



# OPEN Epidemiological characteristics and treatment challenges of chronic hepatitis C in the kashi region of xinjiang china: A retrospective investigation from 2018 to 2022

Mingna Li<sup>1,3</sup>, Kuerbannisa Wulayin<sup>2,3</sup>, Shasha Ma<sup>1</sup>, Lian Zhou<sup>1</sup>, Shutao Lin<sup>1</sup>, Chao Wu<sup>2</sup>✉ & Lubiao Chen<sup>1</sup>✉

Due to the emergence of direct-acting antiviral (DAA), more attention has been devoted to the prevalence and antiviral treatment of chronic hepatitis C in the Kashi region of Xinjiang, China, over the past decade. This study aimed to investigate the epidemiology, genotype (GT) distribution, diagnosis, and antiviral treatment of chronic hepatitis C virus (HCV) infection in this region from 2018 to 2022 and to highlight the challenges in achieving effective management. This retrospective study included individuals with HCV antibody (HCV-Ab) positivity at the First People's Hospital of Kashi from January 1, 2018, to August 31, 2022. Clinical data, including HCV RNA data, GT distribution, and DAA treatment history, were collected. Patients were followed up via telephone to assess treatment adherence and reasons for refusal. The HCV-Ab positivity rate increased from 1.7% in 2018 to 2.9% in 2022. Among the 4,928 HCV-Ab-positive individuals, 2174 (44%) underwent HCV RNA testing, with 1,088 (22%) confirmed positive. Of these patients, 707 were genotyped, with GT1b (70.7%) being the most prevalent GT. Due to limited access to DAA, only 327 (30%) RNA-positive patients received antiviral treatment, 243 (74%) of whom completed the course. Barriers to receiving DAA included high costs, low disease awareness, and limited healthcare access. These findings underscore the severity of the chronic HCV epidemic in Kashi, where healthcare access is inadequate, including limited HCV RNA testing and DAA treatment coverage. Tailored public health interventions and improvements in healthcare infrastructure are essential for better managing chronic HCV infection in this high-burden region.

**Keywords** Hepatitis C virus, Epidemiology, Direct-acting antiviral, Genotype, Kashi

Persistent hepatitis C virus (HCV) infection is a major cause of chronic liver disease, and this virus significantly contributes to the global burden of liver-related conditions<sup>1–4</sup>. In 2020, it was estimated that 56.8 million people worldwide were infected with HCV, resulting in 257,000 HCV-related deaths<sup>5</sup>. China bears a high burden of chronic HCV infection, with approximately 9.487 million people infected in 2020, yet only a small proportion of patients received treatment with direct-acting antivirals (DAAs)<sup>5,6</sup>. In 2019, the incidence rate of hepatitis C was approximately 16 per 100,000 population nationwide, around 36 per 100,000 population in Xinjiang, and approximately 61 per 100,000 population in the Kashi region<sup>7</sup>. From 2005 to 2019, the overall incidence rate of hepatitis C in the general population of the Kashi region exhibited an upward trend, with an average annual increase of 11.5%<sup>7</sup>.

HCV is characterized by high genetic diversity, with eight genotypes (GTs) and over 100 subtypes identified to date<sup>8</sup>. In Asia, particularly in Central Asia, East Asia, Southeast Asia, and the Asia-Pacific region, GT1 (especially subtype 1b) is the most common GT<sup>1</sup>. A nationwide survey conducted in China revealed that the

<sup>1</sup>Department of Infectious Diseases, The Third Affiliated Hospital of Sun Yat-Sen University, 600 Tianhe Road, Tianhe District, Guangzhou 510630, Guangdong, China. <sup>2</sup>Department of Infectious Diseases, The First People's Hospital of Kashi, 120 Yingbin Avenue, Kashi 844000, Xinjiang, China. <sup>3</sup>Mingna Li and Kuerbannisa Wulayin contributed equally. ✉email: 3216233205@qq.com; chenlub@mail.sysu.edu.cn

most prevalent subtype was 1b (63.4%), followed by 2a (17.3%)<sup>9</sup>. The distribution of HCV GTs in Xinjiang is similarly diverse, with GT1b being the most predominant GT, followed by GT2a, GT3a, GT3b, and GT6a<sup>10</sup>. The epidemiological situation of hepatitis C in the Kashi region is alarming, with DAA treatment outcomes being suboptimal. Additionally, there is a lack of relevant literature on this topic. This study retrospectively analysed the epidemiology, diagnosis, and treatment of HCV among a hospital-based cohort from 2018 to 2022 and aimed to enhance the prevention and treatment of HCV infection in China. The ultimate goal is to achieve the ambitious target set by the World Health Organization (WHO) of eliminating viral hepatitis as a public health threat by 2030.

