Third Central Hospital, Tianjin, Tianjin, China; ¹⁴Department of Hepatology, Lanzhou University Second Hospital, Lanzhou, Gansu, China; ¹⁵Department of Infectious Diseases, Peking Union Medical College Hospital, Beijing, China; ¹⁶Department of Infectious Diseases, The Affiliated Hospital of Southwest Medical University, Lanzhou, Gansu, China; ¹⁷Department of Gastroenterology, Shanghai Public Health Clinical Center, Shanghai, China; ¹⁸Department of Hepatology, Xijiang Uygur Autonomous Region Traditional Chinese Medicine Hospital, Urumqi, Xinjiang, China; ¹⁹Department of Infectious Diseases, Shanghai Ruijin Hospital, Jiao Tong University School of Medicine, Shanghai, China; ²⁰Department of Infectious Diseases, The First Affiliated Hospital of Xian Jiao Tong University, Xi'an, Shaanxi, China; ²¹Department of Infectious Diseases, Xiangya Hospital Central South University, Changsha, Hunan, China; ²²Department of Digestive System, Beijing Tiantan Hospital, Capital Medical University, Beijing, China; ²³Department of Infectious Diseases, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China; ²⁴Department of Infectious Diseases, First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China; ²⁵Department of Infectious Diseases, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China; ²⁶Department of Infectious Diseases, Yanbian University Hospital, Yanji, Jilin, China; ²⁷Department of Infectious Diseases, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China; ²⁸Department of Hepatology, The Fourth People's Hospital of Qinghai Province, Xining, Qinghai, China; ²⁹Department of Infectious Diseases, Xinyi Changji Prefecture People's Hospital, Changji, Xinjiang, China; ³⁰Department of Hepatopancreatitis Surgery, Affiliated Hospital of Weifang Medical University, Weifang, Shandong, China; ³¹Department of Infectious Diseases, Hunan Provincial People's Hospital, Changsha, Hunan, China; ³²Department of Gastroenterology, The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei, China; ³³Department of Hepatology, Xi Xi Hospital of Hangzhou, Hangzhou, Zhejiang, China; ³⁴Department of Infectious Diseases, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, China; ³⁵Department of Infectious Diseases, Union Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, China; ³⁶Department of Hepatopancreatitis and Splenic Medicine, The Affiliated Hospital, Logistics University of People's Armed Police Force, Tianjin, China; ³⁷Department of Infectious Diseases, Infectious Disease Hospital of Wuhai, Wuhai, Inner Mongolia, China; ³⁸Department of Infectious Diseases, The Affiliated Hospital of Guizhou Medical University, Guiyang, Guizhou, China; ³⁹Department of Infectious Diseases, The First Affiliated Hospital of Shanxi Medical University, Taiyuan, Shanxi, China; ⁴⁰Department of Infectious Diseases, The Fifth Hospital of Shijiazhuang, Shijiazhuang, Hebei, China; ⁴¹Department of Infectious Diseases, Guizhou Provincial People's Hospital, Guiyang, Guizhou, China; ⁴²Department of Infectious Diseases, Hainan General Hospital, Haikou, Hainan, China; ⁴³Department of Infectious Diseases, The Second Hospital of Shandong University, Jinan, Shandong, China; ⁴⁴Department of Infectious Diseases, Yanan University Affiliated Hospital, Yan'an, Shaanxi, China; ⁴⁵Department of Infectious Diseases, Peking University First Hospital, Beijing, China; ⁴⁶Peking University Hospital Institute, Peking University People's Hospital, Beijing, China; ⁴⁷Institute of Hepatology and Department of Infectious Disease, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong, China; ⁴⁸Artificial Liver Center, Beijing Youan Hospital, Capital
Background and Aims: Chronic hepatitis B virus (HBV) infection remains a major public health problem globally. Here, we describe the baseline characteristics and treatment profiles of HBV-infected patients recruited to the China Registry of Hepatitis B. Methods: Inclusion criteria were patients with different stages of chronic HBV infection and complete key data. Exclusion criteria were patients with hepatocellular carcinoma. The baseline clinical, laboratory and treatment profiles were analyzed. Results: Finally, 40,431 patients were included. The median age was 43 years, with 65.2% being men and 51.3% being positive for hepatitis B e antigen (HBeAg). The most common initial diagnosis was chronic hepatitis B (81.0%), followed by cirrhosis (9.3%), inactive carrier of hepatitis B surface antigen (HBsAg) (6.7%), and immune tolerant phase of hepatitis B infection (3.0%). Among the 21,228 patients who were on treatment, 88.0%, 10.0% and 2.0% received nucleos(t)ide analogues (NAs), interferon or combination of NAs and interferon, respectively. The proportion of patients who received preferred NAs (entecavir or tenofovir disoproxil fumarate) had increased from 13.5% in 2003 to 79.7% in 2016.

