

## Cost–Benefit Evaluation of Interferon and Ribavirin for the Treatment of Hepatitis C in District Dera Ismail Khan, Pakistan

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### Abstract

Hepatitis C Virus (HCV) infection is a significant public health problem in Pakistan, being a leading cause in the development of chronic liver disease, cirrhosis, and hepatocellular carcinoma. In resource-constrained districts like Dera Ismail Khan, a key barrier to effective disease management is the lack of affordability of treatments. To assess the clinical outcomes and cost-effectiveness of therapies for the treatment of hepatitis C, the author focuses on the District Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan, and the use of interferon, pegylated interferon, and ribavirin. A descriptive cross-sectional study was developed based on the physician's data made through the structured questionnaire. Thirty physicians (30) involved in the management of HCV patients were selected to describe treatment preferences, clinical outcomes, adverse effects, and relative costs of the most commonly prescribed brands of interferon and ribavirin. The response rate was approximately 90%. Uniferon was the most frequently prescribed conventional interferon, accounting for 45%. After Uniferon were Hepaferon (30%), Ceron Alpha (15%), and Roferon (10%). Of the most commonly used brands of ribavirin, Ribazole was prescribed (50%). Physicians indicated that Uniferon and Ribazole were effective, with a lower financial burden, than most alternatives. The combination of Uniferon and Ribazole was the most cost-efficient ribavirin and interferon based regimen for the treatment of HCV in Dera Ismail Khan District. These results show that low-resource areas can successfully implement low-cost treatment plans.

**Keywords:** Cost-effectiveness; Ribavirin; Pegylated interferon; Interferon; Hepatitis C Virus.

### Introduction

Hepatitis is an inflammatory disorder of the liver caused by multiple factors contributing to the chief cause of viral infections (Tillman, 2014). Hepatitis A, B, C, D, and E, lead to the highest prevalence of viral infections globally, and of these, Hepatitis C is most severely problematic by virtue of liver-related chronic conditions, cirrhosis and, in some cases, lead to liver cancer (hepatocellular carcinoma) (Riaz et al., 2011; Khan et al., 2022).

HCV infects an estimated 170 million patients worldwide, with the highest concentration of patients belonging to low and middle-income countries, like Pakistan (Fang et al., 2022). The

transmission of HCV mainly results from exposure to infected blood, which can stem from an inadequate blood transfusion, multiple usages of infected syringes, and the sharing of needles (Echeverría et al., 2015).

Pakistan has an estimated HCV prevalence of nearly 6%, contributing to the growing number of end-stage liver disease and liver cancer cases (Raja et al., 2019). Genotype 3 is the most prevalent strain across the country, whereas genotypes 2 and 3 are frequently found in Khyber Pakhtunkhwa (Umar et al., 2016). The HCV early infection stages typically present no symptoms; however, disease progression may trigger fatigue, jaundice, cirrhosis, and hepatic failure (Iftikhar et al., 2020).

In developing nations, the main stay treatment of HCV, has historically centered around conventional interferon (IFN), pegylated interferon (Peg-IFN), and ribavirin (Sulkowski et al., 2004; Irekeola et al., 2022). These regimens are effective, but are associated with high costs, treatment length, and complications, restricting their use in poorer areas, like District Dera Ismail Khan (Deborah et al., 2005; Seth et al., 2005).

Evaluating the cost-effectiveness of generic interferon and ribavirin, given to patients of District Dera Ismail Khan, aids evidence based clinical and policy decisions in Pakistan. This study focuses on assessing the physician-reported clinical outcomes and economic impacts of commonly prescribed interferon-and ribavirin-based therapies in District Dera Ismail Khan.

### **Problem statement**

In District Dera Ismail Khan, the infection of hepatitis C virus is a problem for the public's health, especially for the residents of district Dera Ismail Khan because of the use of Interferon treatments but the cost is very high, which limits a lot of people from being able to receive the treatments. There is very little local data that compares the cost versus effectiveness of available generic formulations for the use of interferon and Ribavirin. Given the description, and in order to minimize the burden and optimize the care, the best available options need to be evaluated (Tandon et al., 2021).

