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*Original Article*

# Liver Insights: Probing Molecular Signatures of Hepatitis C Patients in Hospitals of Lahore- Navigating the Clinical Landscape of Viral Infection and Organ Profiling

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***Conflict of Interest: None.***

*Batool A., et al. (2024). 4(1): DOI: https://doi.org/10.61919/jhrr.v4i1.565*

## ABSTRACT

Background: Hepatitis C virus (HCV) infection is a major public health problem, leading to chronic liver diseases, cirrhosis, and hepatocellular carcinoma. The disease burden is particularly high in developing countries, with significant gender disparities and varied outcomes across different clinical settings.

Objective: The study aimed to assess the prevalence of HCV infections, analyze the clinical correlation of demographic factors with patient outcomes, and examine the age-related duration of hospital stays in a Pakistani cohort.

Methods: A cross-sectional retrospective study was conducted on 230 symptomatic liver patients from three major hospitals in Lahore. Inclusion criteria were based on HCV-related liver conditions, excluding post-liver transplant patients. Data on viral load detections were obtained via semi-automated RT-PCR with commercially available kits. Statistical analysis was performed using SPSS version 25 and GraphPad Prism 9.0 to determine frequency distributions, cross-tabulation analyses, and Pearson correlation coefficients.

Results: Out of the 230 patients, 69% (158) were male, and 31% (72) were female. Age distribution showed 36.7% (58) of males were over 60 years, and 63.3% (100) under 60 years; 55.6% (40) of females were over 45 years, with 44.4% (32) under 45 years. Most referrals came from the Pulmonary ward (35%), followed by the Surgery (30%) and Gastroenterology (20%) wards. HCV RNA detection was positive in 67% (154) of the patients. Cross-tabulation analysis indicated a mortality rate of 39% in the Pulmonary ward. A significant positive correlation ($r=0.494$, $p<0.000$) was observed between patient age and days of hospital stay.

Conclusion: The study demonstrates a higher prevalence of HCV in males and a notable age-related impact on the duration of hospitalization. Interdisciplinary approaches and gender-sensitive healthcare interventions are essential for effective HCV management.

Keywords: Hepatitis C, Prevalence, Gender Disparity, Viral Load Detection, Hospitalization Duration, Cross-Sectional Study, Pakistan, Hepatology, Public Health, Epidemiology.

## INTRODUCTION

Hepatitis C virus (HCV), a member of the Flaviviridae family and genus Hepacivirus, is a small, enveloped RNA virus responsible for causing both acute and chronic liver diseases, such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma (1). Globally, chronic HCV infection affects an estimated 58 million individuals, with around 1.5 million new infections reported annually (2). The World Health Organization highlighted that in 2019, hepatitis C was the cause of approximately 290,000 deaths, predominantly from cirrhosis and hepatocellular carcinoma(3). The challenge of hepatitis C is amplified by the absence of an effective vaccine, marking it as a significant public health concern, particularly in Pakistan (3, 4). In Pakistan, the prevalence of HCV among the adult population is estimated at 11.55%, positioning the country as having the second-highest rate of HCV infections globally. This situation is further complicated by the lack of a national registry or database system and inadequate coordination among provinces, contributing to mortality rates due to hepatitis B and C viruses of 563,000 and 366,000 annually, respectively(4).

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HCV is often described as a "silent epidemic" due to its capacity to progress insidiously, with many individuals remaining asymptomatic for extended periods(5). This silent progression hinders early detection and effective intervention, allowing the virus to establish chronic infections that can lead to severe liver complications, including cirrhosis and hepatocellular carcinoma, over time (5). The virus's ability to persist in the liver for long durations without eliciting noticeable symptoms presents significant challenges in the early detection and management of the disease (6). HCV's transmission through blood exposure, unsafe medical practices, sexual activities, unscreened blood transfusions, and from mother to child during childbirth further emphasizes the critical need for enhanced preventive measures and screening protocols(9).

