



## Prescribing Trends of Hepatitis C in Hospitals of Faisalabad, Pakistan

Sana Shahzad, Sana Javed, Medeha Fatima, Fatima Akber, Fauzia Rehman

Department of Pharmacy, Faculty of Pharmaceutical Sciences, The University of Faisalabad, Faisalabad 38000, Pakistan

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#### Corresponding author

Email:

[sanashahzad.PHARM@tuf.edu.pk](mailto:sanashahzad.PHARM@tuf.edu.pk)

(Sana Shahzad)

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### ABSTRACT

**Background:** Hepatitis is a priority area of public health in Pakistan in which Hepatitis B and C is prevalent at high prevalence and presents the enormous challenge for the healthcare sector.

**Objective:** To find out the trends, risk factors and control strategies for hepatitis in Pakistan.

**Methodology:** This study was conducted on patients who got treatment with hepatitis C virus (HCV) medicines; a comparative cross-sectional survey was done. To do this, 270 patients were given a standardised, closed ended questionnaire to fill out. Data were compared using age, gender, marital status, present medication and side effects. Epidemiology of hepatitis was studied on the basis of English and Urdu data from English and Urdu newspapers, national health databases, as recorded in hospital records and published papers. The chosen technique is in accordance with well-elaborated principles of public health research that guarantee precision and reliability. The results of the Pakistan Health Research Council, the Pakistan Bureau of Statistics and the World Health Organisation were used with the secondary data and carried out retrospective observational analysis based on the secondary data.

**Results:** Infection rates by species, geographic distribution and the success of prevention efforts in place are discussed based on the data given in the national health, research articles. It was seen that unsafe medical procedures, low vaccination coverages and low awareness on the part of the common person brought on a lack of burden of hepatitis, in particular, the rural populace and the individuals who were unfortunate. Changes have been made with government led initiatives including vaccination program and blood screen policies; however, the application is hindered by poor healthcare accessibility and socioeconomic barriers. The study gives an edge to the importance of public health interventions such as mass awareness campaigns, better sanitation and wider vaccination. Healthcare policies be strengthened and hepatitis control strategies be integrated into the primary healthcare services to achieve a great failure in reduction.

**Conclusion:** A multi-sectoral response that combines government agencies, healthcare providers, and community outreach needs to be employed to limit spread of hepatitis in Pakistan.

### INTRODUCTION

About 180 million individuals throughout the world have contracted hepatitis C virus (HCV). Various nations have stated prevalence rates of hepatitis C infection. According to Alberts *et al.* (2022), the rates of HCV were found to be highest in Asia, North Africa, and the Middle East. They were moderate in South Asia, Sub Saharan Africa, Central and Southern Latin America, the Caribbean, Oceania,

Australasia, Middle Eastern and Central Europe, and Tropical Latin America and North America. About 15–20% of those infected with HCV are able to recover, whereas the remaining 75–85% develop hepatitis C. Research shows that, compared to other cities in Pakistan, the prevalence of hepatitis C is on a rise in Faisalabad, where it affects roughly 24% population (Abbas *et al.* 2024). When it comes to liver disease, hepatitis C is at the top of the list for complications, deaths, and transplants. Only 1% of hepatitis



cases in Pakistan are treated (Khan *et al.* 2020). Uninformed people about the disease spread, high treatment costs, and a shortage of qualified medical personnel are reasons for rising hepatitis ratio and the dismal treatment rate (Proquest.com 2021).

Beginning in 1999 as a monotherapy, interferon (IFN) was later shown to be an effective in combination with ribavirin (RBV) in 2001. As of 2004, the gold standard for treatment was the introduction of RBV in conjunction with PEGylated interferon alpha. Significant adverse effects of IFN prevented it from providing the desired therapeutic benefit, which led to discontinuation of its usage (1-6SI). The issue of IFN toxicity persisted even when the dosage was reduced. Myalgias, stomach pains, sleeplessness, anorexia, and fever were the first noted adverse effects. Infections of the urinary tract, the lungs, the brain, hyperthyroidism, hypothyroidism, psychosis, and suppression of the bone marrow were among the adverse effects noted with long-term usage (Salari *et al.* 2022).