### **Study Objectives**

1. To evaluate the clinical impact of interferon, pegylated interferon, and ribavirin therapy among patients with hepatitis C in District Dera Ismail Khan.
2. To assess the cost-effectiveness of various generic brands of interferon and ribavirin based on physician-reported data.
3. To examine changes in hematological and biochemical parameters during interferon-and ribavirin-based therapy.

### **Materials and Methods**

#### **Study Design and Setting**

#### **Study Location**

In the District Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan, a descriptive cross-sectional study was carried out which included both public and private health care facilities.

#### **Study Population**

Participants included physicians actively involved in the management of hepatitis C patients. In clinical evaluations, adult patients ( $\geq 18$  years) who were diagnosed with HCV were included. Patients who had hepatitis B or were co-infected with HIV were excluded.

#### **Data Collection**

Thirty physicians completed a structured questionnaire regarding treatment options and brand-related perceptions of efficacy, side effects, and costs of ribavirin and interferon. Incentive visits were used to improve the participation and to achieve a response rate of 90%.

### Evaluated Treatment Options

1. Conventional interferon: Roferon, Ceron Alpha, Hepaferon, Uniferon
2. Pegylated interferon: Pegasys, Unipeg
3. Ribavirin: Novia, Viron, Zolox, Ribazole

### Clinical Outcomes and Cost-Effectiveness

Based on the clinical outcomes related to the adverse effects and the changes in the blood picture, and the liver enzyme activities, the physicians evaluated the clinical outcomes. The clinical outcomes to price ratio was used to assess cost-effectiveness.

### Ethical Considerations

This research was granted ethical approval by the local ethics committee. The participation was on a voluntary basis and was kept confidential.

### Statistical Analysis

SPSS was used for the analysis of the data. The descriptive statistics which included frequencies and percentages were computed.

## Results

### Physician Response Rate

30 questionnaires were sent to physicians treating hepatitis C patients in District Dera Ismail Khan. 27 were filled out and sent back, leading to a 90% response rate. Response rate for specialist physicians were marginally better at 93% than for general practitioners at 86%, showing good participation from both clinical groups.

**Table 1. Questionnaire distribution and physician response rate.**

Total Questionnaires	Specialists (%)	General Practitioners (%)	Overall Response (%)
30	13 (93%)	14 (86%)	90%

Since so many doctors answered the survey, and since the answers are so representative of the actual state of the prescription practice and the economics of managing hepatitis C, we can state these results with confidence.

