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Original Article

Trends in Mortality of Cirrhosis in China: An Analysis of the China Death Surveillance Database from 2008 to 2020

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Abstract

Background and Aims: China accounts for 14.9% of total cirrhosis deaths worldwide. A detailed and comprehensive understanding of the contemporary status of cirrhosis mortality in China is crucial for establishing strategies for intervention and decreasing the disease burden of cirrhosis worldwide. The study aimed to report the cirrhosis mortality rates in our whole country or province over time. ***Methods:*** Mortality data from 2008 to 2020 were retrieved from the Disease Surveillance Point System (DSPs) of the Chinese Center for Disease Control and Prevention. The crude mortality rate and age-standardized mortality rate of patients with cirrhosis were stratified by sex, residential location, and region. The average annual percentage change (AAPC) in cirrhosis mortality rates from 2008 to 2020 was also calculated. ***Results:*** The crude mortality rate of cirrhosis was 4.57/100,000 people in 2020. Compared with females and individuals living in urban areas, males and people living in rural areas had greater age-standardized mortality. The crude mortality rate and age-standardized mortality rate in provinces in Southwest China (Guangxi, Yunnan, Guizhou, and Qinghai) were greater than those in other provinces. Moreover, with increasing age, the age-specific mortality rate increased significantly. From 2008 to 2020, the mortality rate of cirrhosis in China decreased except for in males aged 50–59 years, females aged 45–49 years and females aged 80–84 years. ***Conclusions:*** The mortality rate of patients with cirrhosis in China decreased from 2008 to 2020. In the future, interventions of cirrhosis mortality control need to pay more attention to all males, females aged 45–49 and 80–84 years, and people living in rural areas and in provinces in Southwest China.

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Introduction

Cirrhosis is the terminal stage of various chronic liver diseases and seriously affects the quality of life and lifespan of patients.[1,2] Cirrhosis is the 13th leading cause of mortality worldwide.[3] According to the data from the Global Burden of Disease Study 2019 (GBD 2019), cirrhosis caused 560.4/100,000 age-standardized disability-adjusted life-years (DALYs).[4,5] Therefore, cirrhosis is still a public health problem that requires worldwide attention. China has an important role in the global burden of cirrhosis and other chronic liver diseases; there are approximately 6,833.3 thousand patients with cirrhosis in China, accounting for 14.9% of the total cases in the world.[6] Thus, the mortality of patients with cirrhosis in China has a greater effect on the global burden of cirrhosis and other chronic liver diseases. It was necessary for us to analyze the current mortality rate of patients with cirrhosis and its changing trends in recent decades in China to establish strategies for intervention and to decrease the mortality burden of patients with cirrhosis worldwide.

There are few reports about the death burden of cirrhosis in China. A previous study used GBD 2016 data to analyze the burden of cirrhosis and other chronic liver diseases and reported that age-standardized mortality has decreased in recent years.[7] Another study used part of data from the Chinese mortality surveillance system (2006–2017) to explore

Keywords: Cirrhosis; Mortality; Trend; China.

Abbreviations: AAPC, average annual percentage change; ASMRC, Age-standardized mortality rates of China; ASMRW, Age-standardized mortality rates of the world; CDC, Chinese Center for Disease Control and Prevention; CI, confidence interval; DAAs, direct-acting antiviral drugs; DALYs, disability-adjusted life-years; DSPs, Disease Surveillance Point System; GBD, Global Burden of Disease; HBV, hepatitis B virus; HCV, hepatitis C virus; ICD, International Classification of Diseases; NAFLD, nonalcoholic fatty liver disease; SDI, sociodemographic index; T2DM, type 2 diabetes mellitus.

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the trends of major liver diseases roughly, and their results were similar to those of previous studies.[8] To the best of our knowledge, no published studies have reported the cirrhosis mortality rates in our whole country or province over time according to the sociodemographic index (SDI) based on detailed national surveillance data from China. In this study, using data from the Disease Surveillance Points system (DSPs) of the Chinese Center for Disease Control and Prevention (CDC), we analyzed the mortality profile of cirrhosis in 2020 and the trend in mortality from 2008 to 2020 stratified by sex, residential location, region, province, and age group.

Methods

Data source

Data on people who died of cirrhosis between 2008 and 2020 were retrieved from the DSPs datasets. The Ministry of Health first introduced the DSPs in 1980 and adjusted its coverage and representativeness in the next few decades.[9] From 2004 to 2013, the number of surveillance points on the DSPs expanded from 161 to 605 (64 urban and 97 rural points in 31 provinces in mainland of China), covering 323.8 million individuals (approximately 24% of the entire Chinese population). The use of data from the DSPs is one of the main sources of detailed mortality data in China.[10–12] To guarantee data quality, provincial and national CDC staff members carry out routine supervision, feedback, and verification every year and every 3 years, they take out an underreported survey to adjust the mortality rate using the following formula: adjusted mortality rate = mortality rate / (1 − underreporting rate).[12,13] The representativeness and credibility of mortality data from the DSPs have been validated in previous studies.[9,14,15] All death data from the surveillance points were collected and reported through an online monitoring system. Causes of mortality were coded according to the International Classification of Diseases, 10th Revision (ICD-10). The ICD-10 codes for cirrhosis were K70.2-70.4 and K74-K74.6.