Conclusions: We concluded that middle-aged men accounted for most of the patients with chronic hepatitis B in this cross-sectional study. About half of the patients were HBeAg-positive. NAs were the most commonly used therapy, and use of the preferred NAs had steadily increased in the past decade.

Citation of this article: Shan S, You H, Niu J, Shan J, Xie W, Zhang Y, et al. Baseline characteristics and treatment patterns of the patients recruited to the China Registry of Hepatitis B. J Clin Transl Hepatol 2019;7(4):322–328. doi: 10.14218/JCTH.2019.00052.

Abstract

Background and Aims: Chronic hepatitis B virus (HBV) infection remains a major public health problem globally. Here, we describe the baseline characteristics and treatment profiles of HBV-infected patients recruited to the China Registry of Hepatitis B. Methods: Inclusion criteria were patients with different stages of chronic HBV infection and complete key data. Exclusion criteria were patients with hepatocellular carcinoma. The baseline clinical, laboratory and treatment profiles were analyzed. Results: Finally, 40,431 patients were included. The median age was 43 years, with 65.2% being men and 51.3% being positive for hepatitis B e antigen (HBeAg). The most common initial diagnosis was chronic hepatitis B (81.0%), followed by cirrhosis (9.3%), inactive carrier of hepatitis B surface antigen (HBsAg) (6.7%), and immune tolerant phase of hepatitis B infection (3.0%). Among the 21,228 patients who were on treatment, 88.0%, 10.0% and 2.0% received nucleos(t)ide analogues (NAs), interferon or combination of NAs and interferon, respectively. The proportion of patients who received preferred NAs (entecavir or tenofovir disoproxil fumarate) had increased from 13.5% in 2003 to 79.7% in 2016.

Conclusions: We concluded that middle-aged men accounted for most of the patients with chronic hepatitis B in this cross-sectional study. About half of the patients were HBeAg-positive. NAs were the most commonly used therapy, and use of the preferred NAs had steadily increased in the past decade.

Citation of this article: Shan S, You H, Niu J, Shan J, Xie W, Zhang Y, et al. Baseline characteristics and treatment patterns of the patients recruited to the China Registry of Hepatitis B. J Clin Transl Hepatol 2019;7(4):322–328. doi: 10.14218/JCTH.2019.00052.

Introduction

Universal vaccination against hepatitis B virus (HBV) in infants has achieved great success but chronic HBV infection remains a major public health problem globally.1 The 2017 World Health Organization (WHO) Global Hepatitis Report estimates that 257 million persons, or 3.5% of the population, are chronically infected by HBV,2 with the highest hepatitis B surface antigen (HBsAg) prevalence (6.2%) being in the Western Pacific region.3–5 Chronic HBV infection is associated with a considerable burden of liver morbidity and mortality, and can lead to cirrhosis, decompensation and hepatocellular carcinoma (HCC).6

In China, with high coverage of HBV vaccination in infants, the estimated prevalence of HBsAg declined to 6.1% in the general population.7,8 However, historical HBV endemicity built a large reservoir of chronically infected persons. It is estimated that there are more than 70 million persons with chronic HBV infection in China.3 To facilitate real-world clinical study of chronic HBV infection, we have established a national HBV registry platform, the China Registry of Hepatitis B (known as the CR-HepB),9 which was launched in July 2012. Currently, it consists of 47 tertiary hospitals in mainland China (ClinicalTrials.gov registry number: NCT03108794).9

In the present cross-sectional study, we described the demographic, baseline characteristics, and treatment profiles of patients recruited in CR-HepB from June 2012 through June 2017.

Methods

Data sources

The CR-HepB was launched in June 2012 but retrospectively captured data of patients from 2000. The current study retrieved data from CR-HepB registrants prospectively or retrospectively from June 2012 to June 2017. The key information includes patients’ age, gender, diagnosis, laboratory results, liver biopsy results, and antiviral treatment profiles.