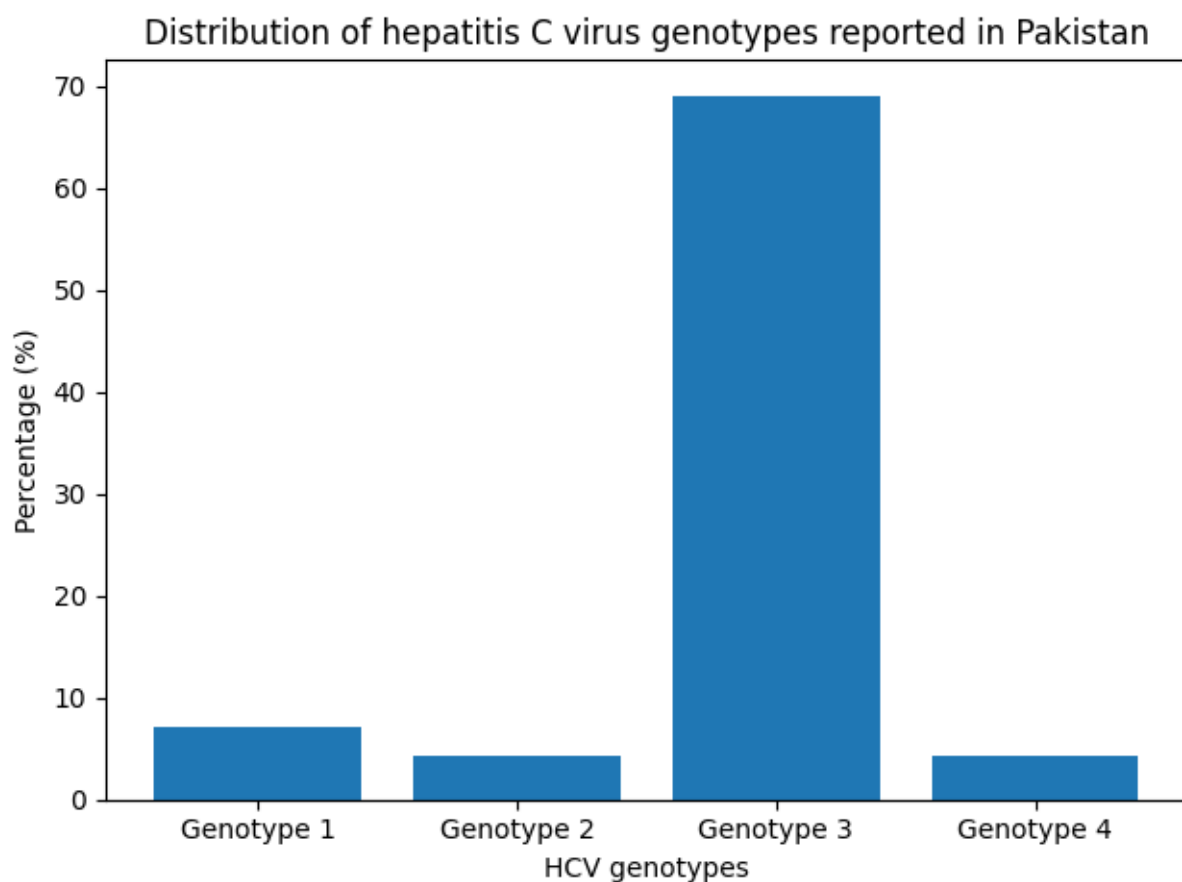
### Distribution of Hepatitis C Virus Genotypes.

69.1% of physicians surveyed considered Geno type 3 hepatitis C virus to be the most prevalent. Genotypes 1 and 2 were present in fewer respondents, and Genotype 4 was the least prevalent.

**Table 2. Distribution of hepatitis C virus genotypes reported in Pakistan.**

Genotype	Percentage (%)
Genotype 1	7.1
Genotype 2	4.2
Genotype 3	69.1
Genotype 4	4.2

Judging by how common the genotype 3 variation is, there is a clinical reason to justify the use of standard interferon-based treatment regimens, which are effective and inexpensive for this genotype in Pakistan.



**Figure 1.** Distribution of hepatitis C virus genotypes reported in Pakistan.

#### **Physician Preference for Interferon and Ribavirin Brands**

Of all the standard interferon brands, the most prescribed Uniferon (45%) followed by Hepaferon (30%), Ceron Alpha (15%) and Roferon (10%). Ribavirin therapy showed that Ribazole was the most preferred by half the physicians while the use of Viron, Zolox and Novia, was considerably less.

