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Yiqun LIU
Fujian Medical University
Li Zongqing
Fujian Medical University
Sha LI
Fujian Medical University
LIAN Qiaoling
Fujian Center for Disease Control and Prevention
Mingya ZHANG
Fujian Center for Disease Control and Prevention
Huang Fan
Jianxin Hospital, Fujian Province
WU Shaobin
Fujian Center for Disease Control and Prevention
WU Shouli
Fujian Center for Disease Control and Prevention
XIE Jianfeng
xjf417@163.com

Fujian Center for Disease Control and Prevention

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Analysis of Genetic Characteristics of Hepatitis C Virus among Sentinel Surveillance Populations in Fujian Province, China from 2022 to 2025

LIU Yiqun[1], Li Zongqing[1], LI Sha[1], LIAN Qiaoling[2], ZHANG Mingya[2], Huang Fan[4], WU Shaobin[2], WU Shouli[2], XIE Jianfeng[2,3*]

[1]The School of Public Health, Fujian Medical University, Fuzhou, Fujian,350000, China；

[2]Fujian Center for Disease Control and Prevention, Fuzhou 350000, China

[3]Fujian Provincial Key Laboratory of Zoonosis Research, Fuzhou 350000, China

[4]Jianxin Hospital, Fujian Province, Fuzhou 350000, China

*Correspondence:

Jianfeng Xie: MS, Fujian Provincial Center for Disease Control and Prevention, Institute of Infectious Disease Prevention and Control, Fuzhou 350000, China

Email: xjf417@163.com

Abstract

Objective： To analyze the genotype distribution, evolution, and characteristics of resistance-associated substitutions (RASs) of Hepatitis C Virus (HCV) among sentinel surveillance populations in Fujian Province from 2022 to 2025, and to provide a scientific basis for HCV prevention and control.

Methods： The hepatitis C incidence report data from 2022 to 2025 in Fujian Province were obtained from the China CDC Information System. Full-length HCV genome sequences were obtained through high-throughput sequencing, and bioinformatics software was employed to analyze genetic characteristics and RAS distribution.

Results： From 2022 to 2025, sentinel surveillance in Fujian Province revealed that HCV infections were predominantly subtype 1b, with escalating trends observed in subtypes 3b and 6a. Phylogenetic analysis demonstrated that most 1b, 3b, and 6a sequences clustered closely with Guangdong Province sequences, while some lineages also grouped with international sequences from Japan and Denmark. Sequences of subtypes 1a and 2a were more likely to cluster with international sequences. In the HCV NS3/4A region, resistance-associated substitutions (RASs) S122G/N/C occurred most frequently in subtypes 1b and 6a (31/91). In the NS5A region, RASs conferring higher drug resistance included L31V and Y93H, R30Q and L28M in subtype 1b, and Q30K+L31M in subtype 3b. In the NS5B region, RASs-C316N was predominantly detected in subtype 1b (21/32), and when coexisting with S556G, it conferred higher resistance to DSV. Concurrent presence of RASs in both NS5B and NS5A regions reduced SOF treatment efficacy.

Conclusions: The genetic distribution of sentinel populations in Fujian Province tends to be increasingly complex. Population mobility and overseas importation are important factors in virus transmission. Drug resistance-related substitution mutations are commonly present in sentinel populations, and using whole-genome sequencing to track drug resistance mutations generated by genetic diversity in epidemic strains is very important for accurately guiding treatment of hepatitis C patients.

Key word： Hepatitis C；Whole genome sequence；Genetic distribution；Resistance-associated substitutions

1. Introduction

Hepatitis C (HCV) is an infectious disease mainly affecting the liver, caused by infection with the Hepatitis C virus (HCV). Without timely treatment, patients are prone to develop chronic hepatitis, and most of these chronic hepatitis patients die from cirrhosis and hepatocellular carcinoma[1], Hepatitis C has become one of the main causes of chronic hepatitis worldwide[2]. According to the World Health Organization (WHO) 2026 Hepatitis Report, it is estimated that 47 million people were infected with the hepatitis C virus in 2024, with approximately 900,000 new hepatitis C infections that year and 242,000 related deaths. The report shows that the number of

hepatitis C virus infections in China is about 7.6 million, ranking third in the world, and together with Pakistan and India, they account for 39% of global hepatitis C infections[3, 4]. The WHO's goal is to reduce the incidence of hepatitis C to fewer than 5 cases per 100,000 people, but in China the incidence is as high as 14.38 cases per 100,000 people, still far from the target[5].

HCV is a single-stranded positive-sense RNA, with a genome of approximately 9.6×10^3 nucleotides, containing a large open reading frame (ORF) that encodes structural proteins (core, E1, E2) and non-structural proteins (p7, NS2, NS3, NS4A, NS4B, NS5A, and NS5B)[6]. NS3, as a serine protease, has multiple functions. NS4A is a highly hydrophobic protein involved in inducing membrane alterations required for the biogenesis of viral replication organelles. NS5A is a multifunctional phosphorylated protein that plays a key role in viral RNA replication and particle assembly. NS5B is the RNA-dependent RNA polymerase of HCV, responsible for genome replication[7, 8].Therefore, NS3/4A, NS5A, and NS5B are usually the targets of direct-acting antiviral drugs (DAAs)[9]. Due to the lack of an efficient proofreading mechanism during its replication process, RNA polymerase has low fidelity, producing an average base mismatch rate of about 10^{-4} to 10^{-5}[10], This leads to the coexistence of multiple genetically distinct viral variants within an individual infected with HCV, forming a complex viral population[11], These differences have led HCV to be classified into 8 genotypes and more than 90 subtypes[12, 13], The pathogenicity of different genotypes and their responses to existing therapies vary[14, 15], Researchers confirm genotyping through NS5B, the core protein Core, and the envelope glycoprotein E1[16, 17].