Methods
Study design and study patients

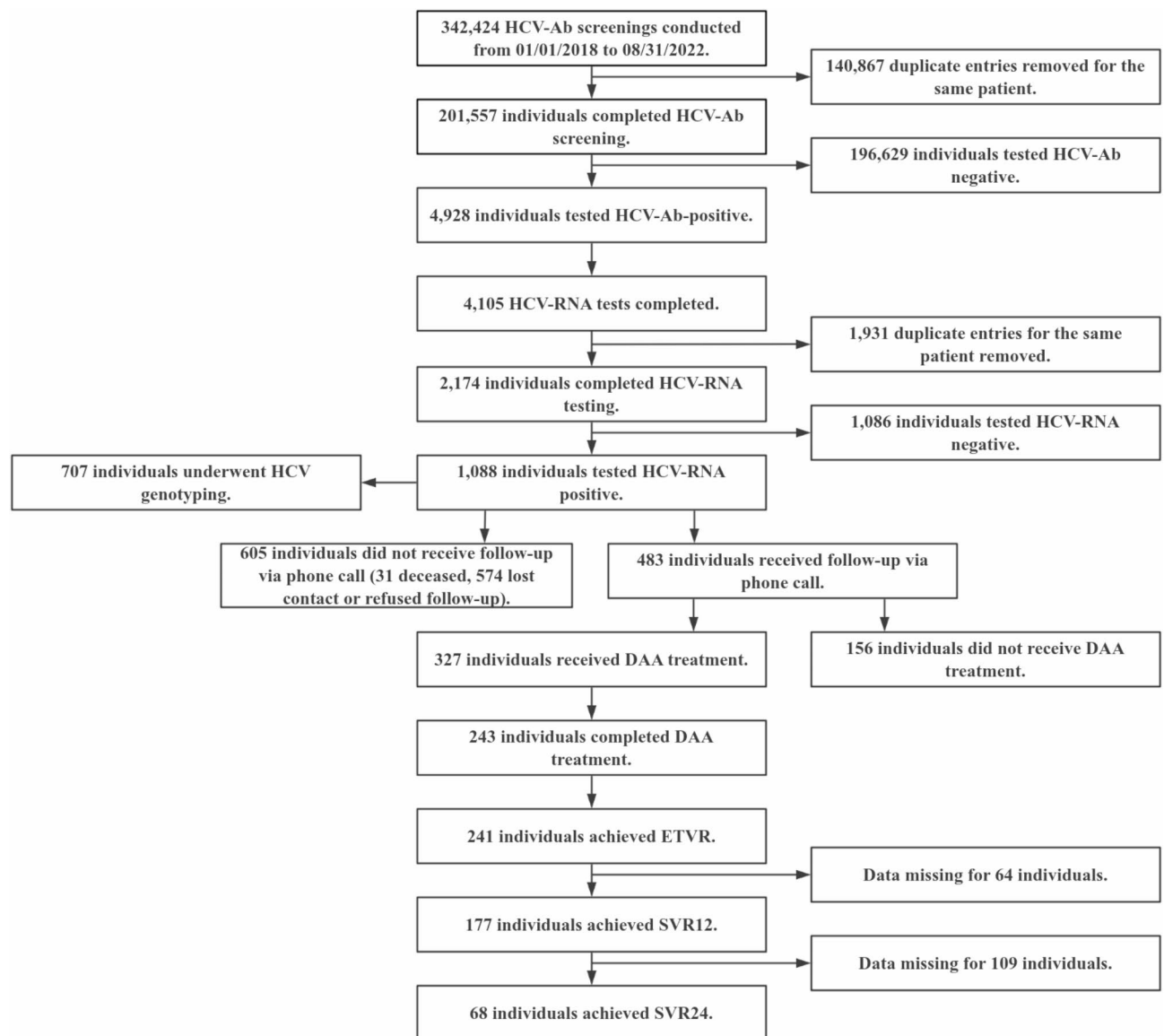
During the investigation period, with the exception of the First People's Hospital of Kashi, the major hospitals in the Kashi region, which includes one city and eleven counties, lacked the capacity for hepatitis C diagnosis, genotyping, and liver fibrosis testing and were limited to HCV antibody (HCV-Ab) screening. In 2018, the First People's Hospital of Kashi began to administer Elbasvir/Grazoprevir (EBR/GZR), thereby becoming the only medical institution in this region equipped with DAA. In 2021, the hospital began to administer Ledipasvir/Sofosbuvir (LDV/SOF) and SOF/Velpatasvir (VEL). During this study period, patients with chronic hepatitis C in this region were primarily treated at the infection department of the First People's Hospital of Kashi (Table 1). This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the First People's Hospital of Kashi. This study was a retrospective analysis involving subjects who tested positive for HCV-Ab at the First People's Hospital of Kashi from January 1, 2018, to August 31, 2022. The exclusion criteria were as follows: HCV-Ab negative, HCV-Ab-positive but HCV RNA negative, and duplicate data for the same patient who completed HCV RNA testing. Additionally, patients who did not participate in the follow-up phone survey or had inaccessible or significantly incomplete medical records were also excluded. The flowchart is shown in Fig. 1.

Study assessment

Patient visit dates, HCV-Ab screening results, and HCV RNA test results were extracted from the hospital's electronic medical records and laboratory information systems by the hospital's information technology department. This process was conducted under strict confidentiality protocols and in compliance with institutional guidelines to ensure patient privacy. Data completeness and accuracy were ensured through cross-referencing between electronic medical records and the laboratory information system. Any discrepancies identified during this process were resolved through manual verification by the research team. Data related to DAA treatment and reasons for treatment refusal were collected through follow-up phone calls using a structured questionnaire. To address communication barriers due to local ethnic languages, two trained local clinicians conducted the phone interviews after undergoing pre-interview training to ensure a standardized data collection process. Reasons for refusing DAA treatment were categorized based on pre-defined themes and analyzed quantitatively to identify trends and barriers. To enhance data quality, validation was performed by comparing collected data with electronic medical records. Priority was given to medical record entries to resolve any inconsistencies, ensuring the reliability of the dataset. For missing or incomplete data, a systematic review and processing approach was employed. Cases with critical data points (e.g., treatment status, treatment outcomes) that were severely missing and could not be

Medical institution	Local availability of diagnostic items				Local availability of DAA		
	HCV-Ab screening	HCV-RNA testing	HCV genotyping	Liver stiffness measurement	EBR/GZR	LDV/SOF	SOF/VEL
First People's Hospital of Kashi	√	√	√	√	√	√	√
Kashi City <sup>a</sup>	√	×	×	×	×	×	×
Shufu County	√	×	×	×	×	×	×
Shule County	√	×	×	×	×	×	×
Yingjisha County	√	×	×	×	×	×	×
Zepu County	√	×	×	×	×	×	×
Shache County	√	×	×	×	×	×	×
Yecheng County	√	×	×	×	×	×	×
Maigaiti County	√	×	×	×	×	×	×
Yuepuhu County	√	×	×	×	×	×	×
Jiashi County	√	×	×	×	×	×	×
Bachu County	√	×	×	×	×	×	×
Taxkorgan County <sup>b</sup>	√	×	×	×	×	×	×

Table 1. The implementation status of hepatitis C diagnosis and treatment programs in the major medical institutions of the Kashi region from 2018 to 2022. <sup>a</sup>Kashi City refers to the main medical institutions in the city, excluding the First People's Hospital of Kashi. <sup>b</sup>Taxkorgan County refers to Taxkorgan Tajik Autonomous County. Ab, Antibody; DAA, Direct-acting antiviral; EBR, Elbasvir; GZR, Grazoprevir; HCV, Hepatitis C virus; LDV, Ledipasvir; SOF, Sofosbuvir; VEL, Velpatasvir.



**Fig. 1.** Investigation flowchart Ab, Antibody; DAA, Direct-acting antiviral; ETVR, End-of-treatment virological response; HCV, Hepatitis C virus; SVR, Sustained virological response.