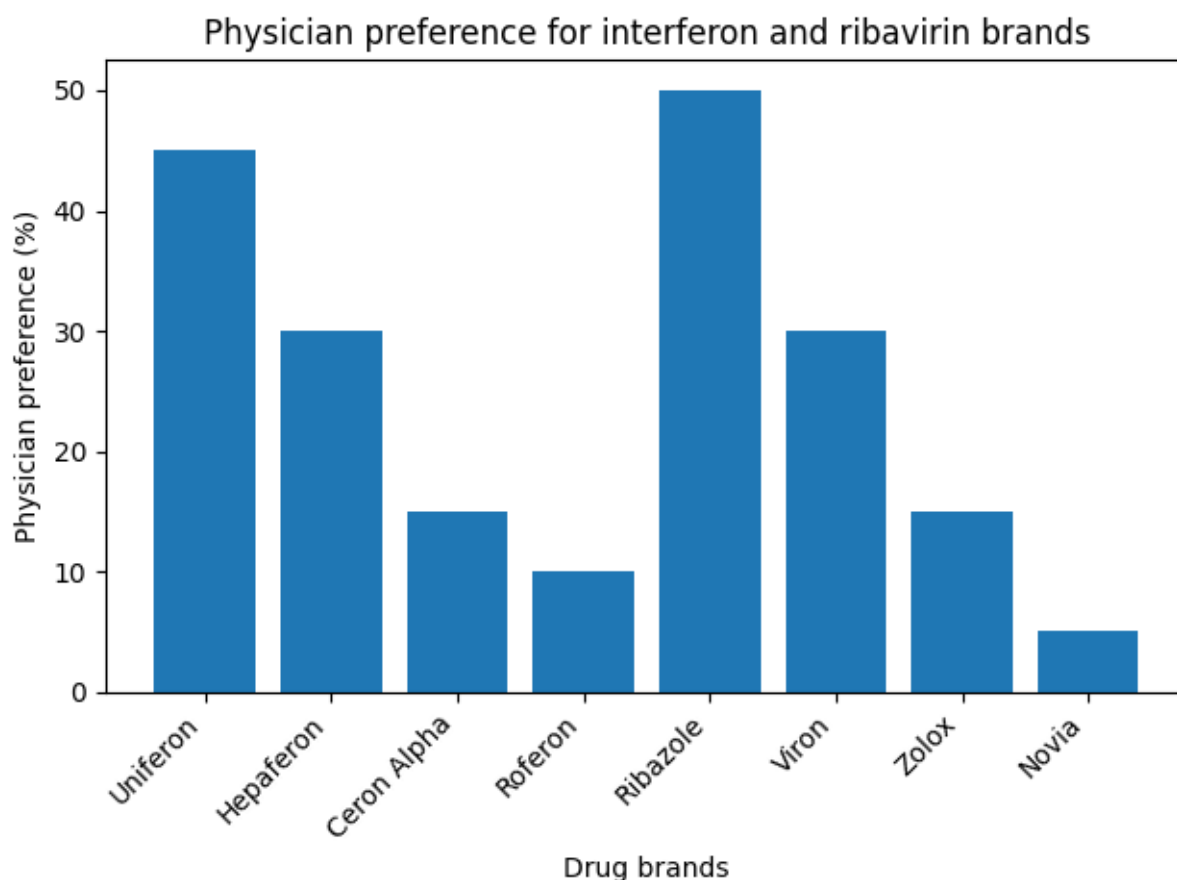
**Table 3. Physician preference for conventional interferon brands.**

<b>Brand</b>	<b>Percentage (%)</b>
Uniferon	45
Hepaferon	30
Ceron Alpha	15
Roferon	10

**Table 4. Physician preference for ribavirin brands.**

<b>Brand</b>	<b>Percentage (%)</b>
Ribazole	50
Viron	30
Zolox	15
Novia	5

Physician preference for Uniferon and Ribazole suggests a balance between perceived therapeutic efficacy, affordability, and availability in the local healthcare market.



**Figure 2.** Physician preference for interferon and ribavirin brands used in hepatitis C treatment.

#### **Cost Comparison of Interferon and Pegylated Interferon Brands**

Different brands of interferon have different prices. The most affordable regular interferon was Uniferon and Roferon was the most pricey. For pegylated interferon, Unipeg was a lot cheaper than Pegasys.

**Table 5. Retail price comparison of conventional interferon brands.**

Brand	Manufacturer	Price (PKR)	Strength
Uniferon	Getz Pharma	550	3 MIU
Ceron Alpha	Bio Care Pharma	700	3 MIU
Roferon	Roche Pakistan	1074	3 MIU
Hepaferon	Pharmadic Pharma	590	3 MIU