Demographic data, including age, sex, residential location (urban/rural areas) and region (Eastern, Central and Western China), were also collected from the DSPs. According to the National Statistics Bureau, China was divided into three main regions: Eastern China (Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong and Hainan), Central China (Heilongjiang, Jilin, Shanxi, Henan, Hubei, Anhui, Jiangxi and Hunan) and Western China (provinces other than the aforementioned). The study was approved by the Ethics Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention in the Chinese Center for Disease Control and Prevention (No. 202219-2) and conformed to the ethical guidelines of the Declaration of 2013 Helsinki.

Data analysis

The crude mortality rates and age-standardized mortality rates (mortality caused by cirrhosis/100,000 people, 1/100,000) were reported by sex, age (<40, 40–85, and >85 years), residential location (urban and rural areas), and region (Eastern China, Central China, and Western China). Age-standardized mortality rates were calculated using two age structures, the 2010 census population of China (ASMRC) and Segi's world population (ASMRW). We also analyzed the changing trend of cirrhosis mortality from 2008 to 2020 by sex, residential location, and region by estimating the AAPC of the ASMRC and its 95% confidence interval (CI). The statistical analysis was performed using Joinpoint Regression software, version 4.9.0.0 (National Cancer Institute, United States), and *p*-values <0.05 were considered significant.

Results

Mortality of patients with cirrhosis in 2020

In 2020, a total of 15,375 deaths from cirrhosis were reported in the DSPs (4.57/100,000 people). The crude mortality rates of cirrhosis for males and females were 6.65 and 2.68/100,000 people, respectively. Higher age-standardized mortality rates were observed in males than females (ASMRC: 5.60 vs. 1.88/100,000 people; ASMRW: 4.25 vs. 1.40/100,000 people). The crude mortality rates for people living in urban and rural areas were 4.63 and 4.49/100,000 people, respectively. After adjustment for age, the mortality rates in urban areas remained lower than those in rural areas (ASMRC: 3.53 vs. 3.72/100,000 people; ASMRW: 2.67 vs. 2.81/100,000 people). After stratification by region (Eastern China, Central China, and Western China), higher age-standardized mortality rates were still observed for males and people living in rural areas (Table 1).

The crude mortality rates and ASMRC for cirrhosis from 31 provinces in 2020 are shown in Figure 1. Provinces from Southwest China (Yunnan and Guizhou) had the highest crude mortality rates of cirrhosis (higher than 8.54/100,000 people) (Fig. 1A). After adjustment for age, the highest ASMRC for cirrhosis was still observed in provinces in Southwest China (Guangxi, Yunnan, Guizhou, Tibet and Qinghai) (6.69–10.93/100,000 people). In addition to the provinces mentioned above, Heilongjiang, Jilin and Inner Mongolia in Northeast China also had higher ASMRCs than other provinces (3.39–6.68/100,000 people). Geographically, the lowest ASMRC for cirrhosis was exhibited in provinces in Eastern China (1.37–2.05/100,000 people) (Fig. 1B). After stratification by sex, there were similar geographical distribution characteristics for the crude mortality rate and ASMRC for cirrhosis among males, females and the entire population (Supplementary Figs. 1, 2).

Age-specific mortality rate of cirrhosis in 2020 stratified by sex, residential location, and region

The age-specific mortality rates of patients with cirrhosis increased with increasing age, reaching a peak in those >85 years of age, while age-specific mortality rates among males were greater than those among females (Fig. 2). A similar trend was also observed after stratification by residential location and region (Supplementary Figs. 3, 4). After stratification by residential location, the age-specific mortality rates in urban people <80 years of age were similar to those in rural people, but people >80 years of age, people residing in urban areas had higher age-specific mortality than people residing in rural areas (Supplementary Table 1, Supplementary Fig. 3). When stratified by region, people living in Eastern China had similar age-specific mortality rates as people living in Central China, while people living in Western China had greater age-specific mortality rates than people living in Eastern China or Central China (Supplementary Table 1, Supplementary Fig. 4).