Patient population

Inclusion criteria were patients with different stages of chronic HBV infection and available information on hepatitis B e-antigen (HBeAg) status and HBV DNA and alanine transaminase levels. Exclusion criteria were patients with HCC.

The diagnostic criteria for immune tolerant phase, HBeAg-positive chronic hepatitis B (CHB), HBeAg-negative CHB, inactive HBsAg carriers, cirrhosis, and HCC were in line with major international and national guidelines10 and described in our previous paper.9

Statistical analyses

We use proportions and percentages to describe the demographic and clinical characteristics of the patients. We present the proportions of patients by their age, sex, HBeAg status, diagnosis, liver biopsy results, and type(s) of treatment received. Descriptive statistics are expressed as medians, lower quartiles, and upper quartiles, or as a number and percentage of patients. All statistical analyses were performed using SPSS v19.0.

Results

After excluding 530 individuals with HCC, 40,431 patients with confirmed diagnoses of immune tolerant phase hepatitis B,
CHB, inactive HBsAg carrier status, and cirrhosis were included in the present study (Fig. 1).

**Demographic and clinical characteristics of patients**

The demographic and clinical characteristics of the patients are shown in Table 1. The median age was 43 years, with a men-to-women ratio of 1.9. Overall, 51.3% were HBeAg-positive. Approximately 81.0% of the patients had initially been diagnosed with CHB, 9.3% with cirrhosis, 6.7% as inactive HBsAg carriers, and 3.0% with immune tolerant phase hepatitis B.

**Age distribution of the 40,431 patients with chronic HBV infection (by sex)**

Among the 40,431 patients included in the present study, the 30–49 years-old age group was the most predominant in both

Table 1. Demographic and baseline data of 40,431 patients with hepatitis B virus-related diseases

|                         | Overall, n = 40,431 | Immune tolerance phase, n = 1,214 | Inactive HBsAg carrier, n = 2,725 | Chronic hepatitis B, n = 32,740 | Cirrhosis, n = 3,752 |
|-------------------------|---------------------|----------------------------------|----------------------------------|---------------------------------|---------------------|
| Age in years            | 43 (33, 53)         | 33 (28, 41)                      | 39 (31, 49)                      | 43 (33, 52)                     | 55 (48, 63)         |
| Sex                     |                     |                                  |                                  |                                 |                     |
| Men, n (%)              | 26,347 (65.2)       | 610 (50.2)                       | 1522 (55.9)                      | 21,472 (65.6)                   | 2743 (73.1)         |
| Women, n (%)            | 14,084 (34.8)       | 604 (49.8)                       | 1203 (44.1)                      | 11,268 (34.4)                   | 1,009 (26.9)        |
| HBeAg-positive, n (%)   | 20,740 (51.3)       | 1214 (100.0)                     | 0 (0)                            | 17,936 (54.8)                   | 1,590 (42.4)        |
| HBV DNA (log_{10} IU/mL)| 3.9 (2.3, 6.6)      | 7.6 (6.3, 8.1)                   | 0 (0, 2.6)                       | 4.2 (2.7, 6.9)                  | 3.9 (2.0, 5.6)      |
| ALT (IU/mL)             | 41.7 (24.6, 87.0)   | 27.0 (21.0, 34.8)                | 24.0 (18.0, 33.0)                | 46.0 (26.0, 99.0)               | 42.0 (27.0, 76.0)   |
| AST (IU/mL)             | 34.0 (23.0, 63.0)   | 22.0 (17.0, 26.0)                | 23.0 (19.0, 28.0)                | 35.6 (24.0, 67.2)               | 47.0 (29.5, 83.6)   |
| ALP (U/L)               | 78.0 (62.0, 101.0)  | 69.0 (56.0, 85.0)                | 70.0 (58.0, 86.0)                | 77.7 (62.0, 99.0)               | 97.8 (73.0, 133.0)  |
| GGT (U/L)               | 27.0 (16.0, 55.0)   | 15.0 (12.0, 21.0)                | 17.0 (12.0, 25.0)                | 28.0 (17.0, 55.2)               | 50.9 (27.9, 99.0)   |
| Bilirubin (µmol/L)      | 14.8 (10.9, 21.5)   | 12.1 (9.3, 15.8)                 | 12.8 (9.7, 17.2)                 | 14.4 (10.8, 20.3)               | 24.5 (15.9, 41.3)   |
| ALB (g/L)               | 44.0 (39.7, 46.7)   | 45.2 (43.2, 47.3)                | 45.4 (43.4, 47.4)                | 44.2 (40.4, 46.9)               | 34.8 (29.4, 41.2)   |
| PLT count (×10^3/L)     | 165.0 (115.0, 208.3)| 200.0 (173.0, 236.0)             | 188.0 (154.0, 225.0)             | 171.0 (129.0, 211.0)            | 81.0 (53.0, 123.0)  |