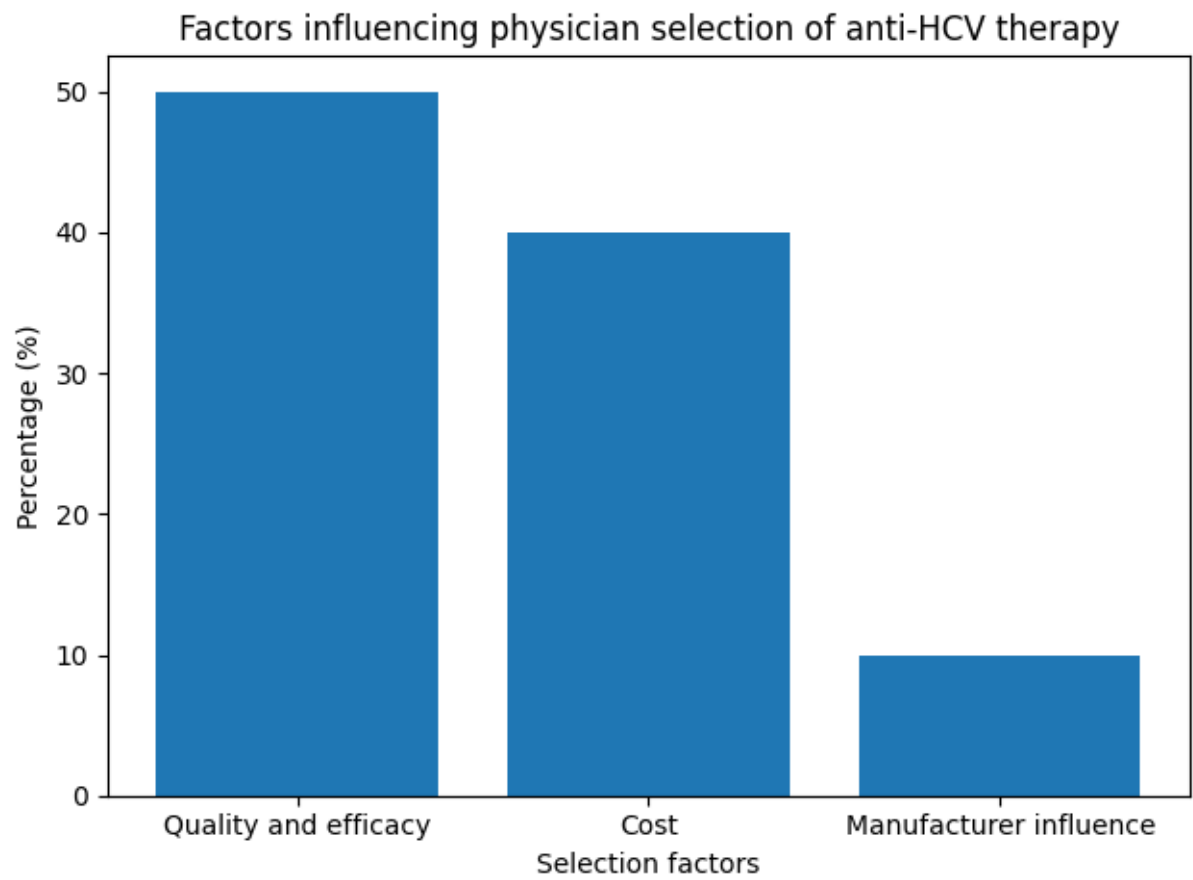
**Table 6. Retail price comparison of pegylated interferon brands.**

Brand	Manufacturer	Price (PKR)	Dose
Unipeg	Getz Pharma	8165	180 mcg
Pegasys	Roche	13000	180 mcg

Uniferon and Unipeg are cheaper options that are more likely to be used in low cost treatment settings where the ability to afford treatment heavily impacts what is prescribed.