Trends in cirrhosis mortality in 2008–2020

In China, the overall ASMRC for cirrhosis patients decreased from 2008 to 2020 (AAPC: −4.8 (−7.3 to −2.3), $p<0.001$). After stratification by sex, residential location, and region, the decreasing trend was still observed (Fig. 3A, B). From 2008 to 2020, there were no differences in the AAPC of cirrhosis between males and females [AAPC: −5.3 (−6.1 to

Table 1. Mortality rates of cirrhosis by sex, region, and location in China in 2020

Region	location	Sex	Crude rate (1/10^5)	ASMRC (1/10^5)	ASMRW (1/10^5)
All	All	Both	4.57	3.63	2.75
		Male	6.65	5.60	4.25
		Female	2.68	1.88	1.40
	Urban	Both	4.49	3.53	2.67
		Male	6.21	5.18	3.95
		Female	2.89	2.01	1.49
	Rural	Both	4.63	3.72	2.81
		Male	6.97	5.93	4.49
		Female	2.51	1.79	1.34
Eastern China	All	Both	3.51	2.68	2.03
		Male	4.91	4.02	3.07
		Female	2.23	1.47	1.09
	Urban	Both	3.46	2.68	2.03
		Male	4.47	3.72	2.87
		Female	2.48	1.66	1.22
	Rural	Both	3.56	2.71	2.05
		Male	5.32	4.34	3.29
		Female	1.98	1.30	0.97
Central China	All	Both	3.72	2.94	2.22
		Male	5.42	4.51	3.43
		Female	2.34	1.65	1.22
	Urban	Both	4.44	3.42	2.61
		Male	6.38	5.19	3.99
		Female	2.77	1.91	1.42
	Rural	Both	3.37	2.70	2.02
		Male	4.95	4.19	3.16
		Female	2.11	1.52	1.12
Western China	All	Both	7.41	6.27	4.73
		Male	11.17	9.83	7.44
		Female	3.80	2.92	2.19
	Urban	Both	6.61	5.35	4.02
		Male	9.63	8.15	6.14
		Female	3.79	2.80	2.09
	Rural	Both	8.01	6.98	5.29
		Male	12.28	11.11	8.43
		Female	3.81	3.01	2.27

ASMRC, age-standardized mortality rate adjusted by the Chinese standard population; ASMRW, age-standardized mortality rate adjusted by the world standard population.

−4.5) vs. −5.3 (−9.1 to −1.4)] or between urban and rural areas [−5.1 (−5.9 to −4.4) vs. −4.9 (−7.6 to −2.1)] (Fig. 3A, Supplementary Tables 2 and 3). However, in rural areas, the highest AAPC in the cirrhosis ASMRC was in 2013–2016 [−12.5 (−23.4 to −0.1), p=0.049)] (Supplementary Table 3). After stratification by region, there were also no differences in the AAPC of the cirrhosis ASMRC among Eastern, Central and Western China (Fig. 3B, Supplementary Table 4). Moreover, in Western China, the highest AAPC in the cirrhosis ASMRC was also detected in 2013–2016 [−11.6 (−21.7 to −0.3), p=0.047] (Supplementary Table 4).

AAPC in the age-specific mortality rate of patients with cirrhosis in 2008–2020

Between 2008 and 2020, the age-specific mortality rates of cirrhosis decreased in males and females (AAPC<0), ex-