Data are expressed as median (range) or n (%).

Abbreviations: ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; PLT, platelet.
men and women, followed by the 50–59 years-old age group. Patients aged between 30–59 years-old accounted for 71.8% of all patients (Fig. 2).

**Disease distribution in different age groups among the 40,431 patients**

The proportion of patients diagnosed with cirrhosis was increased with increasing ages, whereas the proportion of patients diagnosed with immune tolerance phase was decreased with increasing age (Fig. 3).

**Liver histology of 485 patients**

Necroinflammation activity and fibrosis stage were assessed according to the Scheuer grading and staging system. Among the 485 patients who underwent liver biopsy, the proportion of patients with liver inflammation grade ≥2 or the stage of liver fibrosis ≥2 increased with age (Fig. 4).

**Treatment profiles of 21,228 patients and the changing prescription of different nucleos(t)ide analogues**

Nucleos(t)ide analogues (NAs) were the most common therapy among the 21,228 patients with prescription information. A much smaller proportion of patients were treated with interferon (10.0%) or a combination of interferon and NAs (2.0%). Lamivudine (15.3%) and adefovir dipivoxil (18.4%) were widely used before 2011, whereas the use of entecavir (51.4%) and tenofovir disoproxil fumarate (2.1%) dramatically increased after 2011 (Fig. 5).
**Discussion**

In the present study, with large number of patients, we found that middle-aged men represented the major proportion of this cohort. About half of the patients were HBeAg-positive. The most common initial diagnosis was CHB, followed by cirrhosis, inactive HBsAg carrier, and immune tolerant phase of hepatitis B infection. The proportion of patients diagnosed with cirrhosis was increasing with increasing age. Among the patients with prescription information, nearly 90% received NAs and the use of preferred NAs have increased dramatically in the past decade.

Our study showed that men accounted for a significantly higher proportion (65.2%) than women (34.8%), and about half of patients were HBeAg-positive. This is similar to the result of a recent multicenter, real-world study conducted in tier-2 city hospitals in China, which showed that 74% of 3,408 patients with CHB were men, with an overall mean age of 40 years, and that 60% of patients were HBeAg-positive. Not surprisingly, patients with HBeAg-negative infection were older than those with HBeAg-positive infection, also similar to that reported from the USA.

In our study, the middle-aged group was the most predominant in both men and women. This is in line with the recent reports that the prevalence of HBsAg in childbearing-aged men and women still being around 6% in rural and endemic areas in China. Therefore, prevention of mother-to-child transmission is still of paramount importance. Not surprisingly, the proportion of patients diagnosed with cirrhosis was increased with increasing age. Similarly, among the 485 patients who underwent liver biopsy, the majority of these patients had mild to moderate necroinflammation and fibrosis. This may be due to the fact that patients with more disease activity and advanced fibrosis could be identified easily by noninvasive modalities, making them under-represented among patients who received liver biopsy.

In our study, more than half of the patients were prescribed treatment, and nearly 90% of them received NAs due to their favorable efficacy and safety as well as ease of administration. All major international guidelines recommend highly potent entecavir and tenofovir disoproxil fumarate as preferred therapy, since accumulating evidence indicates that long-term therapy with entecavir or tenofovir disoproxil fumarate can prevent or reverse liver fibrosis and...
reduce risk of HCC. However, in real-world practice, lots of patients had been treated with lamivudine, adefovir dipivoxil and tenbivudine, which are not preferred therapy, due to their low antiviral potency and low genetic barrier. This discrepancy between guideline recommendations and real-world clinical practice may be influenced by many factors, including doctors’ knowledge, reimbursement policy, and patients’ economic status and compliance.