With the approval of combination therapy of DAAs in 2014 and achieving very good treatment outcomes[18]. China approved these drugs in 2017, issued the annual guidelines for the prevention and treatment of hepatitis C in 2019, and updated them in 2022. The guidelines indicate that interferon-free pan-genotypic regimens can achieve a sustained virological response (SVR) of over 90% in patients with major HCV genotypes[19]. Currently, no effective vaccine against HCV has been developed. Although DAAs are relatively effective in treatment, some clinical trials for certain genotypes or special HCV-infected populations have not achieved high SVR rates, and appropriate treatment strategies need to be formulated based on the local genotype distribution and special populations. Another important factor related to DAA therapy failure is resistance-associated substitutions (RASs). These mutations may arise spontaneously in the virus or under drug pressure, occurring in the three gene regions of NS3/4A, NS5A, and NS5B. The presence of RASs can reduce the effectiveness of drugs and even lead to treatment failure[20, 21].

Currently, there are relatively few domestic studies using whole genome sequences to describe the distribution of genotypes/subtypes and drug resistance characteristics. This study conducted high-throughput sequencing of the whole genomes of individuals infected with HCV in the sentinel surveillance population in Fujian Province, using whole genome sequences to describe the distribution of HCV genotypes/subtypes, evolution, and resistance mutations in this population. The findings provide scientific evidence for improving treatment plans for patients with different genotypes or those with unsatisfactory treatment outcomes, consolidating HCV prevention and control, and reducing the disease burden.

2 Methods

2.1 Study subjects

Serum samples were collected from 96 HCV-infected individuals identified through sentinel surveillance in nine cities (coastal cities: Fuzhou, Zhangzhou, Putian, Quanzhou, Xiamen, and

Ningde; inland cities: Sanming, Longyan, and Nanping) in Fujian Province from October 2022 to August 2025. The samples were sent to Fujian Provincial Center for Disease Control and Prevention and stored at -80°C. The diagnostic criteria followed the Diagnosis of Hepatitis C: WS213-2018[22].This study was approved by the Medical Ethics Committee of Fujian Provincial Center for Disease Control and Prevention: Min Disease Control Ethics Review (2024) No. (001).

2.2 Research Methods

2.2.1 Epidemiological Data Collection.

Case information was obtained from the China CDC Information System, including sex, age, region, occupation, and other variables.

2.2.2 HCV RNA Extraction

RNA was extracted from a 140 μL serum sample using the QIAamp viral RNA mini kit protocol (Qiagen, Hilden, Germany). Finally, 60 μL of eluted RNA was obtained and kept at −80 °C.

2.2.3 HCV Genome Sequencing

Reverse transcription and amplification of the full-length HCV genome were performed according to the instructions of the nucleic acid capture kit. Reverse transcription was carried out using PT Super Mix reagent (Hangzhou, Baiyi Technology Co., Ltd.) to generate cDNA strands. The same cDNA strand was then amplified separately using Primer Pool A and Primer Pool B. Subsequently, the two amplification products were combined into a 1.5 mL centrifuge tube to obtain the amplified nucleic acid of the full-length HCV genome, and the product was sent to Hangzhou Baiyi Technology Co., Ltd.

2.2.4 HCV Genotyping and Phylogenetic Tree Construction

The obtained whole-genome sequences were uploaded to GenBank under accession numbers PZ746446–PZ746536. Preliminary subtype identification was performed by online alignment in the GenBank database to establish the most similar complete HCV genome sequences and to compare with reference sequences of common HCV subtypes (1a: NC_004102.1, 1b: D90208.1, 2a: D00944.1, 3a: NC_009824.1, 3b: 49374.1, 6a: Y12083.1, 6n: DQ278894.1). These sequences were subsequently used to construct phylogenetic trees. All sequences were aligned using muscle, and phylogenetic trees were constructed using the Neighbor-Joining method in MEGA12.0 software. The resulting trees were then adjusted and visualized using the Chiplot online platform.

2.2.5 HCV-RASs Detection

The whole-genome sequences obtained from sequencing were uploaded to a specialized website (http://hcv.geno2pheno.org/index.php) for resistance-associated substitution analysis. The resistance level of RASs was classified into four categories: Resistance, Reduced susceptibility, Susceptible*, and Susceptible. According to literature reports [23], Resistance refers to the presence of mutations in the virus that have been clearly documented to lead to treatment failure. The efficacy of drugs against such viruses would be severely compromised or even nullified; Reduced susceptibility indicates that mutations present in the virus lead to decreased drug efficacy, although the drug still retains some therapeutic effect; Susceptible* refers to mutations occurring at key sites (i.e., scoring positions) that have a potential impact on drug sensitivity, theoretically affecting drug efficacy, yet lacking clear literature evidence—these are referred to as potential mutation risks in this study; Susceptible is defined as the virus being fully sensitive to the drug, with no mutations present that affect drug efficacy.