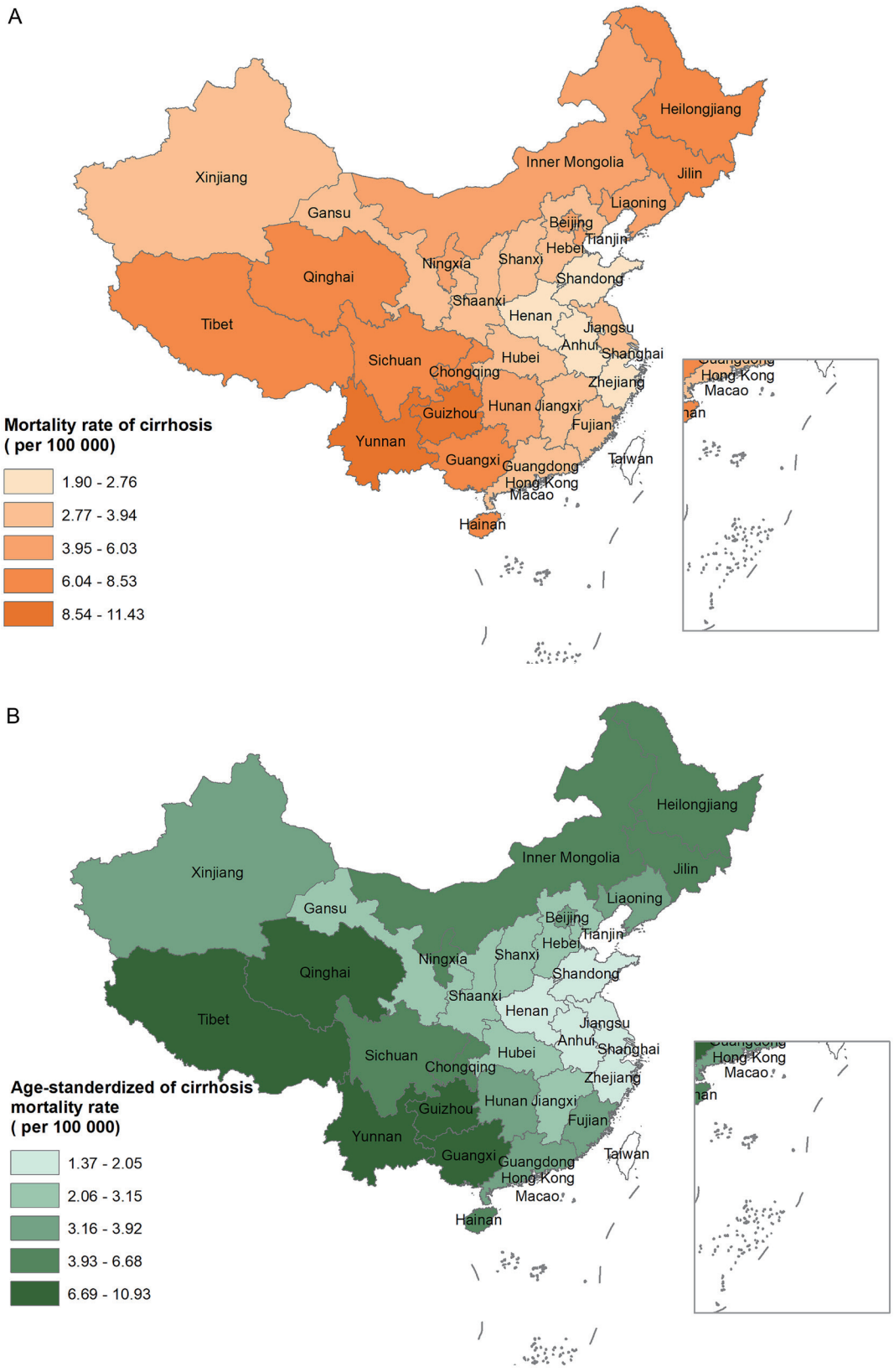

Fig. 1. Crude mortality rates and age-standardized mortality rate in China (ASMRC) for both sexes in 2020, by province. (A) Crude rate of cirrhosis for both sexes. (B) ASMRC of cirrhosis for both sexes.

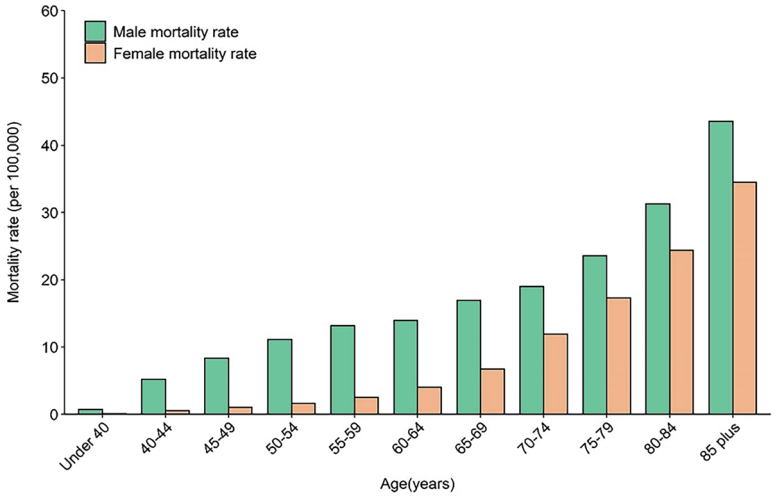

Fig. 2. Mortality rates of cirrhosis by age group and sex in 2020.

cept for males 50–59 and females 45–49 and 80–84 years of age (Fig. 4). The AAPC in the age-specific mortality rates of patients with cirrhosis in the younger 40 years group was greater than that in the older 60 years group. After stratification by residential location, in urban areas, the AAPC in age-specific mortality of cirrhosis in females 55–64 years was greater than that in males, but this characteristic reversed in people aged 80–84 years (Fig. 4).

After stratification by region, in Eastern China, the age-specific mortality rate of cirrhosis decreased across every age group (all AAPCs<0). In Central China, the age-specific mortality rate of cirrhosis did not decrease in males 50–59 or females 55–59 years and 80–84 years of age. However, in Western China, only males (40–44, 50–59, and 75–79 years of age) did not have a decrease in the age-specific mortality rate of cirrhosis.