At the molecular level, HCV is characterized by a single open reading frame flanked by highly conserved untranslated regions (UTRs), which are crucial for the virus's polyprotein translation and genome replication (7). Despite challenges in studying the virus due to the lack of a productive cell culture system, structural analyses of HCV components have shed light on the molecular mechanisms underlying polyprotein processing, RNA replication, and virion assembly, offering valuable insights into the virus's pathogenesis and informing the development of targeted therapies and diagnostic tools (8).

This study aims to explore the prevalence of HCV infections among symptomatic patients in the medical and gastroenterology wards of Lahore hospitals, assessing the clinical correlations with various significant statistical confounders (9, 10). By providing a comprehensive overview of HCV's impact within the clinical landscape, the research seeks to deepen our understanding of the virus's epidemiology, molecular characteristics, and implications for patient care and public health strategies. Through meticulous assessment and analysis, the study aspires to contribute crucial insights toward the global efforts to combat hepatitis C, with the ultimate goal of diminishing its burden on public health.

## MATERIAL AND METHODS

The study adopted a cross-sectional retrospective design, meticulously planned to evaluate the prevalence and clinical correlations of Hepatitis C virus (HCV) infections among liver patients. A total of 230 patients were selected through consecutive sampling, focusing on those exhibiting symptoms of HCV-related liver conditions (11). Participants included males and females over the age of 45, encompassing both outpatient and inpatient individuals referred to or admitted in the departments of Medicine, Gastroenterology, and Hepatology at three major hospitals in Lahore: Shaikh Zayed Hospital, Fatima Memorial Hospital, and Jinnah Hospital. Notably, individuals who had undergone liver transplantation were explicitly excluded from the study to maintain the specificity of the investigated population towards natural progression and management of HCV infections (12).

Inclusion criteria were meticulously defined, centering on patients with liver conditions attributed to HCV infections, who were symptomatic at the time of the study. This approach enabled a focused examination of the disease's impact within a demographic and clinical context that is representative of the broader population afflicted by HCV in the region. The data collection hinged on the availability of HCV viral load detections, with screening for HCV RNA performed using semi-automated RT-PCR. This process utilized commercially available diagnostic kits for both extraction and amplification, ensuring a high degree of reliability and reproducibility in the detection of active viral infections (13).

For the purpose of statistical analysis, data were meticulously documented on a specifically designed performa. The analysis was conducted using SPSS version 25 and GraphPad Prism 9.0, which facilitated a comprehensive exploration of the data. Analyses included gender-wise frequency distribution of patients across different age groups, distribution of patients by referral source, detection rates of HCV RNA in symptomatic patients, and frequency distribution of disease severity among those testing positive (14). Additionally, cross-tabulation was employed to examine the relationship between disease severity and the necessity for isolation, as well as the distribution of disease outcomes among detected cases. Further analysis explored the association between patients' age and length of hospital stay among those isolated, with particular attention paid to the implications for mortality and death rates. This analytical approach allowed for a nuanced understanding of the disease's dynamics and the efficacy of current clinical practices in managing HCV infections (15).

Ethical considerations were paramount throughout the study, with all procedures performed in strict accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This included ensuring informed consent from all individual participants involved in the study, with a keen emphasis on the confidentiality of patient information and the ethical use of clinical data for research purposes. The study's methodological rigor, combined with its adherence to ethical standards, provides a comprehensive and ethically sound framework for investigating the prevalence, clinical characteristics, and outcomes of HCV infections among liver patients in Lahore.

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## RESULTS

In the study of 230 liver patients with Hepatitis C virus infections, 69% (158) were male and 31% (72) were female. Age-wise, among males, 36.7% (58) were over 60 years, and 63.3% (100) were under 60 years; for females, 55.6% (40) were over 45 years, and 44.4% (32) were under 45 years. Referral patterns revealed that most patients, 35% (21 out of 60), were from the Pulmonary ward, followed by 30% (18) from Surgery, 20% (12) from Gastroenterology, 10% (6) from Nephrology, and 5% (3) from Cardiology. Regarding HCV detection status, 67% (154) of the patients tested positive, while 33% (76) were not detected, indicating a significant prevalence and detection rate within the studied population.