2.3 Statistical Analysis

Data were summarized and organized using Excel 2024 and SPSS 21.0 software. The

arithmetic mean was used to describe the age distribution. Based on the demographic characteristics of HCV, Fisher's exact test was employed to compare the genotype/subtype distribution and resistance-associated substitution distribution among sentinel populations with different characteristics, and a *P*-value of <0.05 was considered statistically significant.

3 Result

3.1 HCV Genotype Distribution and Demographic Characteristics

This study extracted RNA from serum samples of 96 nucleic acid-positive individuals and conducted nucleic acid capture and high-throughput sequencing, successfully obtaining 91 full-length HCV genome sequences, including 8 genotypes: 1a, 1b, 2a, 2m, 3a, 3b, 6a, and 6n, which accounted for 2.20% (2/91), 35.16% (32/91), 14.29% (13/91), 1.10% (1/91), 3.30% (3/91), 23.08% (21/91), 19.78% (18/91), and 1.10% (1/91), respectively. The demographic information of the 91 sequences is shown in Table 1. The distribution of HCV viral subtypes among infected individuals differed significantly by gender, age, and population source (*P*<0.05).

Table 1. Genotype distribution according to the demographic characteristics of HCV-infected Individuals

Classification		N (N=91)	Genotype distribution								*P*
			1a (n=2)	1b (n=32)	2a (n=13)	2m (n=1)	3a (n=3)	3b (n=21)	6a (n=18)	6n (n=1)	
Gender											
Male		59	2	17	4	0	3	17	15	1	0.005
Female		32	0	15	9	1	0	4	3	0	
Age											
<40		13	0	2	4	1	0	3	3	0	
40-60		57	1	19	4	0	1	16	15	1	0.030
>60		21	1	11	5	0	2	2	0	0	
Time											
2022-2023		18	1	9	3	0	1	1	3	0	0.283
2024-2025		73	1	23	10	1	2	20	15	1	
Carrer											
Unemployed or retired		40	1	13	5	1	1	10	8	1	
Production and Technical Personnel		38	0	14	7	0	1	9	7	0	0.915
Business service personnel		13	1	5	1	0	1	2	2	0	
Region											
Coastal cities	Fuzhou	6	1	4	0	0	0	0	1	0	0.069
	Putian	23	0	12	6	0	1	1	3	0	
	Quanzhou	1	0	1	0	0	0	0	0	0	
	Xiamen	13	0	4	1	0	1	6	1	0	
	Zhangzhou	2	0	0	0	0	1	0	1	0	
	Ningde	15	0	0	3	0	0	10	2	0	

	Total	60	1	21	10	0	3	17	8	0	
Inland cities	Sanming	3	0	1	0	1	0	1	0	0	
	Longyan	2	0	0	0	0	0	0	1	1	
	Nanping	26	1	10	3	0	0	3	9	0	
	Total	31	1	11	3	1	0	4	10	1	
Crowd Category											
Hospital		71	1	18	11	1	3	20	17	0	0.020
Community		20	1	14	2	0	0	1	1	1	

3.2 HCV Gene Evolution Analysis

The 91 measured whole-genome sequences were compared with the reference sequences in GenBank in MEGA and a phylogenetic tree was constructed (Figure 1), where the measured sequences are named based on sample number, region, population, and time, and the reference sequences are named based on number, region, time, and subtype, with red dots marking the ends of the branches.