Trends in the ASMRC for cirrhosis with SDI

From 2008 to 2020, the ASMRC for cirrhosis decreased with increasing SDI (Fig. 5). After stratification by province, the ASMRC for cirrhosis decreased or stabilized with increasing SDI in most provinces. During our study period, the ASMRCs of cirrhosis in Guangxi, Heilongjiang, Chongqing, and Inner Mongolia Provinces were greater than the expected death rate according to the SDI. However, the ASMRC of cirrhosis in high-income provinces (Jiangsu and Shandong) was lower than the expected death rate according to the SDI (Fig. 5). The greatest decrease in the cirrhosis ASMRC from 2008 to 2020 occurred in Sichuan Province, a province in Southwest China (Fig. 5).

Discussion

In this study, we analyzed the mortality of cirrhosis in 2020 and the change in mortality profile from 2008 to 2020 in China. Overall, in 2020, after adjusting for age, males and people living in rural areas and provinces in Southwest China had higher mortality rates than females and people living in urban areas and provinces in other regions. The age-specific mortality rates of cirrhosis increased with increasing age. In 2008–2020, the cirrhosis mortality rate had a downward trend over 13 consecutive years, and the decrease in age-specific mortality rates was greater in young people and individuals in Eastern China. In addition, the estimated ASMRC in cirrhosis decreased with increasing SDI. Cirrhosis, the end stage of chronic liver disease, is an important public health problem.[16] Our results may lead to the targeting of priority interventions in specific populations in China to decrease cirrhosis mortality.

In this study, we found that the mortality of cirrhosis showed a downward trend, which was first attributed to the prevention and control of chronic viral hepatitis. In Asia, more than half of all cirrhosis cases are caused by chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection.[17] Currently, HBV-related cirrhosis is still the main cause of liver cirrhosis death in China.[16,18] China began to introduce the three-dose HBV vaccine in newborns in 1992. A catch-up plan was implemented for HBV vaccination in children and adolescents in 2009 throughout the country, which significantly reduced the prevalence of HBsAg and mortality from HBV-associated liver diseases, including cirrhosis.[19–21] China has also made great contributions to chronic hepatitis B treatment. For instance, pegylated interferon, entecavir, tenofovir, and other first-line antiviral drugs have been recommended in the national guidelines.[22] Chronic HCV infection is another major cause of cirrhosis.[23] Hepatitis C treatment in China has entered the era of direct-acting antiviral drugs (DAAs), and an increasing number of DAAs are now included in China's medical insurance coverage. DAAs treatment is relatively safe and effective. Its application can significantly reduce the prevalence of HCV,[24,25] and has significantly reduced the mortality burden of hepatitis C cirrhosis. All these efforts are considered to support the decreasing mortality rate of patients with cirrhosis associated with chronic viral hepatitis.

Our results show that the ASMRC for cirrhosis in males was approximately four-fold greater than that in females in 2020, and there was a lower AAPC in cirrhosis ASMRC in males in 2008–2020 (people 55–59 of age and 55–64 years of age in urban areas). The greater number of deaths from cirrhosis in males might be related to the following factors. First, males were more susceptible to HBV and HCV infection than females. For instance, males had a higher HBsAg positive rate than females, and males with chronic hepatitis B and hepatitis C were more likely to progress to liver fibrosis than females[26–29] Second, males consumed ~33-fold more alcohol than females, and the burden of alcoholic liver disease in males was heavy.[30] Finally, the incidence of non-