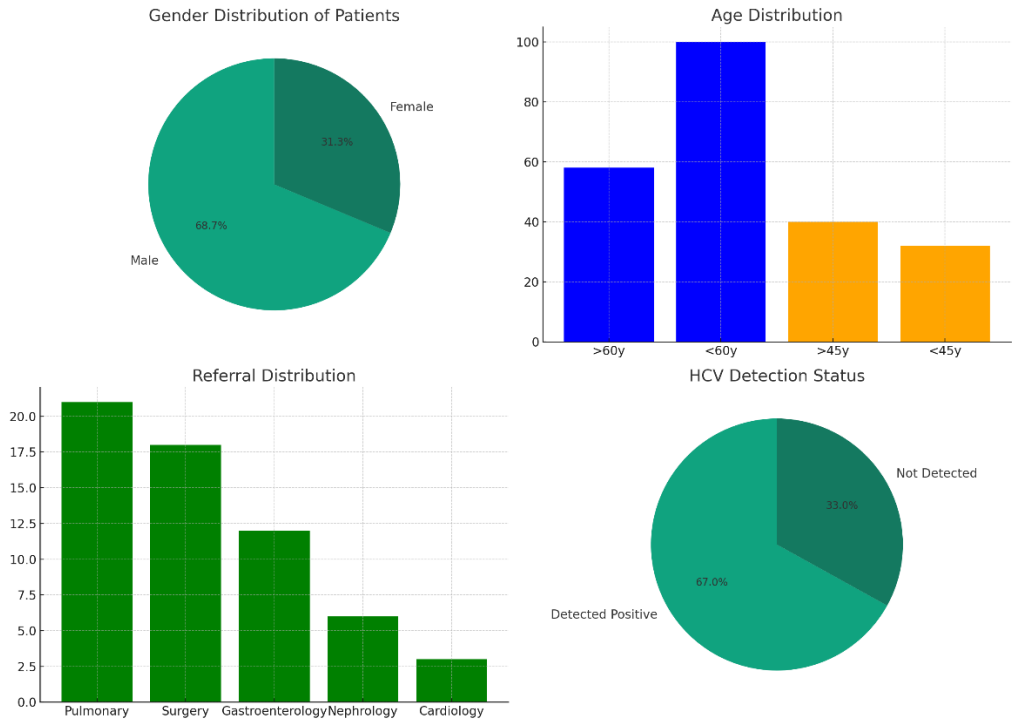


Figure 1 Demographic and Study Characteristics

In a detailed analysis of patient outcomes across different hospital wards, the study revealed distinct patterns in the cross-tabulation analysis (Table 1). Among the 154 patients considered, those from the Cardio ward had 10 patients discharged or alive compared to 8 deaths, totaling 18 cases. The Gastroenterology ward reported similar numbers, with 12 patients discharged or alive and 6 succumbing to the disease, also totaling 18. A significant finding was observed in the Pulmonary ward, where 26 patients were discharged or alive while 39 patients died, accounting for a total of 65 cases, indicating a higher mortality rate in this ward. In the Liver ward, there was an equal split with 16 patients discharged or alive and 16 deaths, summing to 32 cases. The Nephrology ward showed a favorable outcome with 12 patients discharged or alive against 2 deaths out of 14 cases. The Surgery ward reported the most positive outcomes, with all 2 patients being discharged and no deaths. Overall, the study reported 78 patients discharged or alive against 71 deaths out of the total 149 cases accounted for in this analysis.

Descriptive statistical analysis provided an average hospital stay of 27.6786 days with a standard deviation of 5.55994, across 112 patients (Table 2). This suggests a moderate variation in the length of hospital stays among the patients in the study.