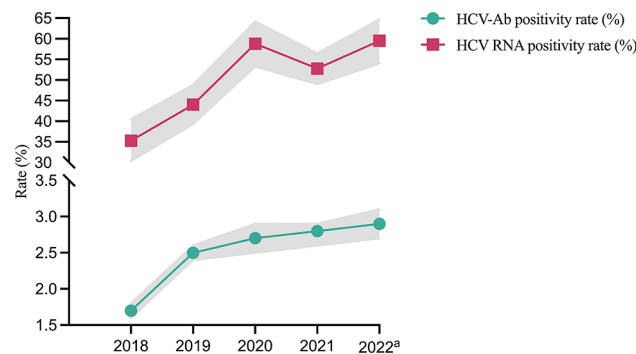
retrieved through follow-up phone calls or verification of medical records were excluded from the relevant analyses to avoid introducing bias. For cases with missing follow-up data where clear trends or reference points were available, the backward fill method was applied. This approach involved supplementing the missing data points using information from subsequent medical records, such as treatment status or laboratory test results. This method was adopted in this study based on the specific circumstances to maximize the balance between data accuracy and the reliability of the results. We conducted a thorough examination of the available data to ensure that the imputed values were consistent with the general trends observed in the cohort. We also carefully considered the nature of the missing data, and filled in gaps based on the assumption that later follow-up data could reasonably reflect earlier trends.

To better understand the diagnosis and treatment of hepatitis C, this study employed two methods to assess progress during the course of care. First, the proportion of patients at each step relative to those with HCV-Ab positivity was calculated. Second, the proportion of patients who moved to the next step of the treatment process was determined.

The primary outcome measures of the investigation were HCV-Ab positivity, HCV RNA positivity, and the achievement of a sustained virological response (SVR). HCV-Ab titres above 1.0 S/co, as measured by an enzyme-linked immunosorbent assay (Abbott, Shanghai, China), were considered positive. The detection limit for the HCV RNA viral load, determined via real-time fluorescent quantitative PCR (Sansure Biotech Inc., Hunan, China), was 100 IU/mL, with levels at or above this threshold considered positive. A more sensitive PCR assay was not available at this hospital during the investigation period. SVR12 and SVR24 were defined as undetectable HCV RNA in serum or plasma at 12 and 24 weeks after completing antiviral therapy, respectively.

Year	HCV-Ab screening, <i>n</i>	HCV-Ab-positive cases, <i>n</i>	HCV-Ab positivity rate, % (95% CI)	HCV RNA testing, <i>n</i>	HCV RNA-positive cases, <i>n</i>	HCV RNA positivity rate, % (95% CI)
2018	51,714	873	1.7 (1.6–1.8)	365	129	35.3 (30.4–40.5)
2019	44,895	1122	2.5 (2.4–2.6)	436	192	44.0 (39.3–48.8)
2020	31,918	865	2.7 (2.5–2.9)	330	194	58.8 (53.3–64.2)
2021	42,323	1170	2.8 (2.6–2.9)	705	372	52.8 (49.0–56.5)
2022 <sup>a</sup>	30,707	898	2.9 (2.7–3.1)	338	201	59.5 (54.0–64.7)
Total	201,557	4928	2.4 (2.4–2.5)	2174	1088	50.0 (47.9–52.2)

**Table 2.** Trends in HCV-Ab and HCV RNA positivity rates from 2018 to 2022. <sup>a</sup>Data for 2022 include only the period from January 1 to August 31. Ab, Antibody; CI, Confidence interval; HCV, Hepatitis C virus.



**Fig. 2.** Trends in HCV-Ab and HCV RNA positivity rates with 95% CIs (2018–2022) <sup>a</sup>Data for 2022 include only the period from January 1 to August 31. Ab, Antibody; CI, Confidence interval; HCV, Hepatitis C virus.

Patients who did not return for follow-up testing were classified as not having achieved SVR. HCV genotyping was performed on serum samples from HCV RNA-positive individuals using the PCR fluorescent probe method (Sansure Biotech Inc., Hunan, China). Due to sensitivity limitations of the genotyping assay, only individuals with an HCV RNA viral load greater than 1000 IU/mL were eligible for genotyping. These procedures were conducted in accordance with the standard diagnostic protocols of the clinical laboratory at the First People's Hospital of Kashi.

### Statistical analysis

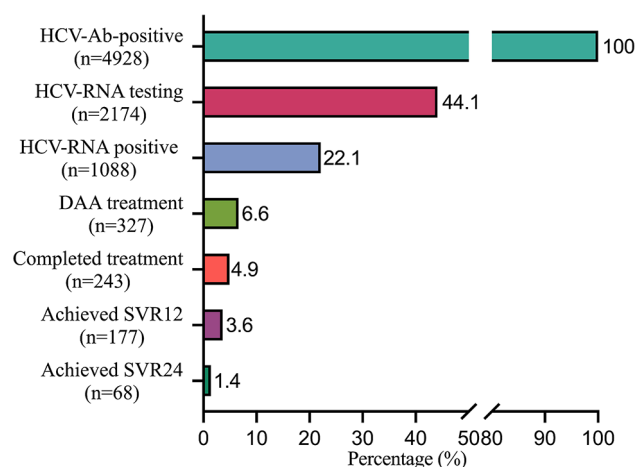
Categorical data are presented as counts and percentages, and 95% confidence intervals (95% CIs) for positivity rates were calculated via the Clopper–Pearson exact method. The data obtained from the structured questionnaire were categorized and quantitatively analyzed by summarizing them into groups and presenting the results in terms of frequencies and percentages. To assess trends over time, a Chi-square test for trend was conducted to evaluate whether there were significant increases or decreases in key variables such as HCV-Ab positivity rates and HCV RNA positivity rates across the study period. A two-tailed *p* value < 0.05 was considered statistically significant. Statistical analysis was conducted via SPSS 29.0 (IBM Corp., Armonk, NY, USA), and bar charts, line graphs, and pie chart were created via GraphPad Prism 10.1.0 (GraphPad Software, San Diego, CA, USA).