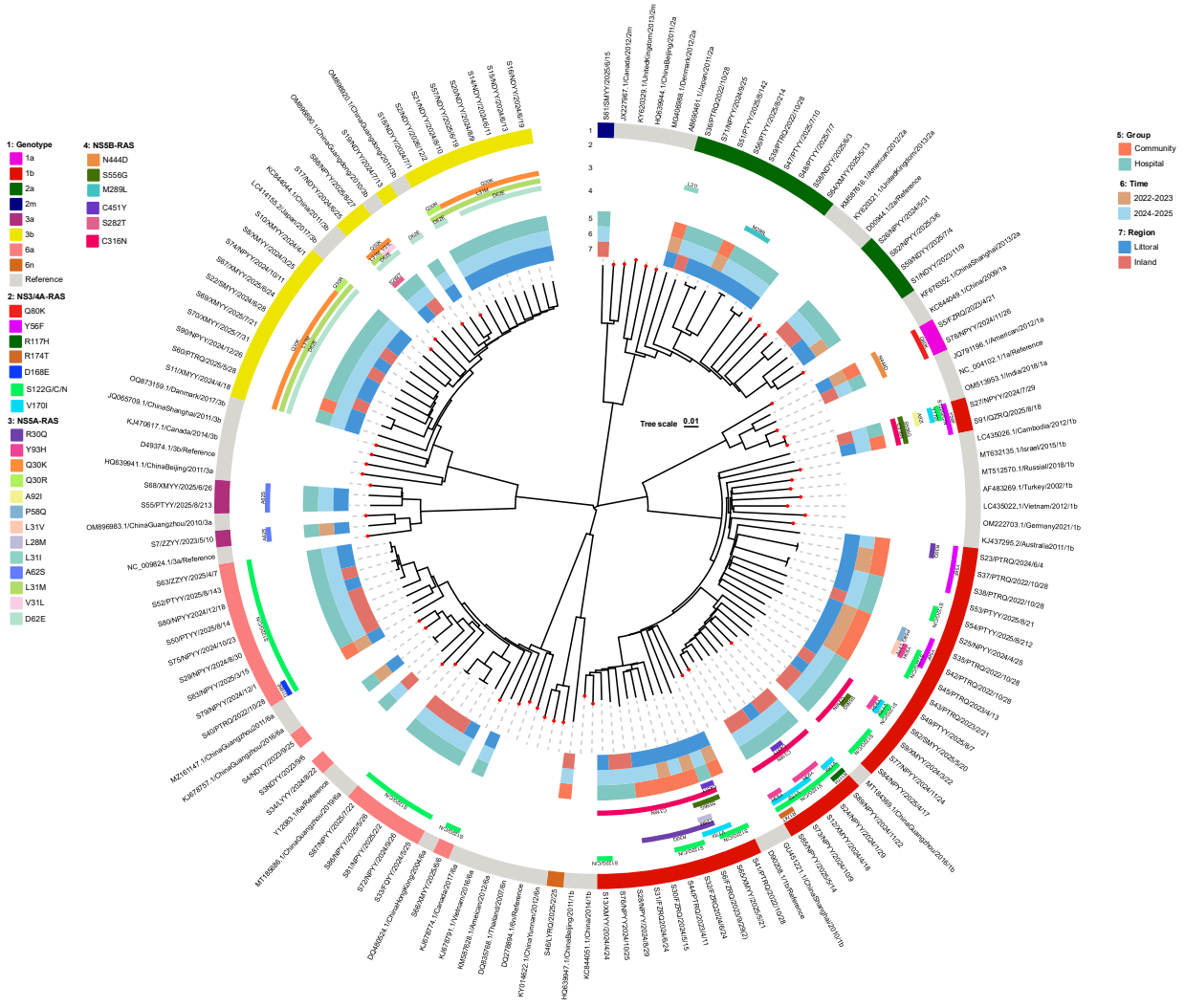


Figure1 HCV Whole Genome Phylogenetic Tree

From the phylogenetic tree, it was observed that subtype 1b sequences not only clustered with previously reported sequences from Beijing, Shanghai, and Guangzhou in China, but sequences from Putian City also belonged to the same branch as sequences from Australia. Sequences of subtypes 1a and 2a were mostly clustered with previously reported foreign sequences (Denmark, the United Kingdom, India, the United States,

and Japan). Both subtypes 3b and 6a were phylogenetically close to previously reported sequences from Guangdong Province, among which subtype 3b also clustered with foreign sequences from Japan and Denmark, while some subtype 6a sequences were located on the same branch as sequences from Hong Kong and Canada.

3.3 The Analysis of HCV Genomic Drug Resistance and RASs

3.3.1 Direct-acting antiviral drug resistance detection rate and resistance level

The DAAs involved in this study included first-generation NS3/4A protease inhibitors Boceprevir (BOC) and Telaprevir (TVR); second-generation inhibitors Simeprevir (SMV), Asunaprevir (ASV), and Paritaprevir (PTR); third-generation inhibitors Glecaprevir (GLE), grazoprevir (GZR), and Voxilaprevir (VOX); NS5A protease inhibitors Daclatasvir (DCV), Velpatasvir (VEL), Ledipasvir (LDV), Ombitasvir (OMB), Elbasvir (EBR), and Pibrentasvir (PIB); and NS5B inhibitors Dasabuvir (DSV) and Sofosbuvir (SOF).

Analysis of the gene sequence information revealed that the HCV in this study was relatively sensitive to the NS3/4A inhibitors VOX and GLE, the NS5A inhibitors VEL and PIB, and the NS5B inhibitor SOF(As shown in Figure 2). Among the NS3/4A inhibitors, only two viruses showed resistance to SMV, while a small number of viruses exhibited reduced susceptibility to TVR (one virus), VOX (three viruses), and GZR (seven viruses). A considerable number of viruses were resistant to multiple NS5A inhibitors, with LDV and EBR being the most frequent (23 viruses each), and 18 viruses showed reduced susceptibility to PIB. Among the NS5B inhibitors, five viruses and one virus were detected to be resistant to DSV and SOF, respectively.