From 2001 to 2011, IFN and RBV were the gold standard drugs for treating HCV. However, several direct acting antiviral (DAA) medication combinations were authorised in 2015 by the European Medicines Agency (EMA) and the Food and Drug Administration (FDA), and these combinations exhibited improved infection treatment response with a decreased risk of side effects. The use of antivirals with direct action has a remarkable positive impact on patient's health while dealing with HCV. According to Naz and Asghar (2023), there are a number of viral protein inhibitors that may aid in the removal of HCV infection from biological systems. These include NS3/4A protease, NS5A, and NS5B polymerase.

Chills, sores, ulcers, pale skin, altered behaviour, lightheadedness, sleeplessness, difficulty breathing, headache, nausea, allergic reactions, constipation, fever, and body aches are some of the antiviral adverse effects that have been seen. Hepatitis C infection spreads via the blood. A chronic infection may develop after an acute infection of HCV. In Faisalabad, where hepatitis affects at least 24% of the population, it is becoming an increasingly pressing issue. The liver may develop cirrhosis and hepatocellular cancer as a result of an HCV infection. Thus, it is crucial to diagnose and treat at an early stage (Guntipalli *et al.* 2021; Kamili and Wester 2024).

The cost of controlling hepatitis is too high all over the world (Lim *et al.* 2021). Despite that it is important to invest in this public welfare program. This study was an attempt to describe and analyze the hepatitis C pharmaceutical therapy prescription pattern in Faisalabad, Pakistan to determine the efficacy of the therapy and patient satisfaction grade of the prescribed drugs.

## MATERIALS AND METHODS

A comparative cross-sectional survey was done on patients who got treatment with HCV medicines. To do this, 270

patients were given a standardised, closed ended questionnaire to fill out. Data was compared using age, gender, marital status, present medication and side effects. Epidemiology of hepatitis was studied on the basis of data from English and Urdu newspapers, national health databases, as recorded in hospital records and published papers. The chosen technique is in accordance with well-elaborated principles of public health research that guarantee precision and reliability. The results of the Pakistan Health Research Council, the Pakistan Bureau of Statistics and the World Health Organisation (WHO) were used with the secondary data and carried out retrospective observational analysis based on the secondary data. It is also based on a review of patient data from a tertiary healthcare institution hospital to provide trends in prevalence. In the analysis of the Hepatitis A, B, C, D and E, infection patterns from 2000 to 2020 (Ullah *et al.* 2022) are presented.

All reported viral hepatitis cases in Pakistan in that period have been analysed in the present study. It includes all dimensions of gender, age and socioeconomic status, and urban and rural residents. There was no study, and when the diagnostic criteria were inconsistent, there were duplicate records. All the strains of hepatitis incidence, prevalence and mortality rates are calculated with the help of SPSS V.17. Descriptive statistics included frequency distribution, standard deviations and means (Falak *et al.* 2020). So, we worked forwards after trending the time series and tried to find a relationship between demographic factors and illness prevalence with Chi square test. In their study, Moradi *et al.* (2020) state that  $P < 0.05$  is statistically significant in this regard.

Patients were not required to provide their permission for this research since it made use of already-public data extracted from an anonymised medical record. Following standard procedures for research ethics and participant confidentiality, the consent from Institutional Review Board of concerned hospitals was obtained to conduct the study before the individuals were enrolled.

From around four months in the beginning of 2019, all of Faisalabad's hospitals were included in the research. We included all HCV patients who were diagnosed without age discrimination and were currently taking treatment for their HCV. The University of Faisalabad's ethics council gave approval for this study. This is because, in accordance with the Declaration of Helsinki Principles, all patients and legal guardians were required to provide written informed permission before they could participate in the trial (Ali 2023). One hundred thirty-seven patients at Allied Hospital, Liver Centre, District Headquarter Faisalabad, Social Security Hospital, and Aziz Fatima Hospital, Faisalabad, who were given medication for HCV infection, filled out a questionnaire created in accordance with national standard treatment guidelines for hepatitis (Saleem *et al.* 2022).

Once several hospital coordinators gave permission, we selected a location for the patient interviews. The completion of the questionnaire was not done in the

presence of any medical professional. Medication, administration method, side effects, treatment satisfaction, treatment cost-effectiveness and diagnostic tests were all included in the questionnaire. Also, details were gathered on the patients age, gender, marital status, occupation, level of education and familiarity with the risk variables (Fung *et al.* 2009; Hashmi *et al.* 2021).

To compare quantitative variables, we used Student's *t*-test, which takes the mean and standard deviation into account. The comparison was considered significant at  $P < 0.05$ . Data were analyzed using SPSS V.17.