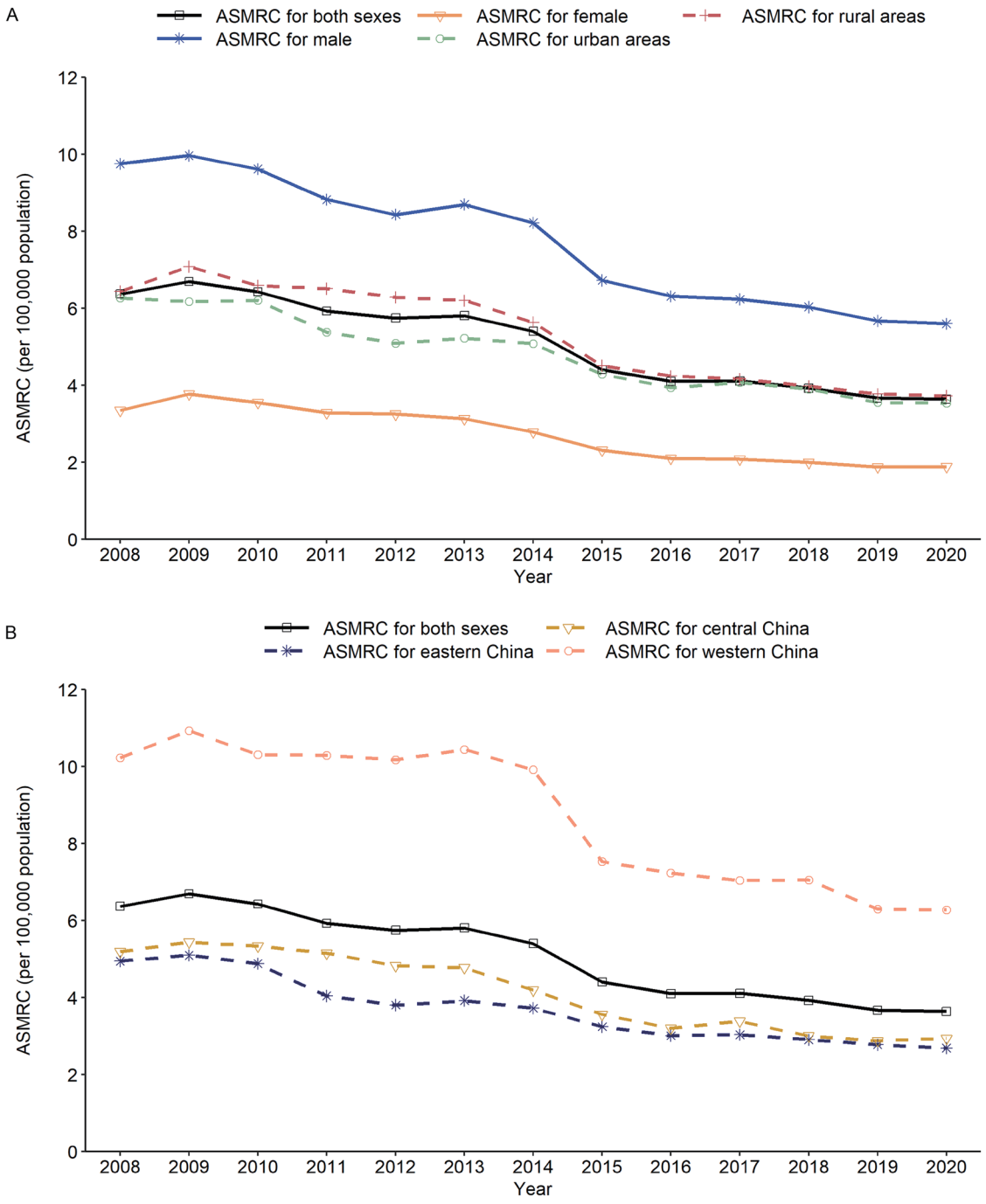

Fig. 3. Trends in the age-standardized mortality rate in China (ASMRC) of cirrhosis by sex, location, and region in 2008–2020. (A) Trends in ASMRC of cirrhosis by gender and residence. (B) Trends in ASMRC of cirrhosis by region. ASMR, age-standardized mortality rate in China.

alcoholic fatty liver disease (NAFLD) is gradually increasing, and the prevalence of NAFLD in males is significantly greater than that in females, which can also lead to the occurrence of end-stage liver disease, including cirrhosis.[31–34]

We found that older people had a greater cirrhosis mortality rate than younger people, and the AAPC in the cirrhosis ASMRC in people >60 years of age was lower than that in people <40 years of age. First, older individuals might be more likely to have HBV-associated cirrhosis because the HBV vaccination system was incomplete when they were young.[35] Second, as the end stage of chronic liver disease, cirrhosis is often ignored before complications occur, the asymptomatic and compensatory period of liver cirrhosis is very long, with a median of ~12 years, and older individuals are more likely to enter the decompensation period according to their natural history of cirrhosis.[1,36] Moreover, the physical function of older people was poor and patients with decompensated cirrhosis often had more serious complications.