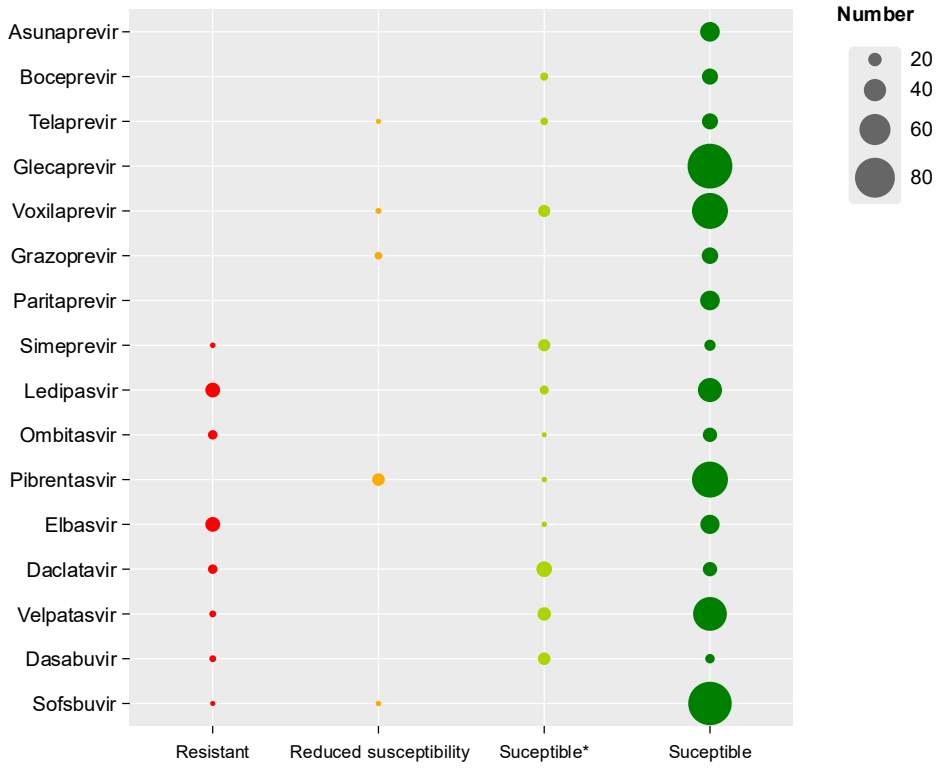


Figure2. Detection rate and resistance level of direct-acting antiviral drugs

3.3.2 Analysis of RASs in the HCV Genome

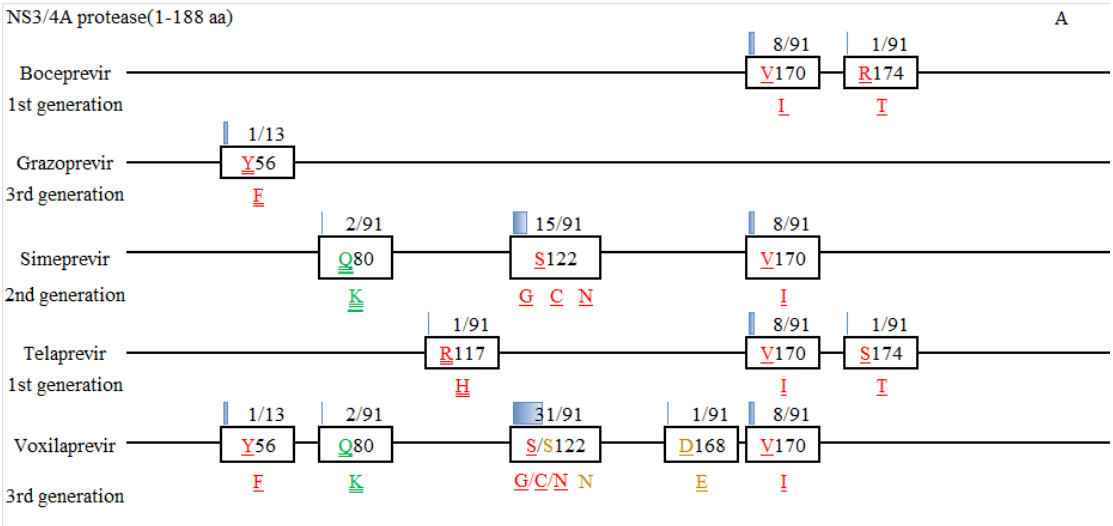
Among the 91 HCV genome sequences, RASs were detected in 72 sequences. The highest frequency of RASs occurred in the non-structural protein NS3/4A region (43.96%, 40/91), followed by the NS5A region (41.76%, 38/91). A total of 17.58% (16/91) of the sequences harbored mutations in both regions, and 8.79% (8/91) of the sequences had resistance-associated substitutions in all three regions. In this study, RASs were predominantly identified in subtypes 1b, 3b, and 6a, with only a small number detected in other subtypes (1a,

2a, and 3a).

In the non-structural protein NS3/4A region, the most frequently detected RASs was S122G/C/N (31/91). V170I was the substitution detected against the most NS3/4A protease inhibitors in this study; the highest number of resistance mutations detected against VOX were identified in the sequences, although the vast majority were potential mutation risks. RASs-Q80K mainly conferred resistance to SMV and reduced susceptibility to VOX in subtype 1a sequences. The detected RASs also varied across different subtypes, with subtype 1b sequences exhibiting the greatest diversity of RASs (Y56F, R117H, S122G/C/N, V170I, S174T), while S122N and D168E were detected in subtype 6a, and only Q80K was detected in subtype 1a(Figure 3 is shown blow).