## RESULTS

Of the 270 patients participating in research, a lesser number of patients ( $n=99$ ) were under the age of 40, while the vast majority (63.3%,  $n=171$ ) were older than 40 years (Table 1). Out of 270 patients, 156 were female (57.2%) and 114 were male (42.2%) (Table 1). With  $P < 0.001$ , 91.5% of the individuals ( $n=247$ ) were married, while 8.5% ( $n=23$ ) were never married. (Table 1).

The occupations represented among the 270 patients were: 124 (45.5%) were housewives, 15 (5.6%) were government employees, 13 (4.8%) were farmers, 17 (6.3%) were businessmen, 29 (10.7%) were teachers, 3 (1.1%) were mill employees, 2 (0.7%) were bankers, 6 (2.2%) were wholesalers, 51 (18.9%) were labourers, and 10 (3.7%) were students (Fig. 1). Of the patients surveyed, 100 (37% of the total) gave a positive response when asked about a family history of hepatitis C, whereas 170 (67%) did not ( $P < 0.001$ ) (Fig. 2).

Among DAAs, Sofosbuvir was used by 24.8% of the participants, Daclatasvir by 24.4%, Entecavir by 0.4%, Acyclovir by 0.7%, RBV by 7.8%, and PEGylated alpha2b by 1.5%. The most common combinations used were Velpatasvir and Sofosbuvir (38.9% of all prescriptions) and IFN and RBV (1.5% each). Patients older than 40 years were more likely to use a combination therapy (34.1% vs. 8.8% for patients younger than 40) (Fig. 3). Sofosbuvir (24.8%), Daclatasvir (24.4%), RBV (7.8%), and PEGylated alpha-2b (1.5%) were the antiviral medications most often administered. Together, Velpatasvir and Sofosbuvir accounted for 38.9% of all combination therapies, with IFN and RBV coming in at 1.5% (Fig. 4). A high cost of HCV therapy was mentioned by 233 patients (86.3%). Among all patients, just 37 (13.7%;  $P < 0.001$ ) were exempt (Fig. 4).

Among 270 patients prescribed HCV medication, 167 (61%) were on it for 1–6 months, 38 (14.1%) for 6 months to a year, 28 (10.4%) for 1–2 years, 18 (6.7%) for 2–4 years, 8 (3%) for 4–5 years, and 11 (4.1%) for 5–10 years (Fig. 5). Although 5.6% of patients were dissatisfied, 94.4% were satisfied with their drug treatment (Fig. 6).

In patients receiving antiviral treatment, the following adverse events were noticed most frequently: weakness (19.6%), constipation (20.0%), dizziness (12.6%), fever

(9.6%), and sleeplessness (9.6%). Tolerance responses (4.8%), nausea (5.2%), headache (4.4%), and bodyaches (8.5%) were the mild adverse events. Shortness of breath (1.1%), pale complexion (1.9%), chills (2.2%), and blisters (0.4%) were minor adverse events (Fig. 7).

There are a number of comorbid illnesses that might aggravate HCV infections. Comorbidities were seen in 160 out of 270 individuals. Hypertension accounted for in 70 patients (58.5%), diabetes in 58 patients (25.9%), and anaemia in 32 patients (11.9%) among the top ranking conditions. No comorbidities were found in 110 individuals (Table 2).

## DISCUSSION

Consistent with other research showing age-related susceptibility owing to protracted exposure to risk factors, such as risky medical procedures and blood transfusions, the study shows a significant incidence of HCV in Faisalabad, especially among those over 40 years old. Existing research suggests intra-household transmission, possibly via shared hygiene items or close contact, and the much higher infection incidence in married persons supports this idea (Farooq *et al.* 2024).

According to Younas *et al.* (2021), patients older than 40 years were more likely to have combination treatment. The most widely given combination, with a prevalence of 38.9%, was Velpatasvir + Sofosbuvir (Fig. 1), which shows a move away from IFN-based therapy and towards DAAs. Because of their greater effectiveness and reduced side-effect profile, DAAs are recommended in worldwide treatment recommendations (Curry *et al.* 2015). Still, a huge problem is the lack of accessibility; 86.3% of patients indicated high cost of medicine as a big obstacle. This is in line with Hill *et al.* (2019) who found that high cost was the greatest obstacle to treatment, especially in low-income nations.