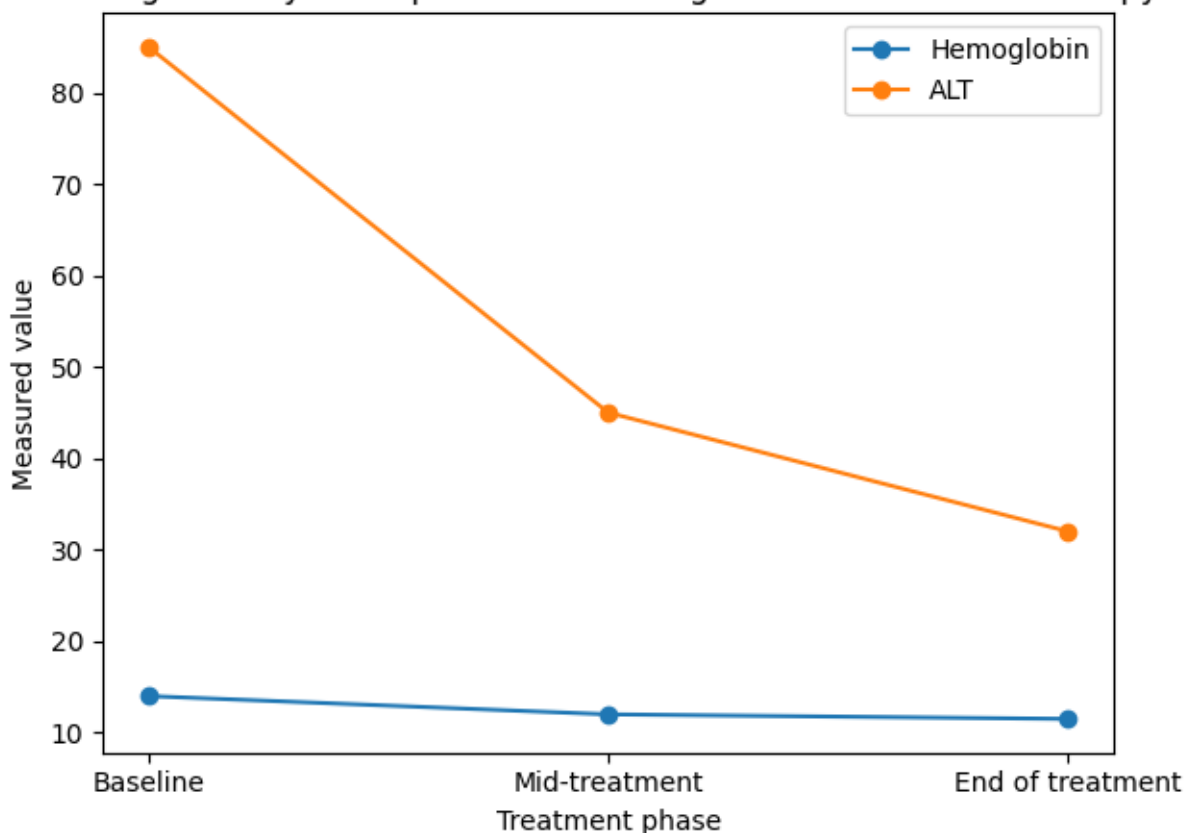
#### **Barriers to the Selection of Drugs and Clinical Factors**

Due to the lack of marketing and advertising by pharmaceutical companies, physicians have the freedom to choose drugs, and most believe that drug quality and effectiveness are the biggest motivators in treating a patient followed by cost. Most patients were treated on an out patient basis and lab monitoring showed routine changes that are expected with treatment, including small decreases in hemoglobin and an achievement of normal values for alanine aminotransferase (ALT) during treatment.



**Figure 3.** Factors influencing physician selection of anti-HCV therapy, including quality, cost, and manufacturer influence.

### Changes in key blood parameters during interferon-ribavirin therapy



**Figure 4.** Changes in key blood parameters (hemoglobin and alanine aminotransferase levels) during interferon-ribavirin therapy.

It is important to note that there are significant economic influences for prescribing that are considered hematological and biochemical changes. Changes that support the use of the interferon-ribavirin regimen continue to be utilized as an outpatient service.

### Discussion

This study was conducted in a resource-constrained region of District Dera Ismail Khan to analyze the costs and effectiveness of therapies that include both interferon and ribavirin for the management of hepatitis C. Given the results of the study, it was determined that the combination of Uniferon, a more economical generic interferon, with Ribazole offers the best economic and therapeutic solution. These results confirm previous work that has highlighted the need for cost-sensitive approaches toward treatment in low-resource settings (Singh et al., 2020; Liu et al., 2021).