In the NS5A region, RASs were detected in subtype 1b, 2a, 3a, and 3b sequences, among which Q30K (18/91), L31M (19/91), and D62E (20/91) were most commonly identified in subtype 3b. Compared to the other two regions, a greater number of multi-RAS combinations leading to resistance were detected in the NS5A region. Specifically, Q30K and Q30K+L31M conferred resistance to LDV and EBR, respectively, in subtype 3b. Other RASs conferring resistance included R30Q and R30Q+L28M, as well as Y93H and Y93H+L31V, all of which were detected exclusively in subtype 1b sequences. The former mainly conferred resistance to DCV and OMV, while the latter conferred resistance to multiple NS5A inhibitors except PIB. For PIB, although no resistance-associated mutations were detected, the mutation Q30K—which reduced susceptibility to PIB—was detected in 18 subtype 3b sequences.

In the NS5B region, fewer RASs were detected compared to the other inhibitor classes. RASs conferring resistance to DSV were predominantly composed of multi-RAS combinations such as C316N+S556G and C316+C451Y+S556G. The single mutation C316N mainly represented a potential mutation risk for DSV in subtype 1b sequences. For the NS5B nucleotide inhibitor SOF, RASs-S282T, which conferred resistance to SOF in subtype 3b sequences, and RASs-M289L, which reduced susceptibility to SOF in subtype 2a sequences, were detected in this study.



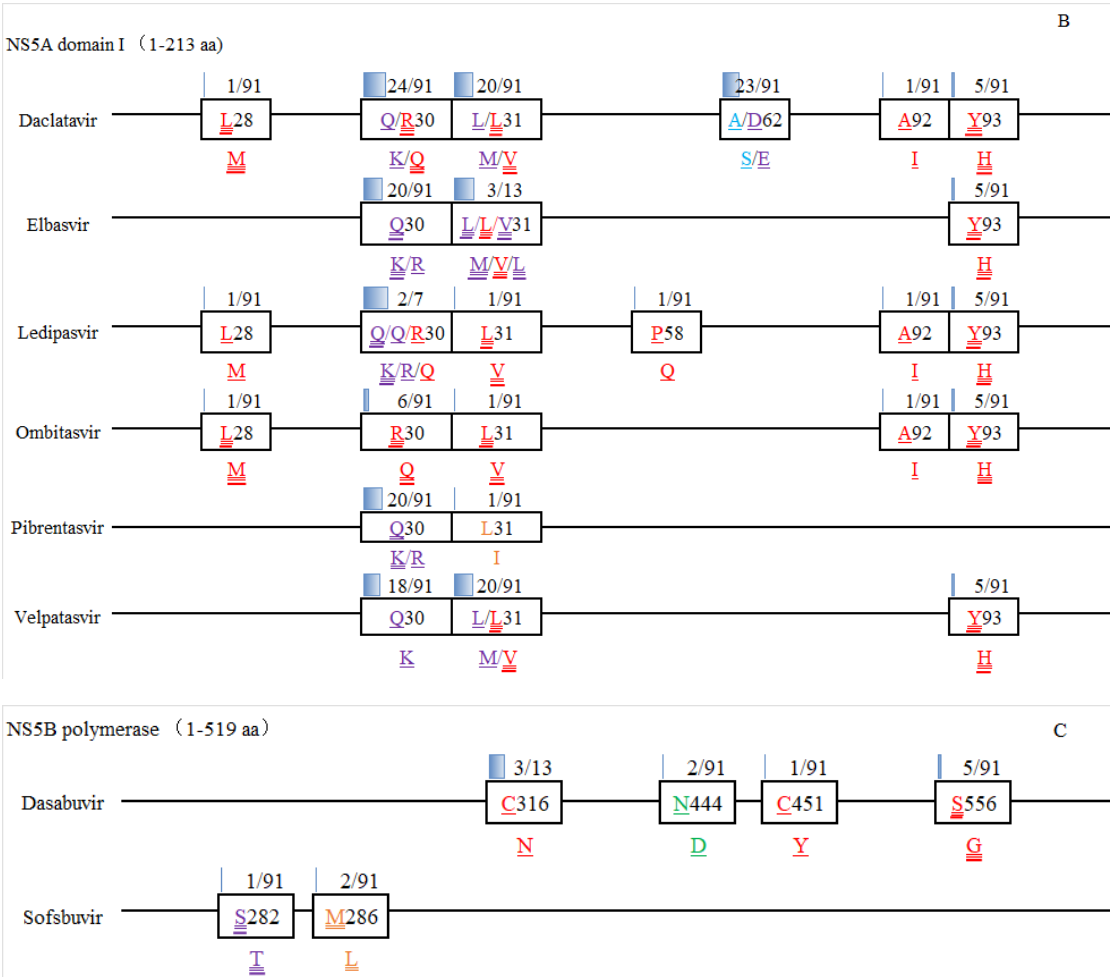


Figure3. Summary of substitutions associated with resistance to Direct-Acting Antiviral Drug

A: NS3/4A protease inhibitors, B: NS5A protease inhibitors, C: Nucleoside and non-nucleoside NS5B inhibitors. HCV genotypes and subtypes are represented by different colors: 1a-Green, 1b-Red, 2a-Orange, 3a-Light blue, 3b-Purple, 6a-Golden.The level of resistance is indicated by underlining: No underline indicates Susceptible, one underline indicates Susceptible*； tow underline indicates Reduced susceptibility；three underline indicates Resistance. The data bars and numbers represent the proportion of sequences with this mutation site.