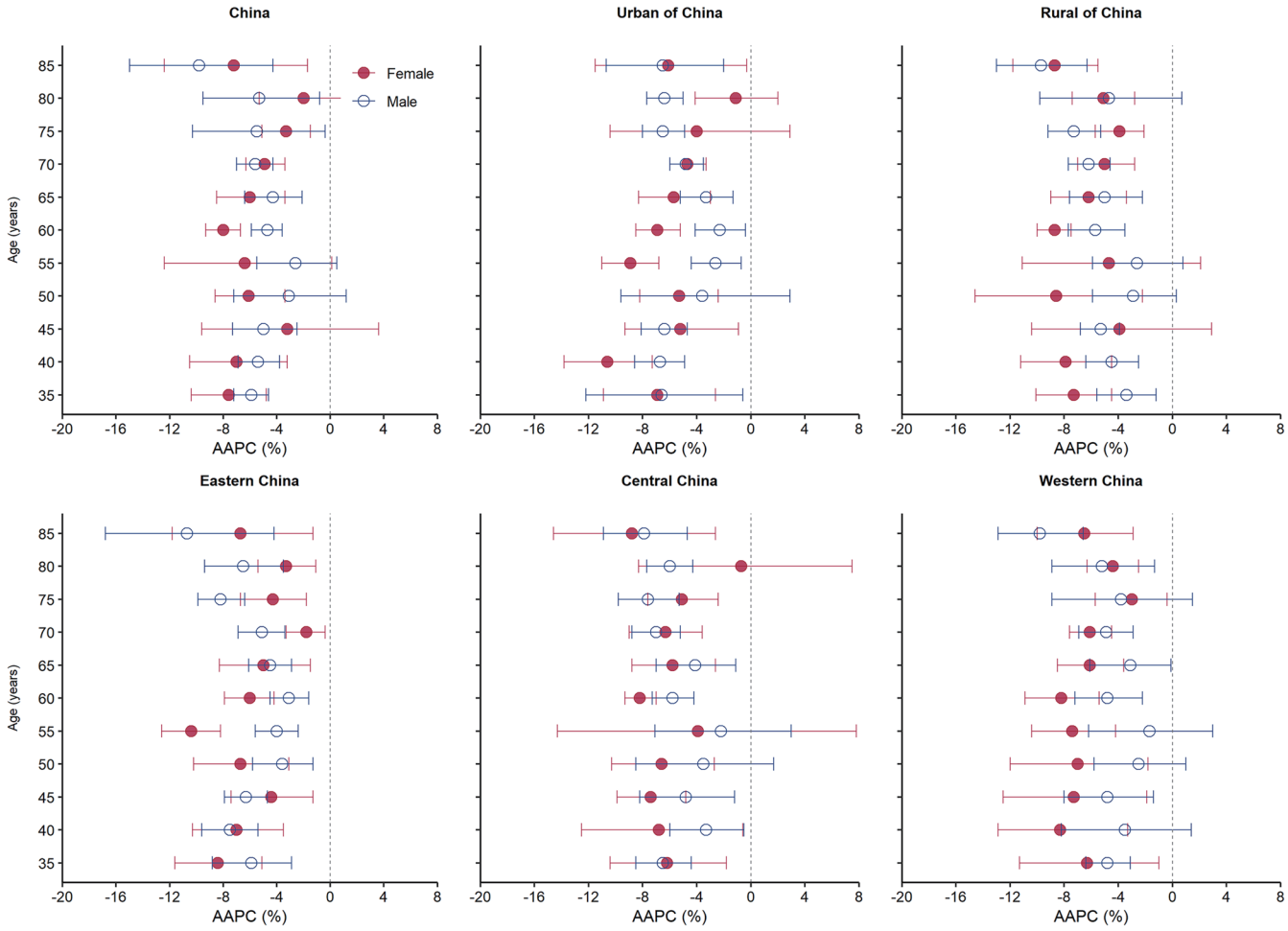

Fig. 4. Average annual percentage change (AAPC) of cirrhosis by sex, region, and location in 2020 in China. AAPC, average annual percentage change.

People residing in rural areas had a higher mortality rate than those residing in urban areas. The following reasons might explain the differences between urban and rural areas. (1) Individuals from rural areas have higher rates of chronic HBV infection.[37] (2) Despite the coverage of the New Rural Cooperative Medical Scheme, there are inadequate medical resources in rural areas; for example, antiviral therapy for viral hepatitis and end-stage liver disease including cirrhosis.[38] However, people ≥80 years of age and people who lived in urban areas had higher age-specific cirrhosis mortality rates than people who lived in rural areas, which might be attributed to the presence of other diseases combined with cirrhosis, for example, type 2 diabetes mellitus (T2DM). T2DM is an endocrine disease with a high incidence in middle-aged and older people. The incidence of T2DM in people living in urban areas is higher than that in people living in rural areas. Data from China and Singapore indicate that T2DM was associated with the incidence and mortality of cirrhosis.[39,40]

In our study, we found that the mortality of cirrhosis in provinces in Southwest China, especially in rural areas, was significantly higher than that in the other two regions. On one hand, the incidence of viral hepatitis in the provinces of Western China was very high, especially for chronic hepatitis B and hepatitis C.[35,41] One study from China also reported that provinces in Western China (Qinghai, Guizhou, Yunnan, and Guangxi) and Taiwan had the highest age-standardized DALY rates of HBV-associated cirrhosis and other chronic liver diseases in 1990–2016.[42] On the other hand, medical conditions in Western China were worse than those in Eastern and Central China, and there was an uneven distribution of medical staff, especially in rural areas of Western China.[43] From 2013 to 2016, the AAPC in the cirrhosis ASMRC was highest in Western China, which might be attributed to improvements in economic status and antiviral treatment after 2013. The mortality rate of cirrhosis in 2008–2020 decreased with increasing SDI, which is consistent with a previous study in which the SDI was negatively correlated with age-standardized mortality.[7] As far as we know, with the increase in SDI, sanitary, and medical conditions (for instance, antiviral treatment) and people's awareness of seeking medical treatment improved, may have contributed to the decreasing trend of cirrhosis with SDI.