## Results

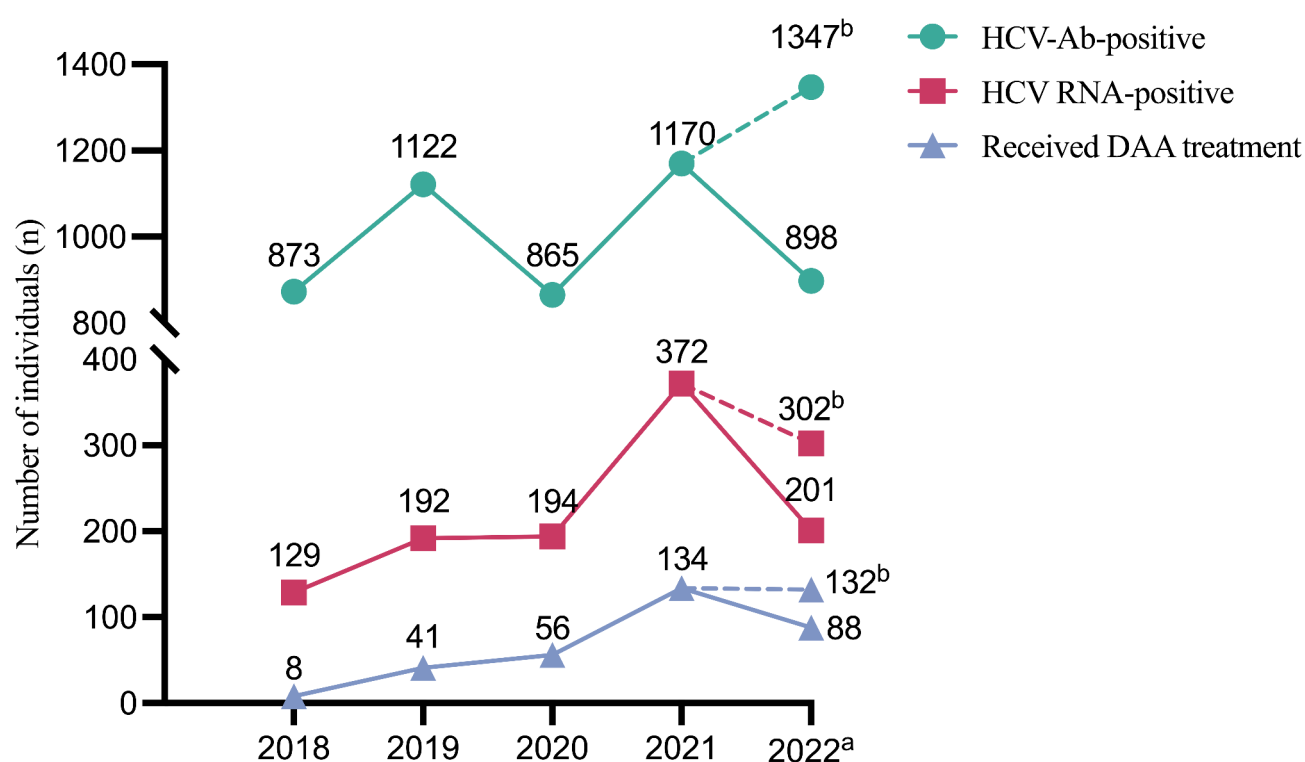
### Raw epidemiological data on HCV-Ab positivity

The patients included in this study were from all 12 counties and cities within the Kashi region, representing both urban and rural populations, as well as diverse ethnic groups, including Han Chinese and various ethnic minorities. However, due to the inability to obtain complete demographic data for all patients, a systematic analysis could not be performed.

The HCV-Ab and HCV RNA positivity rates from 2018 to 2022 are shown in Table 2; Fig. 2. As indicated in the table, the overall HCV-Ab positivity rate was 2.4% (95% CI: 2.4–2.5%), and the overall HCV RNA positivity rate was 50.0% (95% CI: 47.9–52.2%). Over the period from 2018 to 2022, both the HCV-Ab and HCV RNA positivity rates in the Kashi region showed an increasing trend. A Chi-square test for trend was conducted to evaluate this change over time. The HCV-Ab positivity rate demonstrated a significant linear increase (Pearson Chi-square = 181.854, *df* = 4, *p* < 0.001; linear association = 145.397, *df* = 1, *p* < 0.001). Similarly, the HCV RNA positivity rate also showed a significant increasing trend, with a Pearson Chi-square of 62.037 (*df* = 4, *p* < 0.001) and a linear association value of 47.621 (*df* = 1, *p* < 0.001), further emphasizing the significant rise in HCV positivity over the study period.



**Fig. 3.** DAA treatment cascade percentages among 4,928 HCV-Ab-positive individuals Ab, Antibody; DAA, Direct-acting antiviral; HCV, Hepatitis C virus; SVR, Sustained virological response.



**Fig. 4.** Comparison of confirmed hepatitis C cases and DAA treatment numbers from 2018 to 2022 <sup>a</sup>Data for 2022 include only the period from January 1 to August 31. <sup>b</sup>Estimated full-year data for 2022. Ab, Antibody; DAA, Direct-acting antiviral; HCV, Hepatitis C virus.

### Gaps between the diagnosis and treatment of hepatitis C

Among the 4,928 HCV-Ab-positive individuals, 44% (2,174/4,928) underwent confirmatory HCV RNA testing, with 50% (1,088/2,174) testing positive. However, only 30% (327/1,088) of the HCV RNA-positive patients received treatment with DAA, and 74% (243/327) completed the treatment course. Among those who completed treatment with DAA, 73% (177/243) achieved SVR12, and among those who achieved SVR12, 38% (68/177) further achieved SVR24 (Fig. 3). Aside from two patients who experienced virological breakthrough, all patients who did not achieve SVR12 or SVR24 were lost to follow-up.

The status of hepatitis C diagnosis and DAA treatment in the Kashi region from 2018 to 2022 is shown in Fig. 4. Since data for 2022 were only available from January 1 to August 31, we estimated the full year's data by multiplying the average monthly data by 12 months. When excluding the data from 2022, both the number of confirmed hepatitis C cases and the number of individuals receiving DAA treatment increased annually. There

was a particularly significant increase in 2021. However, the number of confirmed hepatitis C cases was much lower than the number of positive HCV-Ab screenings, and the number of individuals receiving DAA treatment was also significantly lower than the number of confirmed cases.

### HCV GT distribution

Among the 1,088 confirmed hepatitis C patients, genotyping data were available for 707 individuals (Fig. 5). Among the 707 individuals, 90.4% (639/707) were from ethnic minority groups. In the Kashi region, HCV included four GTs and seven subtypes: 1a, 1b, 2a, 2b, 3a, 3b, and 6a. The predominant subtype was 1b, accounting for 70.7% of the cases.