4 Discussion

This study analyzed the genotype distribution and resistance-associated substitutions in 96 HCV nucleic acid-positive patients identified through sentinel surveillance in nine cities of Fujian Province, providing a preliminary understanding of the genotype distribution and resistance-associated substitution patterns in this population. In this study, HCV cases were detected in all cities, with the majority originating from coastal cities (60/91), particularly Putian City (23/60), and cases were distributed across each year from 2022 to 2025. Among inland cities, Nanping City had the highest number of cases (26/31), with all cases concentrated in 2024, which is consistent with previous analyses of the epidemiological characteristics of hepatitis C in Fujian Province[24]. From a geographical perspective, the higher number of cases in coastal cities compared to inland cities is associated with population mobility, economic and educational factors, and healthcare institutions. The relatively large number of cases in Putian City is related to behaviors such as the sharing of syringes and infusion sets and non-standard disinfection practices in local health clinics[25]; The situation in Nanping City may be related to the lower educational level of the population and weaker

awareness of health protection[26]. In addition, most HCV-infected individuals were male, middle-aged and elderly individuals aged 40-60 years, and unemployed/retired or technical/production workers, which was associated with educational level, non-standard medical practices in local healthcare settings, high-risk behaviors, and occupational characteristics—findings that are consistent with domestic studies[27-30].

HCV is mainly of the 1b subtype globally, followed by 3a and other subtypes[31-35], while in China, the distribution of HCV subtypes shows obvious geographical heterogeneity[5]. This study showed that the sentinel population in Fujian Province was predominantly infected with subtype 1b (32/91), followed by subtypes 2a, 3b, and 6a (13/91, 18/91, and 21/91, respectively). While subtype 1b remained the dominant subtype in Fujian Province, an increasing trend was observed for genotypes 3 and 6, which is consistent with previous research findings[36, 37], It is indicated that there is diversity in gene subtypes in Fujian Province, with Xiamen and Ningde mainly having 3b, Nanping having a balance of 1b and 6a subtypes, and most of the other cities mainly having 1b. In the phylogenetic tree, the 1b subtype from Xiamen and Nanping and the 3b subtype from Ningde were observed to be closely related to previous sequences from Guangdong Province, while most 1b subtype sequences from Putian are on the same branch as sequences from Australia. Some city-specific 3b subtype branches (Xiamen, Nanping, Ningde) also cluster with foreign sequences from countries such as Japan and Denmark. In terms of treatment, there are reports indicating that genotype 3 is more difficult to manage[38], according to the 2022 Hepatitis C Prevention and Treatment Guidelines[19], the therapeutic effect of subtype 3b is worse compared to other subtypes, The pan-genotypic treatment regimen SOF/VEL shows good efficacy against genotype 3, but its effectiveness is poor in patients with cirrhosis, and there is a high prevalence of dual point mutations A30K and L31M. In this study, all 3b subtype sequences had Q30K and L31M mutations, which can affect the susceptibility to NS5A inhibitors. This is similar to previous studies on 3b subtype patients in the southwestern region[38, 39]. In Xiamen and Ningde, where subtype 3b is predominant, we should strengthen the tracking of treatment outcomes for patients with subtype 3b and the surveillance of viral strain circulation. In addition, the genotype 6 strains in Ningde and Nanping cluster with those from Hong Kong and Guangzhou, and are also on the same branch as sequences from Canada. Although subtype 6a is more distantly related to strains from Vietnam, we still need to be alert to the importation of foreign strains, and there are related studies reporting that the 6a subtype in our country originated from Vietnam[40], circulated from neighboring Guangxi and Yunnan, and further spread to Guangdong Province. Today, the 6a subtype in Guangdong Province has become the prevalent subtype and is expected to become the second region to spread 6a to other provinces. The genotypes 3 and 6 involved in this study are both more closely related to Guangdong Province. Previous studies[41] speculate that with the rapid development of China's high-speed rail, increased transportation convenience and population movement will introduce more genetic subtypes from Southeast Asian countries, leading to a more complex distribution and spread of genotypes across different regions, which will affect the prevention and control of hepatitis C in our country. This requires us to strengthen the management of the floating population in sentinel cities such as Putian, Xiamen, Nanping, and Ningde, and strictly prevent the importation of cases from abroad.

Currently, various DAA regimens are applied to hepatitis C virus infection. Most HCV patients receiving treatment can achieve good therapeutic effects, but resistance to DAAs remains a major challenge in eliminating HCV. Mutations associated with resistance to direct-acting antivirals can be detected in NS3/4A, NS5A, and NS5B, and RASs vary among different HCV subtypes and drug classes. Studies have shown[42] that factors associated with DAA failure include treatment regimen (drug combination and duration), resistance-associated mutations (RASs on the NS5A region), genotype/subtype (genotypes 1a and 3 have a higher risk of failure), and disease severity (cirrhosis). In this study, the sequences in which RASs

were detected were mostly subtypes 1b, 3b, and 6a.