There were several limitations of our study. First, because of the unavailability of etiological data from the DSPs, the mortality data for patients with cirrhosis due to specific etiologies were not analyzed. This might be the main limitation of this study. In the future, we will actively promote the integrity of this database and look forward to obtaining etiological analysis results. Second, our study did not analyze mortality from other coexisting causes (e.g., hypertension or T2DM, which may also be attributed to incomplete data. Despite these limitations, our study facilitates the identification

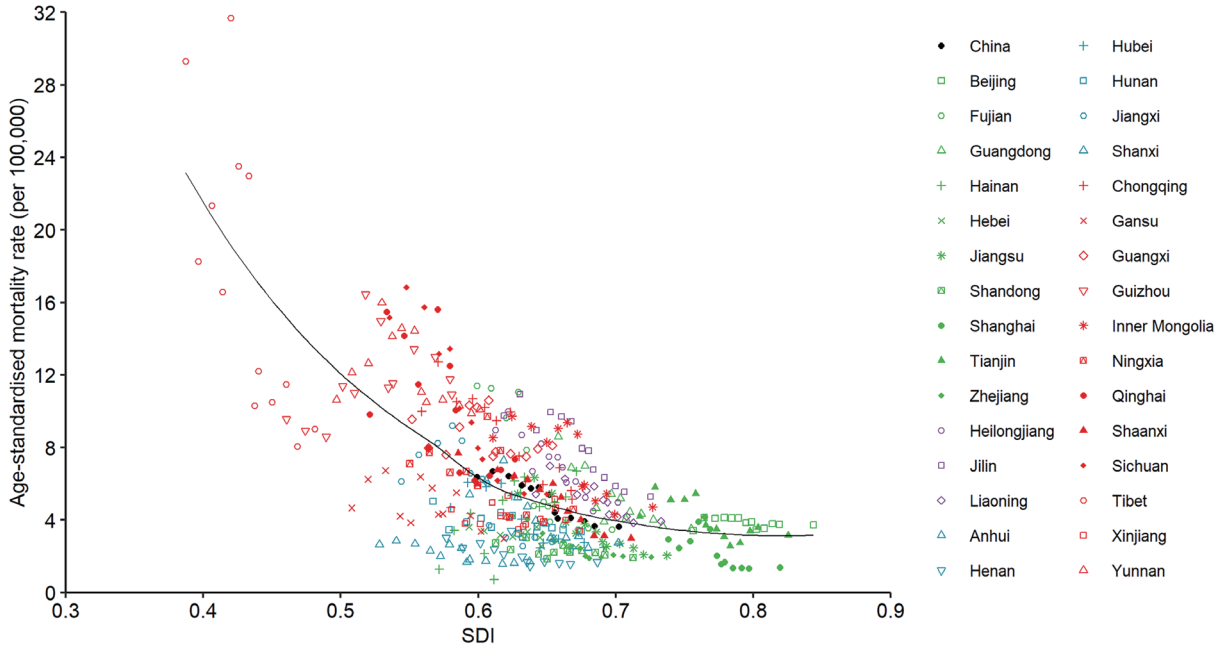

Fig. 5. Age-standardized mortality rates/100 000 for cirrhosis by SDI in China, 2008–2020. SDI, sociodemographic index.

of high-risk populations and provides guiding assistance for the formulation of preventive strategies in China.

Conclusions

We analyzed mortality data of cirrhosis between 2008 and 2020 in China using data extracted from the CDC-DSPs. In those consecutive 13 years, the mortality of cirrhosis decreased in China, except for males 50–59 and females 45–49 and 80–84 years of age. A greater cirrhosis mortality burden was observed in males, older individuals, and people living in rural areas and provinces in Southwest China. In the future, healthcare providers should pay more attention to those people during the intervention and control of cirrhosis mortality.

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Conflict of interest

LW has been an Executive Associate Editor of *Journal of Clinical and Translational Hepatology* since 2013. HR has been an Editorial Board Member of *Journal of Clinical and Translational Hepatology* since 2023. The other authors have no conflicts of interest related to this publication.

Author contributions

Study concept and design (XW, HL, MZ, HR), acquisition of data (JQ, LW, PY), analysis and interpretation of data (FL, LW), drafting of the manuscript (XW, HL, YW, MZ), critical revision of the manuscript for important intellectual content (XW, HL, MZ, HR). All authors have made significant contributions to this study and have approved the final manuscript.

Ethical statement

This study was approved by the Ethics Committee of National Center for Chronic and Noncommunicable Disease Control and Prevention in Chinese Center for Disease Control and Prevention (No. 202219-2). The study protocol also conformed to the ethical guidelines of the Declaration of Helsinki revised in 2013. The individual consent for this retrospective analysis was waived.

Data sharing statement

No additional data are available.

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