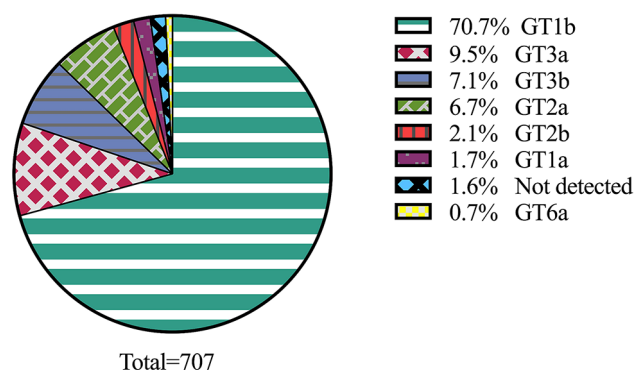
### Reasons for 156 patients not receiving DAA treatment

We conducted follow-up surveys via telephone, and 156 patients provided reasons for refusing DAA treatment (multiple responses were allowed). The reasons included the high cost of DAA treatment (41.7%), coinfection with infectious diseases such as HIV or syphilis (31.4%), unawareness of the harm of hepatitis C (17.9%), asymptomatic patients refusing treatment (14.7%), not being informed about the need for treatment (10.3%), inconvenience of frequent follow-ups (9.0%), unavailability of DAA at local hospitals (7.1%), long duration of DAA treatment (5.8%), long distance to the hospital (5.8%), patients being under 12 years old (4.5%), concerns about the side effects of DAA (1.3%), and pregnancy (0.6%) (Fig. 6). All patients who cited the high cost of DAA treatment were unaware that it could be covered by basic medical insurance. Among these patients, 62 were only willing to receive DAA if the total cost was less than 1,000 RMB, whereas 3 were willing to pay between 1,000 and 3,000 RMB out of pocket.

### Discussion

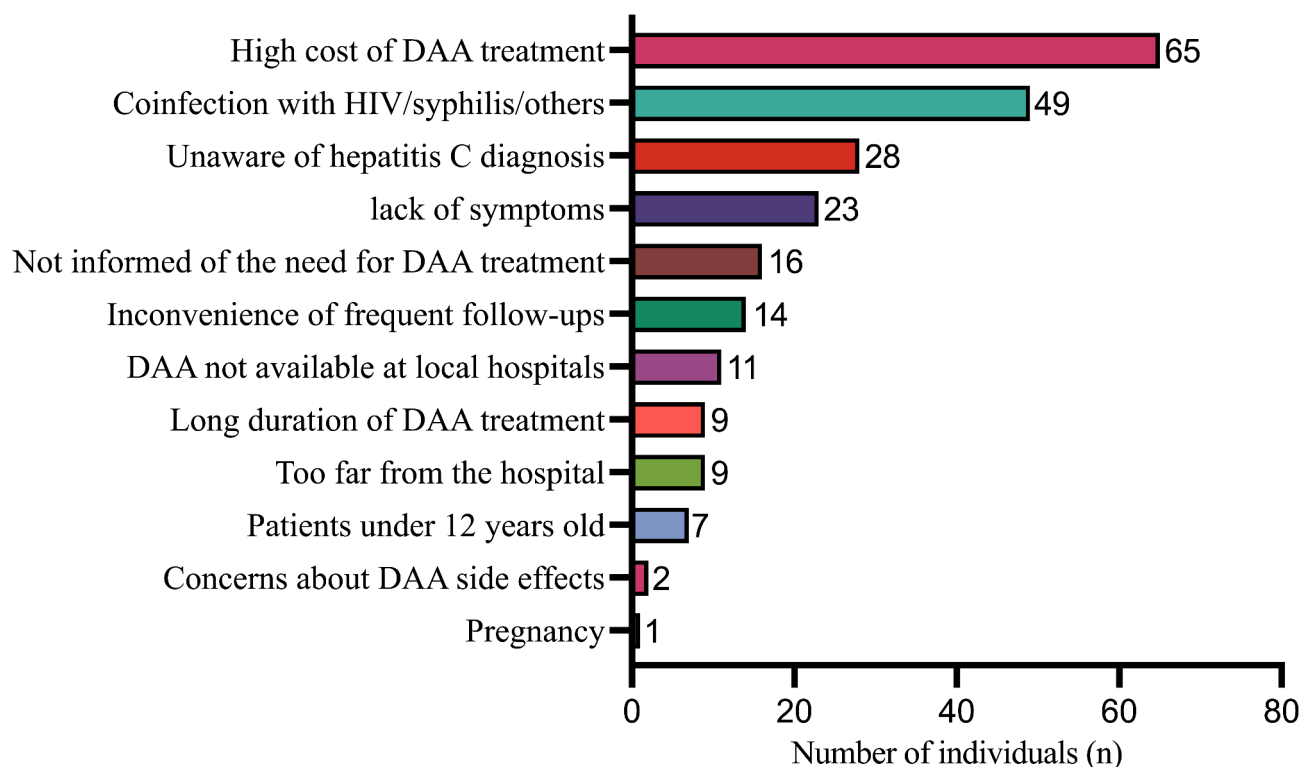
HCV poses a significant threat to public health, leading to liver failure and hepatocellular carcinoma. The global distribution of HCV is uneven. HCV infections in mainland China account for one-sixth of all cases worldwide, making it the country with the highest absolute number of infections worldwide<sup>5</sup>. Given the substantial number of HCV-positive individuals in China, the government's efforts to achieve the WHO's targets of 90% diagnostic coverage and an 80% treatment rate by 2030 could significantly impact the global burden of HCV-related diseases<sup>11</sup>. In 2019, reported cases from Kashi accounted for 28.66% of all cases in Xinjiang. From 2015 to 2019, Kashi reported an average of 2,007 hepatitis C cases annually, and there was an uneven distribution across the region<sup>7</sup>. Our investigation retrospectively analysed the HCV-Ab positivity rate, HCV GT distribution, hepatitis C diagnosis status, and treatment status in the Kashi region. Although the HCV-Ab positivity rate and the number of confirmed cases have increased in recent years, the proportion of patients receiving DAA remains relatively low. The results indicate that the hepatitis C epidemic in this area is critical, with suboptimal treatment outcomes, and that local health authorities and medical institutions face considerable challenges.