Table 1: Cross-tabulation Analysis of Reference Wards & Outcome of Infection among Patients (n=154)

| Reference Ward | Discharged / Alive | Death | Total |
|---|---|---|---|
| Cardio | 10 | 8 | 18 |
| Gastro | 12 | 6 | 18 |
| Pulmonary | 26 | 39 | 65 |
| Liver | 16 | 16 | 32 |
| Nephrology | 12 | 2 | 14 |
| Surgery | 2 | 0 | 2 |
| Total | 78 | 71 | 149 |

Table 2: Descriptive Statistics

| Descriptive Statistics | Mean | Std. Deviation | N |
|---|---|---|---|
| Days of Stay in Hospital | 27.6786 | 5.55994 | 112 |

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Table 3: Correlation Analysis of Age of Patients with Days of Stay in Hospital among Isolated Patients (n=112)

| | Age of Patients | Days of Stay in Hospital |
|---|---|---|
| Pearson Correlation | 1 | .494** |
| Sig. (2-tailed) | | .000 |
| N | 112 | 112 |

Moreover, the study conducted a Pearson correlation analysis to assess the relationship between the age of patients and the duration of their hospital stay among those who were isolated (Table 3). A significant positive correlation was found (r=0.494), with a two-tailed significance of p<0.000, indicating that older patients tended to have longer hospital stays. The number of patients included in this part of the analysis was 112.

These results provide a comprehensive numerical insight into the outcomes of HCV infection across different clinical settings and the influence of patient age on hospital stay duration, highlighting areas for potential improvement in patient management and care.

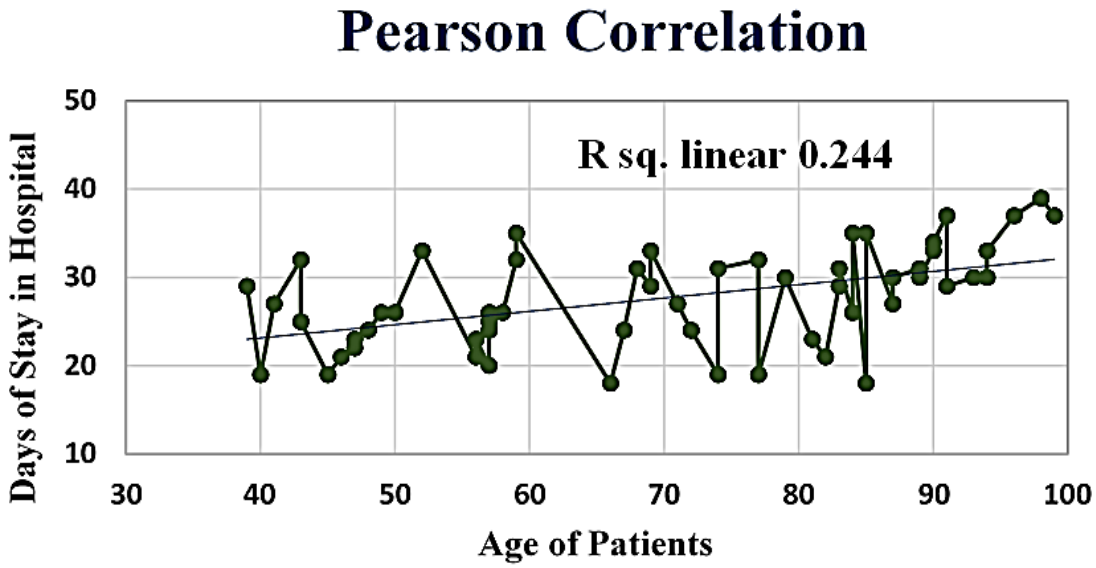


Figure 2 Hospital Stay and Age Correction

The graph presents a Pearson correlation analysis between the age of patients and the duration of their stay in the hospital. It depicts a scatter plot with individual data points representing patient ages (ranging from 30 to 100 years) against the corresponding days of hospital stay (spanning from approximately 10 to 50 days). The trend line across the data points indicates a moderate positive correlation, with an R-squared value of 0.244. This suggests that as the age of patients increases, there is a tendency for the duration of hospital stay to increase as well, although the correlation is not strong, implying that age alone does not account for all the variation in the length of hospital stays.

## DISCUSSION

The pathogenesis of Hepatitis C, a critical health concern, is characterized by the virus's entry and replication within hepatocytes, utilizing the host's cellular machinery to proliferate. This viral propagation elicits an immune response which, failing to clear the infection, leads to a chronic inflammatory state within the liver (16). The chronicity of inflammation is a precursor to liver fibrosis, as evidenced by collagen accumulation and hepatic stellate cell activation, which may ultimately progress to cirrhosis and increase the risk of liver failure and hepatocellular carcinoma (8, 13).