Fortunately, this study showed the prescription of different NAs has changed in the past years, with entecavir prescription increased from less than one-third to more than half. This trend may reflect the following facts: 1) evidence from clinical trial and real-world studies convincingly demonstrates the efficacy and safety of antiviral therapy; 2) update of evidence-based national guidelines recommends entecavir and tenofovir disoproxil fumarate as first-line therapy; 3) evolving national and local reimbursement policy offers more potent antiviral therapy for people who are covered by basic social medical insurance. All these improved the standard of care in clinical practice for CHB treatment. Tenofovir disoproxil fumarate was used only in less than 10%, simply because it had not been proved for HBV until mid-2014 in mainland China.

We hope this large nationwide database could provide a point of view of clinical profiles of chronic HBV infection and the treatment landscape in mainland China. However, several limitations in our study need to be mentioned. First, since CR-HepB is a hospital-based registry system, the proportion of inactive HBsAg carriers may be underestimated, as these patients are usually asymptomatic and may not seek medical service. Second, the cross-sectional design made it difficult to identify factors associated with disease progression or regression. However, CR-HepB registrants are advised to received follow-ups every 3 to 6 months, so we could expect this limitation may be solved in the future. A final limitation is potential selection bias, as the majority of patients in the CR-HepB are from tertiary hospitals, therefore not necessarily reflecting the clinical practice in secondary or primary medical care settings where the resources and expertise are far less privileged.

Conclusions

In conclusion, this hospital-based cross-sectional study provides a snapshot of demographic and baseline profiles of Chinese patients with different stage of chronic HBV infection, as well as the landscape of clinical management.

Ethics Approval

The registry protocol was reviewed and approved by the ethics committee of Beijing Friendship Hospital, Capital Medical University (Approval Number: BJFH-EC/2014-044). Each participating institution also obtained approval from its institutional ethics committee.

Acknowledgments

We thank the China Foundation for Hepatitis Prevention and Control, Chinese Society of Hepatology, Chia Tai-Tianqing Pharmaceutical Group Co., Ltd and Shanghai Ashermen Healthcare Communications, Ltd, for their administrative coordination, technical assistance, and unrestricted grant to the CR-HepB and this paper.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Designed the study (JJ, HY, HZ, LW, JH, ZD), drafted the manuscript (SS), data management (YK). Served as the project leader and extensively and critically revised this manuscript (JJ). The other authors are the team members. All authors have read and approved the final version of the manuscript.

References

[1] Naghavi M, Wang H, Lozano R, Davis A, Liang X, Zhou M, et al. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;385:117–171. doi: 10.1016/S0140-6736(14)61662-2.
[2] World Health Organization. Global hepatitis report, 2017. Available from: https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565452-eng.pdf;jsessionid=7DA50E712691-FED0909855C3796A3A7?sequence=1.
[3] Schweitzer A, Horn J, Nikolajczyk RT, Krause G, Ott J. Estimations of world-wide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet 2015;386:1546–1555. doi: 10.1016/S0140-6736(15)61412-X.
[4] Ott J, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infections: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012;30:2212–2219. doi: 10.1016/j.vaccine.2011.12.116.
[5] Tian Q, Xia J. Hepatitis B virus genotypes: epidemiological and clinical relevance in Asia. Hepatol Int 2016;10:854–860. doi: 10.1016/s12072-016-9745-2.
[6] Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet 2016;388:1081–1088. doi: 10.1016/S0140-6736(16)30579-7.
[7] Liang X, Bi S, Yang W, Wang L, Cui G, Cui F, et al. Reprint of: Epidemiological survey of Hepatitis B in China: the serosurvey of Hepatitis B in China – 2013. Arch Virol 2013;158:221–230. doi: 10.1007/s01199-012-1995-2.
[8] Shan S, Wei W, Kong Y, Niu J, Shang J, Xie W, et al. Baseline and treatment for CR-HepB: Protocol and implementation of a nationwide hospital-based registry of hepatitis B. Scand J Public Health 2018:1403494818772188. doi: 10.1177/1403494818772188.
[9] Shan S, Wei W, Kong Y, Niu J, Shang J, Xie W, et al. Baseline and treatment for CR-HepB. Scand J Public Health 2018:1403494818772188. doi: 10.1177/1403494818772188.
[10] Hou J, Wang G, Wang F, Cheng J, Ren H, Zhuang H, et al. Guideline of prevention and treatment for chronic hepatitis B (2015 update). J Clin Transl Hepatol 2017;5:297–318. doi: 10.14218/JCTH.2016.00019.
[11] Scheuer PJ. Classification of chronic viral hepatitis: a need for reassessment. J Hepatol 1991;13:372–374. doi: 10.1016/0168-8278(91)90084-o.
[12] Jia J, Tang H, Ning Q, Xiong J, Hou J, Liu L, et al. Real-world evidence for nucleoside/nucleotide analogues in a 5-year multicentre study of antiviral-naive chronic hepatitis B patients in China. J Gastroenterol Hepatol 2017;32:752–760. doi: 10.1111/jgh.13886.
[13] Spradling PR, Xing J, Rupp LB, Moorman AC, Gordon SC, Teshale ET, et al. Distribution of disease phase, treatment prescription and severe liver disease among 1598 patients with chronic hepatitis B in the Chronic Hepatitis Cohort Study, 2006–2013. Aliment Pharmacol Ther 2016;44:1080–1089. doi: 10.1111/apt.13802.
[14] He T, Jia J. Chronic HBV: which pregnant women should be treated? Liver Int 2016;36 Suppl 1:105–108. doi: 10.1111/liv.13010.
[15] Cui F, Liang X, Gong X, Chen Y, Wang F, Zheng H, et al. Preventing hepatitis B though universal vaccination: reduction of inequalities through the GAVI China project. Vaccine 2013;31 Suppl 9:329–335. doi: 10.1016/j.vaccine.2012.07.048.
Shan S. et al: Baseline and treatment for CR-HepB