From 2018 to 2022, the overall HCV-Ab positivity rate in the Kashi region was 2.4% (95% CI: 2.4–2.5%). This positivity rate is significantly higher than the national HCV-Ab prevalence rate of 0.43% reported in 2006 and the prevalence rate of 0.40% reported among populations in western China<sup>12</sup>. Additionally, the HCV-Ab positivity rates in Gansu (1.08%) and Chongqing (1.7%) are also higher than the national HCV-Ab prevalence rate reported in 2006<sup>13,14</sup>. This evidence suggests that there may have been a certain degree of increase in the HCV-Ab positivity rate in China in recent years, particularly in the western regions. Statistical analysis using the Chi-square test for trend demonstrated that both the HCV-Ab positivity rate ( $p < 0.001$ ) and HCV RNA positivity rate ( $p < 0.001$ ) showed significant upward trends. These findings suggest that the burden of HCV infection in the region has been rising steadily over the past several years, indicating a potential increase in the incidence of HCV in this area. This increasing trend may be attributed to several factors. The first factor may be increased screening efforts: China's "Action Plan for Eliminating the Public Health Hazard of Hepatitis C (2021–2030)" advocates for comprehensive screening in medical institutions, with strategies such as "testing all who should be tested" for key populations and "testing all who wish to be tested" for the general population. With strong support from national policies, public awareness of hepatitis C has gradually increased, leading more people to undergo HCV screening either voluntarily or as a result of medical protocols and thereby identifying



**Fig. 5.** Genotype distribution among 707 HCV-infected individuals GT, Genotype; HCV, Hepatitis C virus.





**Fig. 6.** Reasons for 156 patients not receiving DAA treatment DAA, Direct-acting antiviral; HIV, Human immunodeficiency virus.

more potential cases. Second, there has been increased exposure among high-risk populations. In recent years, due to advancements in medical technology, the frequency of invasive medical procedures in the Kashi region has gradually increased, leading to a corresponding increase in infection risk. Additionally, high-risk groups in this region, such as blood transfusion recipients and intravenous drug users, are more susceptible to infection. Analysis of global trends and regional data suggested that the issue of injection drug use in China has been worsening annually<sup>15</sup>. The prevalence of HCV-Ab positivity among intravenous drug users in mainland China is approximately 70.8%<sup>16</sup>. Third, socioeconomic factors may play a role in the prevalence of HCV. Kashi is one of China's impoverished regions and is characterized by poor public sanitation, low individual awareness of self-protection, and a high incidence of risky behaviours, all of which contribute to the spread of HCV. Additionally, the low socioeconomic status in this region may limit access to healthcare services, and inadequate oversight and monitoring mechanisms may further increase the risk of HCV transmission.

Among the 707 HCV-infected individuals, the predominant subtype was 1b (70.7%), which is consistent with the national distribution of HCV GTs<sup>17</sup>. However, the proportions of subtypes 3a (9.5%) and 3b (7.1%) were greater than that of subtype 2a (6.7%), in contrast with the findings of a previous study, which indicated that the predominant HCV GTs in Xinjiang were subtypes 1b, 2a, 3a, 3b, and 6a<sup>10</sup>. This difference may be related to the demographic composition of the 707 HCV-infected individuals in this study, 90% of whom were from ethnic minority groups. The proportion of HCV GT3 was higher among ethnic minorities than among the Han population<sup>10</sup>. However, due to the limitations inherent in retrospective studies, this research lacks detailed demographic information, which restricts the representativeness of the sample and the external validity of the findings.

According to estimates by the Polaris Observatory HCV Collaborators, China's hepatitis C diagnosis rate increased to 40% in 2022, but it still falls significantly short of the global target of 90%<sup>11,18</sup>. Insufficient awareness of the harm of chronic HCV infection, combined with the often asymptomatic nature of the virus, reduces public attention to the dangers of HCV, thereby making it challenging to achieve target diagnosis rates<sup>19</sup>. Excluding the incomplete statistics for 2022 (which only include data from January 1 to August 31, 2022), the number of confirmed hepatitis C cases and those receiving DAA in the Kashi region has increased annually, with a particularly significant increase observed in 2021. This encouraging upwards trend may be related to the introduction of LDV/SOF and SOF/VEL at the First People's Hospital of Kashi in 2021, which improved drug accessibility. The cascade of care for HCV-Ab-positive individuals in the Kashi region, from the screening stage to the diagnosis and treatment stages, highlighted vital issues in this region's screening and treatment processes. Fewer than half (44%) of the 4,928 HCV-Ab-positive individuals underwent HCV RNA testing, which is consistent with a study conducted in Jiangsu Province, which reported a testing rate of 51.3%<sup>19</sup>. An online survey conducted in China revealed that individuals with lower educational attainment, residents of rural or western regions, and current alcohol consumers presented insufficient knowledge about HCV and were less

likely to undergo HCV testing<sup>20</sup>. During the investigation period, HCV RNA testing was not widely available in medical institutions across the Kashi region, with only the First People's Hospital of Kashi able to perform this test. The Kashi region covers a total area of 162,000 square kilometres. Except for Kashi city, gaining access the First People's Hospital of Kashi from the surrounding counties involves long distances and inconvenient transportation. Additionally, the two-step diagnostic process, which includes HCV-Ab screening followed by HCV RNA confirmatory testing, is time-consuming. The delayed availability of test results can lead to difficulties in follow-up for patients who initially test positive. The high cost of HCV RNA testing also makes it unaffordable for low-income individuals. Moreover, patients' lack of awareness about the importance of HCV RNA testing contributed to low testing rates. Many individuals did not fully understand the necessity of confirmatory testing after screening positive for HCV-Ab, which is common in regions with lower levels of public health education regarding viral hepatitis. These factors hinder the timely diagnosis of HCV infection and delay the initiation of prompt antiviral treatment.

In our investigation, only 30% of confirmed patients with chronic HCV infection received treatment with DAA, indicating a low treatment coverage rate. Similarly, a study conducted in Jiangsu reported that only 38.7% of patients received treatment with DAA<sup>19</sup>. Both figures fall significantly short of the WHO's treatment target of 80%<sup>11</sup>. Among the 483 patients who participated in the follow-up survey in this study, 67.7% received treatment with DAA. The relatively high proportion of patients receiving DAA treatment may be due to a greater willingness to participate in follow-up among those who were treated. In contrast, patients who did not receive treatment may have been less inclined to participate, possibly due to a loss of hope or other reasons. Among the 327 patients who received treatment with DAA, 243 (74%) completed the full course, based on their GTs and the presence or absence of liver cirrhosis. Some patients discontinued treatment after only 28 days of initial DAA treatment, whereas others abandoned further treatment because of the long distances from their places of residence to the hospital. Poor treatment adherence may also be related to economic pressure and limited awareness of hepatitis C. Among the patients who completed the full course of treatment, 73% (177/243) achieved SVR12, and 38% (68/177) achieved SVR24. Patients who did not return for follow-up testing were considered not to have achieved SVR. Aside from two patients who experienced virological breakthrough, all patients who did not achieve SVR12 or SVR24 were lost to follow-up. After completing the DAA treatment course, many patients believed that they were cured and were therefore unwilling to return to the hospital for follow-up testing. While our study did not perform a detailed analysis of specific patient characteristics such as socioeconomic status, distance from the hospital, lack of public awareness, or other factors that may have influenced loss to follow-up. Patients who face financial difficulties, long travel distances, or other logistical barriers may be less likely to complete follow-up appointments, which in turn could affect their treatment outcomes, including achieving SVR12 or SVR24. Despite the fact that follow-up could theoretically be conducted remotely via phone or telemedicine, practical logistical barriers such as difficulties in maintaining consistent patient contact, lack of reliable communication channels, and limited resources for follow-up contributed to the observed loss to follow-up. In addition, time constraints and the need for intensive staff involvement for data collection further limited our ability to perform a comprehensive analysis of these factors.