Reflecting on the demographic data from this study, which analyzed 230 patients, a significant gender imbalance was identified, with males constituting 69% of the patient cohort. This gender disparity in HCV prevalence necessitates a tailored approach to healthcare interventions that are sensitive to gender differences (17). A deeper analysis of the age distribution within each gender category provided a comprehensive view of the patient demographics, a necessary consideration for devising effective healthcare strategies (17).

The study highlighted the interdisciplinary nature of HCV cases, as evidenced by the diverse origins of referred patients from various hospital wards. A significant number of referrals from the Pulmonary ward, in particular, suggests a potential intersection between respiratory complications and HCV, necessitating an integrated approach to patient care that spans multiple specialties (18, 19). The contrast in patient outcomes between wards, with the Pulmonary ward exhibiting higher mortality rates and the Nephrology ward

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demonstrating a higher incidence of patient recovery, emphasizes the heterogeneity of HCV impacts across different medical contexts (19).

A thorough investigation of patient age in correlation with the duration of hospital stay revealed a moderate positive correlation (r=0.494), suggesting that older patients may experience longer hospital stays, which could have significant implications for healthcare resource allocation and patient care management, especially for those above 50 years of age (20).

The study's strength lies in its comprehensive approach to understanding the multifaceted nature of HCV infection and its outcomes. However, the study is not without limitations. The gender imbalance within the sample may have influenced the study outcomes and may not fully represent the demographics of the broader HCV-infected population. Moreover, the retrospective design may limit the ability to infer causality from the observed associations (5, 14).

In light of these findings and limitations, the study offers valuable insights for healthcare providers. It underscores the necessity of gender-specific healthcare strategies and the importance of interdisciplinary collaboration in managing HCV. Future research should aim to include a more balanced gender representation and consider prospective designs to further elucidate the complexities of HCV pathogenesis and its clinical implications (2, 10).

## CONCLUSION

In conclusion, this retrospective analysis not only sheds light on the demographic and clinical facets of HCV infection but also underscores the intricate interplay between patient characteristics and healthcare outcomes. These findings serve as a critical resource for healthcare practitioners to refine their approaches towards HCV management, with an emphasis on personalized and interdisciplinary care.

This study illuminates the intricate dynamics of Hepatitis C infection, revealing a pronounced gender disparity in prevalence and the multi-disciplinary impact of the virus across different hospital wards. The correlation between patient age and hospital stay duration underscores the need for age-specific management strategies in HCV care. While providing valuable insights for targeted healthcare interventions, the research also highlights the necessity for a more gender-balanced representation in future studies to enhance the generalizability of the findings. Consequently, these insights hold significant implications for the optimization of healthcare resources and the development of comprehensive, patient-centered approaches to managing HCV, ultimately aiming to improve patient outcomes and quality of care.