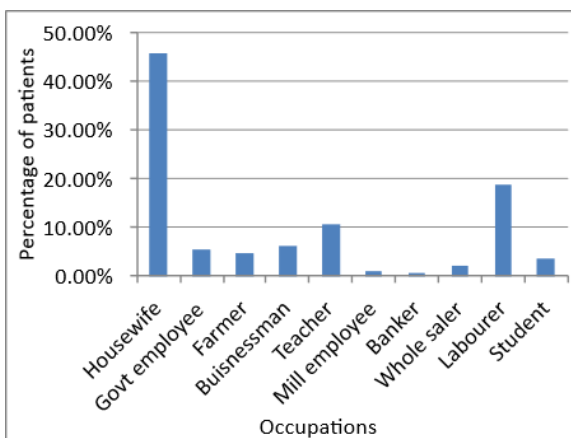
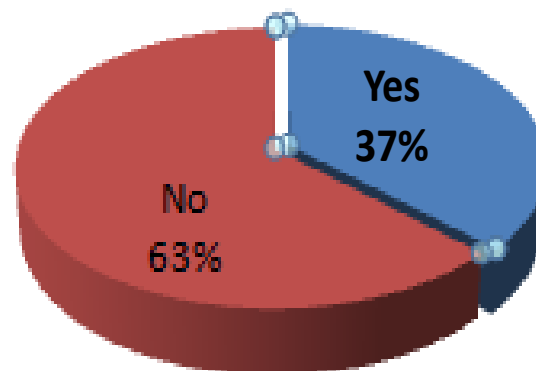
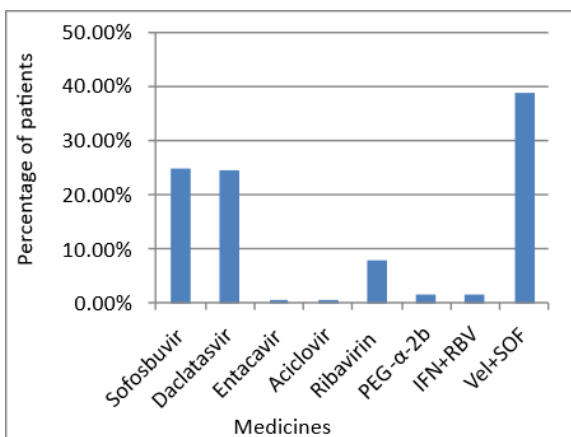
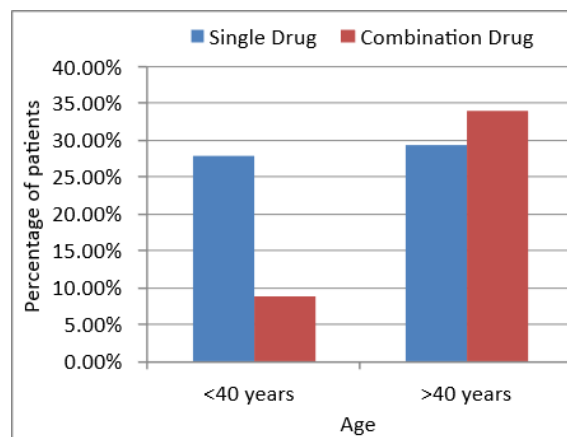
A high prevalence of comorbidities like diabetes and hypertension among HCV patients lends credence to earlier studies that established a connection between long-term HCV infection and metabolic diseases as well as cardiovascular problems (Bozkurt *et al.* 2016; Petrie *et al.* 2018; Nasrallah *et al.* 2024). Based on these results, healthcare providers should work together to treat HCV and any co-occurring diseases (Tariq *et al.* 2023).

Majority of the patients were satisfied with their treatments (94.4%), although a small percentage had side effects, including fatigue (19.6%), constipation (20%) and vertigo (12.6%). These results are somewhat different from those of Western populations, where reports of exhaustion and gastrointestinal problems were more prevalent, which may indicate that medication tolerance and patient-reported outcomes vary by geography (Bibi *et al.* 2023; Marcellin *et al.* 2023).