To enhance follow-up adherence, we propose several approaches. Patient education programs should be strengthened to increase awareness of the importance of SVR monitoring and the risk of reinfection. Telemedicine and remote monitoring can facilitate follow-up consultations, particularly for patients in rural areas, reducing logistical barriers. Integrating post-treatment monitoring into primary healthcare services can improve accessibility and reduce the burden on specialized centers. Additionally, providing incentives, such as cost reductions, transport reimbursement, or mobile clinics, may encourage follow-up adherence. Finally, establishing patient support systems, such as dedicated care coordinators, can help ensure that patients remain engaged in long-term monitoring. These strategies, when tailored to local healthcare infrastructure, may improve retention and optimize treatment outcomes.

An analysis was conducted on the reasons for treatment refusal among the 156 patients who declined DAA therapy. The treatment refusal rate in the Kashi region was 32.3%, which is higher than the 10.5% reported in a study from Taiwan<sup>21</sup>. However, patients in both regions reported similar reasons for refusing treatment. A study in the United States reported that 69% of patients faced barriers when initiating DAA treatment, including issues related to psychosocial factors, healthcare providers, medical systems, and insurance coverage<sup>22</sup>. The reasons for refusing treatment are varied and often multifactorial, making them difficult to overcome through a single intervention. A research indicated that the majority of patients who did not receive DAA (96.9%) continued to visit hospitals and clinics for other medical care<sup>21</sup>. These findings highlight the need for substantial improvements in public knowledge about hepatitis C prevention and treatment in the Kashi region. There is still much work to be done to raise awareness and ensure better health outcomes.

During the study period, the First People's Hospital of Kashi was the only medical institution in the region capable of performing HCV RNA testing and providing DAA treatment. However, with the implementation of China's "Action Plan for Eliminating the Public Health Hazard of Hepatitis C (2021–2030)", major healthcare institutions in the Kashi region have progressively enhanced their diagnostic capabilities. According to this plan, each district is required to establish a mechanism for eliminating the public health threat of HCV, with at least one healthcare institution per county designated to provide HCV antiviral treatment. Additionally, all secondary and tertiary general hospitals, specialized infectious disease hospitals, and disease control centers are mandated to have the capacity to perform both HCV-Ab and HCV RNA testing. Currently, eight types of DAA are included in the National Health Insurance list in China. The First People's Hospital of Kashi has introduced five of these DAA, and it is expected that other healthcare institutions in the region may also incorporate additional DAA in the future, further improving accessibility. The inclusion of these DAA in the national health insurance list has significantly alleviated the financial burden on low-income patients. However, further expansion of the insurance coverage is necessary. We recommend expanding the coverage of DAA to include more treatment



regimens and implementing national or provincial-level subsidies to further reduce patient out-of-pocket expenses. Such measures will improve treatment accessibility, encourage more patients to seek and complete treatment. In addition to expanding coverage, we suggest drawing from the experiences of countries such as Egypt and Pakistan, which have successfully negotiated lower DAA prices through centralized procurement or national agreements with pharmaceutical companies<sup>23,24</sup>. These strategies can help reduce the cost of DAA further. To improve accessibility in remote and rural areas, we recommend implementing mobile clinics that provide screening and treatment services to underserved populations. Increasing public education on HCV and available treatment options is crucial. We propose raising awareness about the importance of HCV RNA testing and DAA treatment through community outreach programs. This can be achieved by collaborating with local media, community health workers, and public health campaigns. Egypt has successfully established a model for managing and treating HCV, which has significantly reduced the national HCV infection rate<sup>23</sup>. Egypt's success has been regarded as a benchmark for other low- and middle-income countries in addressing the HCV epidemic. We believe that applying similar strategies could help improve HCV control in China, particularly in underserved areas such as Kashi region.

This study had several inevitable limitations. First, this was a retrospective investigation, which might be subject to selection bias and incomplete data collection. Second, the investigation population was limited to those who sought care at the First People's Hospital of Kashi, potentially excluding a broader representation of HCV-infected individuals in this region. Third, the reliance on telephone-based follow-up surveys may have produced response bias, as those who were more compliant or engaged with the healthcare system were more likely to participate.

## Conclusions

GT1b was the most prevalent HCV GT in the Kashi region, followed by GT3a and GT3b. Ongoing challenges in this area include the high prevalence of chronic HCV infection and the limited coverage of HCV RNA testing and DAA antiviral treatment. To achieve the WHO's hepatitis C elimination goals, much greater efforts are needed to improve healthcare services, particularly the availability of DAA, and to increase awareness among both medical staff and the public about HCV elimination.

## Data availability

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding authors.