## REFERENCES

1. Ball LE, Agana B, Comte-Walters S, Rockey DC, Masur H, Kottilil S, et al. Hepatitis C virus treatment with direct-acting antivirals induces rapid changes in the hepatic proteome. Journal of Viral Hepatitis. 2021;28(11):1614-23.
2. Butterworth J, Gregoire D, Peter M, Roca Suarez A, Desandré G, Simonin Y, et al. Zine El Aabidine, A.; Guivarch, M.; Flandrau, J.-C.; et al. GOLT1B Activation in Hepatitis C Virus-Infected Hepatocytes Links ER Trafficking and Viral Replication. Pathogens 2022, 11, 46. s Note: MDPI stays neutral with regard to jurisdictional claims in published …; 2021.
3. Che Z, Zhou Z, Li S-Q, Gao L, Xiao J, Wong N-K. ROS/RNS as molecular signatures of chronic liver diseases. Trends in molecular medicine. 2023.
4. Dalzell CG, Taylor AC, White SB. New Insights on Liver-Directed Therapies in Hepatocellular Carcinoma. Cancers. 2023;15(24):5749.
5. Farhan M, Fazal F, Dave T, Butt A, Basit J, Maqbool S. National hepatitis registry in Pakistan: a dire need for hepatitis surveillance and control. Tropical Medicine and Health. 2023;51(1):41.
6. Franco S, Buccione D, Tural C, Martinez MA. Circulating microRNA signatures that predict liver fibrosis progression in patients with HIV-1/hepatitis C virus coinfections. Aids. 2021;35(9):1355-63.
7. Fujiwara N, Kubota N, Crouchet E, Koneru B, Marquez CA, Jajoriya AK, et al. Molecular signatures of long-term hepatocellular carcinoma risk in nonalcoholic fatty liver disease. Science translational medicine. 2022;14(650):eabo4474.
8. Hsu MH. Identification and Validation of a Common Molecular Signature of Progressive Fibrosis in Human Livers. 2020.
9. Huang CH, Fan JH, Jeng WJ, Chang ST, Yang CK, Teng W, et al. Innate-like bystander-activated CD38+ HLA-DR+ CD8+ T cells play a pathogenic role in patients with chronic hepatitis C. Hepatology. 2022;76(3):803-18.
10. Li H, Huang M-H, Jiang J-D, Peng Z-G. Hepatitis C: From inflammatory pathogenesis to anti-inflammatory/hepatoprotective therapy. World journal of gastroenterology. 2018;24(47):5297.
11. Lim HK, Jeffrey GP, Ramm GA, Soekmadji C. Pathogenesis of viral hepatitis-induced chronic liver disease: role of extracellular vesicles. Frontiers in Cellular and Infection Microbiology. 2020;10:587628.

Journal of Health and Rehabilitation Research 2791-156X JHRR

12. Lindqvist K, Thorin Z, Kåberg M. Real-world hepatitis C treatment outcomes and reinfections among people who inject drugs at a needle and syringe program in Stockholm, Sweden. Harm Reduction Journal. 2023;20(1):1-11.

13. Moorman AC, Rupp LB, Gordon SC, Zhong Y, Xing J, Lu M, et al. Long-term liver disease, treatment, and mortality outcomes among 17,000 persons diagnosed with chronic hepatitis C virus infection: current chronic hepatitis cohort study status and review of findings. Infectious Disease Clinics. 2018;32(2):253-68.

14. Nasir S, Majeed MI, Nawaz H, Rashid N, Ali S, Farooq S, et al. Surface enhanced Raman spectroscopy of RNA samples extracted from blood of hepatitis C patients for quantification of viral loads. Photodiagnosis and Photodynamic Therapy. 2021;33:102152.

15. Nosaka T, Naito T, Matsuda H, Ohtani M, Hiramatsu K, Nemoto T, et al. Molecular signature of hepatitis B virus regulation by interferon-γ in primary human hepatocytes. Hepatology Research. 2020;50(3):292-302.

16. Pimenov N, Kostyushev D, Komarova S, Fomicheva A, Urtikov A, Belaia O, et al. Epidemiology and Genotype Distribution of Hepatitis C Virus in Russia. Pathogens. 2022;11(12):1482.

17. Shanmuganathan M, Sarfaraz MO, Kroezen Z, Philbrick H, Poon R, Don-Wauchope A, et al. A cross-platform metabolomics comparison identifies serum metabolite signatures of liver fibrosis progression in chronic hepatitis c patients. Frontiers in Molecular Biosciences. 2021;8:676349.

18. Rafiq S, Majeed MI, Nawaz H, Rashid N, Yaqoob U, Batool F, et al. Surface-enhanced Raman spectroscopy for analysis of PCR products of viral RNA of hepatitis C patients. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2021;259:119908.

19. Shafat Z, Farooqui A, Tamkeen N, Islam A, Chaudhary AA, Alawam AS, et al. Identification of Stage-Specific Differentially Expressed Genes and Network Meta-Analysis Reveals Potential Molecular Signatures in Chronic Hepatitis E Virus Infection. 2023.

20. Poma AM, Basolo A, Bonuccelli D, Proietti A, Macerola E, Ugolini C, et al. Activation of type I and type II interferon signaling in SARS-CoV-2-positive thyroid tissue of patients dying from COVID-19. Thyroid. 2021;31(12):1766-75.