The current research confirmed that married people had a greater HCV prevalence. Factors like sex and sharing

**Table 1:** Demographic data of the patients

Category	Frequency	Percentage data	P-value
Age			
• <40 years	99 /270	36.7%	<0.001
• >40 years	171/270	63.3%	
Gender			
• Male	114	42.2%	<0.001
• Female	156	57.8%	
Marital status			
• Married	247	91%	<0.001
• Single	23	8.5%	

**Fig. 1:** Occupational distribution among the patients for the prevalence of HCV**Fig. 2:** Distribution of patients with respect to family history of HCV**Fig. 3:** Trend of DAAs prescription to the HCV patients**Fig. 4:** Trend of using drugs combination among age groups

housing may contribute to the transmission of HCV from one partner to the other. Prior research by Osmond *et al.* (1993) and Piazza *et al.* (1997) provided evidence that sex may transmit HCV. The discovery of HCV RNA in saliva lends credence to the idea that the virus could have spread through non-sexual and non-parental household transmission (Ackerman *et al.* 2000).

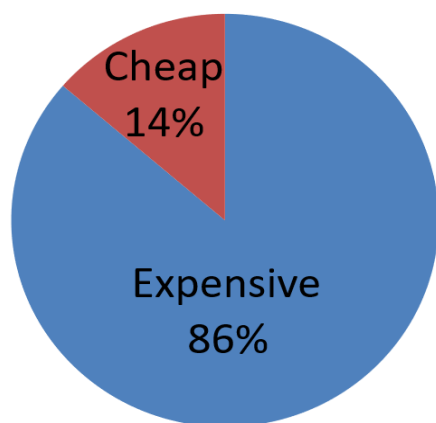
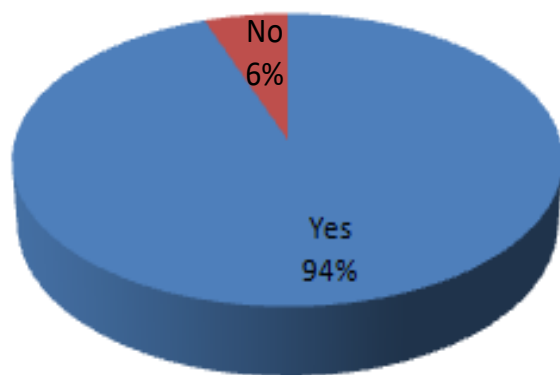
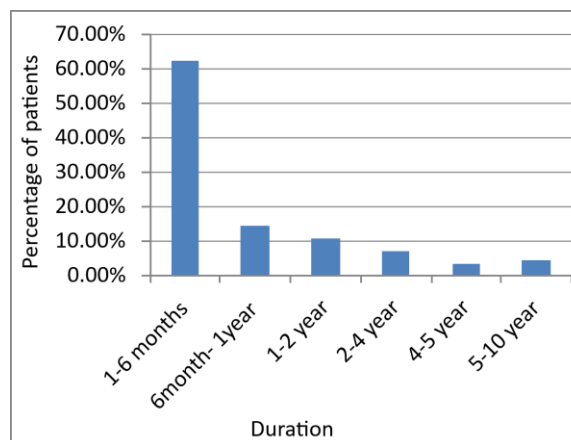
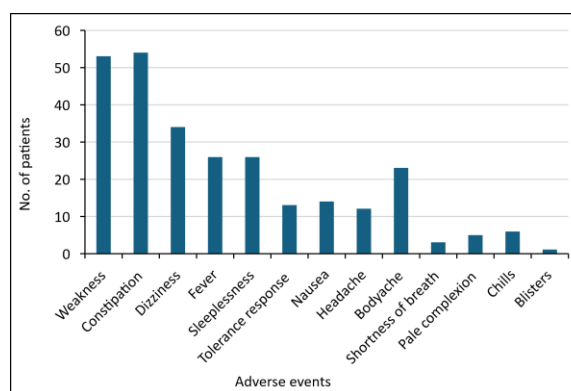
Among the individuals in this research, females were more affected by HCV than males, according to research by Sood *et al.* (2018), out of a sample size of

5543 patients, females had a greater prevalence of HCV (53.8%) than males (46.2%), that had 5543 patients. Contrarily, Mahmood *et al.* (2021) indicated a greater prevalence of HCV in males (67.14%) compared to females (32.85%).