While studies have found that pegylated interferon-based treatments may lead to a higher sustained virological response, the increased costs, adverse effects, and limited accessibility in low-resource settings are significant barriers (Linan et al., 2023; Hayashi et al., 2021). In the analysis conducted by Singh et al., (2020), pegylated interferon was mainly used for paying patients with genotypes 1 and 2, while for genotype 3, due to economic reasons, the use of conventional interferon was more significant (Umar et al., 2016).

Some patients on interferon-ribavirin therapy may develop mild leukopenia and anemia, and although such hematological adverse events are manageable in the outpatient setting, they are characteristic of the toxicity profile of ribavirin and are explained in the literature (Sulkowski and others, 2004). These observations allow us to conclude that interferon-based regimens can continue to be used in areas where the latest antiviral agents cannot be obtained.

From this perspective, the purchase and subsidization of the Uniferon and Ribazole generics in the most cost-effective markets would increase the treatment coverage and decrease the burden of disease in the most disadvantaged areas (Tandon et al., 2021).

### Conclusion and Recommendations

In the District Dera Ismail Khan, Uniferon with Ribazole can be considered the most economical interferon-based therapy available for patients with hepatitis C. It is advisable that the government health authorities facilitate the access by the people to such therapies by making them subsidized or available for free, in order to achieve the better public health results. A recommendation for further study is to include patient level outcome indicators.

### References

- Deborah, L., Smith, J., & Allen, R. (2005). Absorption and pharmacokinetics of interferon. *Pharmacology Research*, 25(4), 79–86.
- Echeverría, M., de la Fuente, A., & Pérez, J. (2015). Transmission routes of hepatitis C virus. *Journal of Clinical Microbiology*, 53(9), 3050–3055.
- Fang, Y., Liu, H., & Wang, X. (2022). Hepatitis C virus: Clinical implications and management. *Liver Disease Review*, 28(2), 103–115.
- Hayashi, K., Tanaka, Y., & Itoh, Y. (2021). Economic outcomes of interferon and ribavirin treatment in Japan. *Journal of Hepatology*, 75(3), 568–577.
- Iftikhar, S., Ahmad, R., & Malik, A. (2020). Symptoms and progression of chronic hepatitis C. *Liver Disease Journal*, 24(3), 189–197.
- Khan, A., Shah, N., & Ali, S. (2022). Hepatitis C in Pakistan: Prevalence and management. *Pakistan Journal of Medical Sciences*, 38(4), 245–250.
- Linas, B. P., Barter, D. M., & Leff, J. A. (2023). Cost-effectiveness analysis of pegylated interferon and ribavirin for hepatitis C treatment. *Journal of Viral Therapy*, 19(1), 45–52.
- Liu, Y., Zhang, W., Chen, X., & Li, J. (2021). Cost implications of interferon-based therapies in LMICs. *Hepatology International*, 15(4), 623–630.
- Raja, A., Khan, M., & Hussain, Z. (2019). Hepatitis C prevalence in Pakistan. *Journal of Epidemiology*, 29(7), 1123–1131.
- Riaz, A., Javed, S., & Ahmad, N. (2011). Hepatitis C and liver complications. *World Journal of Hepatology*, 3(9), 288–296.
- Singh, R., Verma, P., & Sharma, S. (2020). Economic impact of interferon-based therapies in India. *Indian Journal of Hepatology*, 32(5), 70–76.
- Sulkowski, M. S., McHutchison, J. G., & Fried, M. W. (2004). Ribavirin and interferon combination therapy in hepatitis C. *American Journal of Gastroenterology*, 99(6), 956–964.
- Tandon, S., Akhtar, M., & Qureshi, H. (2021). Cost-utility of interferon-based treatment in Pakistan. *Pakistan Journal of Gastroenterology*, 26(4), 112–118.
- Tillman, H. L. (2014). Hepatitis and liver inflammation. *Clinical Liver Disease*, 18(3), 1–10.
- Umar, M., Bilal, M., & Khokhar, N. (2016). Hepatitis C genotype distribution in Pakistan. *Pakistan Journal of Gastroenterology*, 25(2), 55–62.
- World Health Organization. (2022). Global hepatitis report. WHO Publications.