Received: 22 October 2024; Accepted: 17 March 2025

Published online: 21 March 2025

## References

1. Polaris Observatory, H. C. V. C. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol. Hepatol.* **2**, 161–176. [https://doi.org/10.1016/S2468-1253\(16\)30181-9](https://doi.org/10.1016/S2468-1253(16)30181-9) (2017).
2. Pimpin, L. et al. Burden of liver disease in Europe: epidemiology and analysis of risk factors to identify prevention policies. *J. Hepatol.* **69**, 718–735. <https://doi.org/10.1016/j.jhep.2018.05.011> (2018).
3. Ouyang, G. et al. Incidence trends of acute viral hepatitis caused by four viral etiologies between 1990 and 2019 at the global, regional and National levels. *Liver Int.* **42**, 2662–2673. <https://doi.org/10.1111/liv.15452> (2022).
4. Huang, D. Q. et al. Global epidemiology of cirrhosis - aetiology, trends and predictions. *Nat. Rev. Gastroenterol. Hepatol.* **20**, 388–398. <https://doi.org/10.1038/s41575-023-00759-2> (2023).
5. Collaborators, P. O. H. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol. Hepatol.* **7**, 396–415. [https://doi.org/10.1016/S2468-1253\(21\)00472-6](https://doi.org/10.1016/S2468-1253(21)00472-6) (2022).
6. Thrift, A. P., El-Serag, H. B. & Kanwal, F. Global epidemiology and burden of HCV infection and HCV-related disease. *Nat. Rev. Gastroenterol. Hepatol.* **14**, 122–132. <https://doi.org/10.1038/nrgastro.2016.176> (2017).
7. Saimaiti, A., Xie, C. M., Maimaiti, H. & Hei, F. X. Epidemiological characteristics of hepatitis C in Kashgar, Xinjiang during 2005–2019. *Chin. J. Dis. Control Prev.* **27**, 244–248. <https://doi.org/10.16462/j.cnki.zhjbkz.2023.02.019> (2023).
8. Vo-Quang, E. & Pawlotsky, J. M. Unusual HCV genotype subtypes: origin, distribution, sensitivity to direct-acting antiviral drugs and behaviour on antiviral treatment and retreatment. *Gut* <https://doi.org/10.1136/gutjnl-2024-332177> (2024).
9. Huang, K. et al. Molecular evolution of hepatitis C virus in China: A nationwide study. *Virology* **516**, 210–218. <https://doi.org/10.1016/j.virol.2018.01.015> (2018).
10. Anaerguli, M. et al. Distribution characteristics of hepatitis C virus genotypes in Xinjiang. *Chin. J. Hepatol.* **28**, 494–498. <https://doi.org/10.3760/cma.j.cn501113-20190522-00181> (2020).
11. WHO. *Global Health Sector Strategy on Viral Hepatitis 2016–2021. Towards Ending Viral Hepatitis*. 53 (World Health Organization, 2016).
12. Chen, Y. et al. A sero-epidemiological study on hepatitis C in China. *Chin. J. Epidemiol.* 888–891. <https://doi.org/10.3760/cma.j.isn.0254-6450.2011.09.009> (2011).
13. Chen, Z. W. et al. Large disparity between prevalence and treatment rates for hepatitis C in Western China. *J. Clin. Transl Hepatol.* **6**, 385–390. <https://doi.org/10.14218/JCTH.2018.00027> (2018).
14. Du, Q. et al. Distribution and genotyping of hepatitis C virus (HCV) infection in Gansu Province, China. *J. Infect. Dev. Ctries.* **18**, 458–463. <https://doi.org/10.3855/jidc.18331> (2024).
15. Trickey, A. et al. The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. *Lancet Gastroenterol. Hepatol.* **4**, 435–444. [https://doi.org/10.1016/S2468-1253\(19\)30085-8](https://doi.org/10.1016/S2468-1253(19)30085-8) (2019).
16. Bao, Y. et al. Prevalence of HIV, HCV and HBV infection and sociodemographic characteristics of people who inject drugs in China: A systematic review and meta-analysis. *Int. J. Drug Policy.* **70**, 87–93. <https://doi.org/10.1016/j.drugpo.2019.05.005> (2019).
17. Guideline for the prevention and treatment of hepatitis C. *Chinese Journal of Hepatology* **30**, 1332–1348, (2022). version <https://doi.org/10.3760/cma.j.cn501113-20221220-00605> (2022).
18. Polaris Observatory, H. C. V. C. *HCV Infections* (2022), (2024). <https://cdafound.org/polaris-countries-dashboard/#footnote-hcv>
19. Yang, D. et al. Diagnosis, treatment, and associated factors among patients with HCV Infection - Jiangsu Province, China, 2004–2020. *China CDC Wkly.* **6**, 1–5. <https://doi.org/10.46234/ccdcw2024.001> (2024).

20. Liu, Y. et al. Hepatitis C knowledge and Self-Reported testing behavior in the general population in China: online Cross-Sectional survey. *JMIR Public. Health Surveill.* **9** <https://doi.org/10.2196/39472> (2023).
21. Chang, L. J. et al. Factors associated with the refusal of Direct-Acting antiviral agents for the treatment of hepatitis C in Taiwan. *Med. (Kaunas)*. **58**. <https://doi.org/10.3390/medicina58040521> (2022).
22. Malespin, M. et al. Barriers to treatment of chronic hepatitis C with direct acting antivirals in an urban clinic. *Ann. Hepatol.* **18**, 304–309. <https://doi.org/10.1016/j.aohep.2018.06.001> (2019).
23. Esmat, G., Elbaz, T., Elsharkawy, A., Abdullah, M. & El Kassas, M. Emerging from the screening of 57 million citizens and treating 4 million patients: future strategies to eliminate hepatitis C from Egypt. *Expert Rev. Anti Infect. Ther.* **18**, 637–642. <https://doi.org/10.1080/14787210.2020.1758065> (2020).
24. Qureshi, M. A. & Health Systems Strengthening approach to address the high burden of hepatitis C in Pakistan. *J. Viral Hepat.* **32**, e14050. <https://doi.org/10.1111/jvh.14050> (2025).

## Acknowledgements

We extend our gratitude to the patients and the Guangdong Provincial Department of Science and Technology for their support of this study.

## Author contributions

Study concept and design: Chao Wu and Lubiao Chen; Methodology: Mingna Li and Kuerbannisa Wulayin; Data collection: Mingna Li, Lian Zhou and Shutao Lin; Analysis and interpretation of data: Mingna Li, Kuerbannisa Wulayin and Shasha Ma; Draft manuscript preparation: Mingna Li and Kuerbannisa Wulayin; Funding acquisition: Lubiao Chen; Supervision: Lubiao Chen. All authors read and approved the final manuscript.

## Funding

This work was supported by the Special Project of Guangdong Rural Science and Technology Commissioner of China (KTPY2021014).

## Declarations

## Ethics approval and consent to participate

The work was conducted according to the Helsinki Declaration as revised in 2013. It was approved by the Institutional Review Board of the First People's Hospital of Kashi (No. 2022-03). Due to the retrospective nature of the study, an exemption from informed consent was granted by the Institutional Review Board of the First People's Hospital of Kashi.

## Competing interests

The authors declare no competing interests.

## Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

## Consent to publish

Not applicable.

## Additional information

**Correspondence** and requests for materials should be addressed to C.W. or L.C.

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