In the NS3/4A region, the detection rate of RASs in subtype 1b sequences was 71.88% (23/32), lower than 97.14% (68/70) in Huaibei City and 85% (53/62) in western regions[43, 44]. The most frequently detected RAS in subtype 1b was S122G, which is the most common RAS in Asia[45], and in this study, it mainly indicates a potential risk of resistance of subtype 1b sequences to SMV and VOX. Studies have shown that different mutations at amino acid position V170 can cause resistance of the virus to different direct-acting antivirals [46], In this study, amino acid position 122 in subtype 1b sequences involved three different mutations (S122/N/C/G). When formulating treatment regimens, the high genetic variability of HCV should be considered, as it can lead to drug resistance.

In the NS5A region, RASs-Y93H detected in subtype 1b sequences, as well as its combination with L31V, conferred resistance to multiple NS5A inhibitors except PIB in subtype 1b, with a detection rate of 15.63% (5/32) among subtype 1b sequences, which was higher than the 14.1% reported for subtype 1b in China[47]; Among subtype 2a sequences, L31M, which has a relatively high prevalence in domestic subtype 2a populations, was not detected in this study[47, 48], only one case of RASs-L31I was identified. From the phylogenetic tree, it was observed that subtype 2a sequences were predominantly found in Putian and formed a distinct cluster, which may be consistent with studies from Guangdong Province[41], suggesting differences in resistance profiles between southern and southwestern regions; Significant differences existed between genotypes 3a and 3b: subtype 3a had only three cases of the A62S mutation, whereas mutations at amino acid positions 30 and 31 were detectable in the vast majority of subtype 3b sequences. Specifically, 80.95% (17/21) of subtype 3b sequences harbored Q30K+L31M, which was lower than the 94% of subtype 3b sequences with A30K+L31M mutations reported in southwestern China[39], he Q30K+L31M detected in this study represents a natural polymorphism at amino acid position 30 in the NS5A region of subtype 3b sequences[49], primarily conferring resistance to EBR in subtype 3b; No RASs in the NS5A region were detected in genotype 6, consistent with domestic studies[48].

In the NS5B region, RASs-C316N is commonly detected in subtype 1b sequences, which presents a potential mutation risk. However, when the combination of C316N and S556G is detected in the sequence, it causes resistance to DSV, consistent with previous studies[45]. In subtype 3b sequences, RASs-282T, which confers resistance to SOF, was detected. Mutations Q30K, L31M, and D62E were also present in the NS5A region of these sequences. Research has shown that the coexistence of baseline RASs in the NS5A and NS5B regions can affect the efficacy of SOF/VEL treatment, leading to treatment failure[50]. In this study, 17.58% of sequences had mutations detected in both regions, highlighting the need to be aware of the impact of coexisting RASs in different regions on drug efficacy. When using pan-genotypic treatment regimens, RASs testing for patients can help avoid such effects.

5 Conclusions

In summary, the sentinel population in Fujian Province was predominantly infected with subtype 1b, with an increasing trend observed for subtypes 3b and 6a, suggesting a trend toward diversification of genetic distribution. Phylogenetic analysis revealed that the locally prevalent subtypes were phylogenetically related to those in Guangdong Province and certain foreign countries, indicating that population mobility and importation from abroad are important factors in viral transmission. Resistance-associated substitutions (RASs) are prevalent in the sentinel population in Fujian Province, and the profiles of RASs vary across different subtypes. Particular attention should be paid to the impact of multi-RAS combinations in the NS5A region and cross-regional co-existing RASs on drug efficacy, especially for subtypes 1b and 3b. Therefore, tracking resistance mutations arising from genetic diversity through whole-genome sequencing is of great importance for precisely guiding the treatment of hepatitis C patients.

List of abbreviations

HCV	Hepatitis C virus
WHO	World Health Organization
RNA	Ribonucleic acid
ORF	open reading frame
DAAs	direct-acting antiviral drugs
SVR	sustained virological response
RASs	resistance-associated substitutions
BOC	Boceprevir
TVR	Telaprevir
SMV	Simeprevir
ASV	Asunaprevir
PTR	Paritaprevir
GLE	Glecaprevir
GZR	Grazoprevir
VOX	Voxilaprevir
DCV	Daclatasvir
VEL	Velpatasvir
LDV	Ledipasvir
OMB	Ombitasvir
EBR	Elbasvir
PIB	Pibrentasvir
DSV	Dasabuvir
SOF	Sofosbuvir

Declarations

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Author contributions

XJF and LYQ conceived and designed the study. LYQ and LZQ analyzed the data and wrote the main manuscript. HF and LS contributed to the analysis tools. WSB, ZMY contributed to data collation and interpretation. LQL and WSL helped to draft the manuscript. XJF provided advice and critically reviewed the manuscript. All authors read and approved the final manuscript.

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Data availability statement

The data presented in the study are deposited in the GenBank repository, accession numbers PZ746446–PZ746536.

Ethical approval and consent to participate

The studies involving humans were approved by the Medical Ethics Committee of Fujian Provincial Center for Disease Control and Prevention. The studies were conducted in accordance

with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]The School of Public Health, Fujian Medical University, Fuzhou, Fujian,350000, China；

[2]Fujian Center for Disease Control and Prevention, Fuzhou 350000, China

[3]Fujian Provincial Key Laboratory of Zoonosis Research, Fuzhou 350000, China

[4]Jianxin Hospital, Fujian Province, Fuzhou 350000, China

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