This research confirms the findings of Butt *et al.* (2007) and Younossi *et al.* (2013) that demonstrated the greatest rate of co-morbidity between HCV and hypertension. The risk of coronary artery disease (CAD) was greater in HCV infected individuals compared to HCV

**Table 2:** Comparison for occurrence of comorbidity among the patients

Variables	No. of patients	Percentage	P value
Hypertension	70	58.5%	<0.001
Diabetes	58	25.9%	<0.001
Anemia	32	11.9%	<0.001
No disease	110	40.7%	<0.001

**Fig. 5:** Opinion of patients with respect to cost of the medicines**Fig. 7:** Level of satisfaction of patients with the DAAs for the treatment of HCV**Fig. 6:** Duration of use of HCV medication by the patients**Fig. 8:** Adverse events experienced by patients with the use of HCV drugs during treatment

uninfected patients, according to Butt *et al.* (2007) A high prevalence of congestive heart failure (CHF) was observed in patients infected with HCV (Younossi *et al.* 2013). Völzke *et al.* (2004) on the other hand, could not detect a correlation between HCV and CVD. Our findings corroborate those of Sir Ganga Ram Hospital Karachi, where researchers found that people with diabetes, particularly type 2 diabetes mellitus, had an increased chance of contracting HCV infection (Guo *et al.* 2013). Additionally, this research found that HCV and anaemia often occur together. Smith *et al.* (1998) found that Homeostatic Iron Regulator gene mutations are more common in HCV patients and are linked to higher iron storage in HCV patients. On the other hand, Thorburn *et al.* (2002) found no evidence that HFE mutation contributed to

iron buildup in liver biopsies taken from HCV infected individuals.

The current research demonstrated that Velpatasvir and Sofosbuvir were often used together. Curry *et al.* (2015) and Feld *et al.* (2015) showed that this combination is quite successful, with SVR rates ranging from 98–99% after 12 weeks of therapy. Additionally, our research found that antiviral medication for hepatitis C often comes with side consequences. In contrast to our findings, the previous study found that 47.6% of patients experienced fatigue, 38.1% experienced GIT disturbance, 14.3% had headaches, and only 2 patients experienced dyspnoea (Mehmood *et al.* 2019).

Eighty percent of HCV-positive individuals should be treated by 2030, according to the WHO (Raja *et al.* 2020). A

high cost of medication therapy is a major barrier to treatment in many nations. High cost of hepatitis C medicines was a concern for 86.3% of patients (Fig. 2). In their 2016 study, Hill *et al.* (2019) found that current prices for Sofosbuvir for a 12-week therapy range from \$84,000 in the United States to \$53,400 in the United Kingdom, \$46,139 in France, \$27921 in Spain and Portugal, \$7,000 in Brazil, and \$483 in India. Siddique *et al.* (2020) estimated that cost of a 12-week course of generic Sofosbuvir would be ~\$150 USD.

The current investigation confirmed the prevalence of side effects associated with hepatitis C antiviral treatment. We found that 47.6% of patients had tiredness, 38.1% had GIT disruption, 14.3% had headaches, and just 2 individuals had dyspnoea.

In order to increase early detection and accessibility of HCV medicines in Pakistan, this research highlights the immediate need for treatment techniques that are both cost-effective and part of better public health programs. Expanding screening programs and assessing cost-effective generics should be the primary goals of future research aimed at reducing disease burden. Our research showed that hepatitis C was more common in people over the age of 40 compared to younger people under the age of 40. This finding is in line with what Sood A *et al.* found in their study, which also found that the prevalence of HCV increases with age (Abbas *et al.* 2024; Kashif *et al.* 2024).

## CONCLUSIONS

Lack of continuous medical care and the expense of therapy are big obstacles to eradication HCV. There has been clear progress in treating HCV infection with minimal side effects and significant clinical efficacy in recent years. However, the enthusiasm of IFN-free DAAs has been muted by very high cost of drugs. Majority of the recently established regimens are expensive, making their broad use impractical. Pakistan needs to make hepatitis C treatment and prevention a top priority because the infection affects ~5% Pakistanis. Prevalence of hepatitis C was highest among married people in Faisalabad, and that the disease disproportionately affects those who are over 40 years of age. Velpatasvir + Sofosbuvir is the most frequently prescribed combination as DAAs, which has improved treatment efficacy. A multidisciplinary approach to healthcare is necessary due to frequent occurrence of comorbid conditions like hypertension and diabetes. There should be more government intervention to subsidise antiviral treatments, raise awareness about HCV infections and contacts, and expand screening programs. Long-term efficacy of inexpensive generic DAAs needs to be studied, and ways to incorporate HCV management into primary health care be explored. Improved healthcare infrastructure and universal treatment access are essential to achieve the WHO's goal of eradicating hepatitis C as a public health threat by 2030.

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## DATA AVAILABILITY

The data will be made available upon request to the author

## ETHICS APPROVAL

This paper is not relevant

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