[16] Liu J, Zhang S, Wang Q, Shen H, Zhang M, Zhang Y, et al. Seroepidemiology of hepatitis B virus infection in 2 million men aged 21–49 years in rural China: a population-based, cross-sectional study. Lancet Infect Dis 2016;16:80–86. doi: 10.1016/S1473-3099(15)00218-2.

[17] Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018;67:1560–1599. doi: 10.1002/hep.29800.

[18] Lampertico P, Agarwal K, Berg T, Buti M, Janssen HLA, Papatheodoridis G, et al. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67:370–398. doi: 10.1016/j.jhep.2017.03.021.

[19] Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HL, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. Hepatol Int 2016;10:1–98. doi: 10.1007/s12072-015-9675-4.

[20] Varbobitis I, Papatheodoridis GV. The assessment of hepatocellular carcinoma risk in patients with chronic hepatitis B under antiviral therapy. Clin Mol Hepatol 2016;22:319–326. doi: 10.3350/cmh.2016.0045.

[21] Papatheodoridis GV, Chan HL, Hansen BE, Janssen HL, Lampertico P. Risk of hepatocellular carcinoma in chronic hepatitis B: assessment and modification with current antiviral therapy. J Hepatol 2015;62:966–967. doi: 10.1016/j.jhep.2015.01.002.

[22] Sun Y, Zhou J, Wang L, Wu X, Chen Y, Piao H, et al. New classification of liver biopsy assessment for fibrosis in chronic hepatitis B patients before and after treatment. Hepatology 2017;65:1438–1450. doi: 10.1002/hep.29009.

[23] Lim SG, Amarapurkar DN, Chan HL, Crawford DH, Gane EJ, Han KH, et al. Reimbursement policies in the Asia-Pacific for chronic hepatitis B. Hepatol Int 2015;9:43–51. doi: 10.1007/s12072-014-9593-x.

[24] Shan S, Cui F, Jia J. How to control highly endemic hepatitis B in Asia. Liver Int 2018;38 Suppl 1:122–125. doi: 10.1111/liv.13625.

[25] Wei L, Jia JD, Weng KH, Dou XG, Jiang JJ, Tang H, et al. Treating chronic hepatitis B virus: Chinese physicians’ awareness of the 2010 guidelines. World J Hepatol 2016;8:762–769. doi: 10.4254/wjh.v8.i18.762.

[26] Zeng N, Zou C, He Z, Ma H, Ou X, You H, et al. Systematic review on the reporting quality of randomized controlled trials in patients with hepatitis B or C in China. Int J Infect Dis 2018;67:58–64. doi: 10.1016/j.ijid.2017.11.011.