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*Research Article*

# Epidemiology and Determinant of Persistent Hepatitis C Virus Infection in an Endemic Focus of Uttar Pradesh, India

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## Abstract

Background: Hepatitis C Virus (HCV) infection is a major public health issue worldwide and its long term persistence may lead to progressive liver damage and even liver cancer in the number of cases of HCV.

Objective: In the present study we aimed to analyze the incidence of HCV infection in rural setting population of Uttar Pradesh, India in order to highlight the risk factors for continued transmission.

Materials and methods: A total of 200 patients who visited or were admitted to Sharda hospital, U.P., India were screened for HCV infection and associated comorbidities.

Results: District wise observation showed a significant prevalence of HCV in Gautam Buddha Nagar with highest rate of 39%. Of the comorbidities observed associated with HCV infection, smoking, alcohol intake, weight loss, pain in abdomen, conditions like low hemoglobin, thrombocytopenia etc emerged. Each of these factors were then observed for is possible association with HCV proteins. It was found that almost all of these had an association. In addition, environmental exposure to arsenic-contaminated drinking water was found as possible contributory factor for liver disease which may worsen the liver via oxidative stress and up regulation of TNF-$\alpha$ and subsequent progression towards fibrosis.

Conclusion: The study thus highlights need to consider minute factors occurring in patients of HCV which if not taken care of may exaggerate the liver disease conditions, leading to possibility of HCC in the future. The study also underlines the importance of integrated public health strategies such as early detection of HCV, lifestyle changes and environmental interventions to improve drinking water quality parameters.

**Keywords:** Hepatitis C Virus; Epidemiology; Oxidative Stress; HCV Proteins; Cirrhosis

## Introduction

Hepatitis C virus or HCV also known as hepatotropic RNA virus leads to Acute and Chronic Hepatitis and if prevailed for a longer time can lead to cirrhosis, decompensated liver disease and Hepatocellular Carcinoma (HCC) [1]. It belongs to the Flaviviridae family and the genus Hepacivirus. HCV is a blood-borne virus that is primarily transmitted through blood-to-blood contact, with the most common routes being injectable drug use, unsafe blood transfusions and unsanitary medical procedures [2]. In addition, sexual transmission and vertical transmission from mother to child may also contribute to the spread of the virus [3,4].

According to the World Health Organization (WHO) statistics of 2019, there were around 58 million people living with chronic HCV infection, 1.5 million were found to be newly infected people and 290,000 deaths world-wide [2]. The estimated incidence of HCV infection in India is known to be in between 0.5% to 1.5% [5]. In accordance to a study by Chaudhary and coworkers, the prevalence rate of HCV in Uttar Pradesh, India was 1.93% during the year 2014 [6].

The HCV often progresses slowly and without symptoms for many years and so may sometimes go misdiagnosed, leading to significant liver damage. Since it is a blood borne infection, hence there is a need to keep a real time check on the numericals/quantitative levels in terms of infectivity and mortality caused due to HCV infection. The lack of widespread screening, especially in rural and underserved areas, has made it more difficult to control the disease in states like Uttar Pradesh (UP), India. In the present study, we have focused on the incidence of HCV infection reported from different districts of Uttar Pradesh, India. The results from this survey will provide valuable insights into the epidemiology of Hepatitis C in this region, contributing to the broader understanding of its prevalence and risk factors in Uttar Pradesh.

**Materials and Methods**

The study comprised of hospital-based survey in the state of Uttar Pradesh. Patients visiting the Sharda Hospital, UP with various types of ailments and who were tested positive for the presence of Hepatitis C Virus (HCV) infection and Hepatocellular Carcinoma (HCC) were taken. We recorded details of 200 patients who were from different districts of Uttar Pradesh.

The inclusion criteria for the study required that participants be adults (aged 18 and above) who had not previously been diagnosed with Hepatitis C or had undergone treatment for the infection. The patients were approached during their visits to the hospital and their informed consent was obtained before participation. A structured questionnaire was used to collect data on demographic details, medical history, risk factors (such as history of intravenous drug use, unsafe blood transfusions, surgical procedures and other possible exposures) and any known symptoms associated with liver disease.

Blood samples were taken from each participant to confirm the presence of HCV infection through serological testing for anti-HCV antibodies.

**Results**

Out of the 200 study participants, 97 (48.5%) were males and 103 (51.5%) were females. Of the 75 districts present in the state of U.P., it was seen that there were 30 districts from where cases of HCV were reported. The maximum patients were from Gautam Buddha Nagar (39%), followed by Bulandshahr (19%), Amroha (11%) etc. (Fig. 1). The symptoms appearing in the patients were also recorded.

The HCV patients were also investigated for few peculiar habits such as intake of tobacco, cigarette smoking, alcohol intake etc., any type of co-morbidities existing viz; diabetes, Thrombocytopenia, Cholelithiasis, Hepatomegaly, Hypertension, weakness etc. It was observed that 60.5% of the patients complained of fatigue/body pain followed by pain in the abdominal area (53.0%) and smoking habits (52.5%) (Fig. 2, Table 1).

The age wise data indicated that fatigue/body pain, pain in the abdominal area, weight loss etc was found to be more in age group of 40-59 years in both male and female. Smoking habits was found to be more in males in the age group above 60 years, however in females, it was between 40-59 years (Table 2). Five patients were found to be diagnosed with HCC; liver cirrhosis, jaundice, blood transfusion was also observed in age group of 40-59 in few patients.

These peculiar habits found in the infected HCV patients were also attempted to correlate with the presence of HCV virus in previously reported studies. It was observed that few studies have reported role of Tobacco, Cigarette Smoking, Alcohol, Ascites, Hematemesis, Cataract, Type 2 Diabetes mellitus, Kidney calculi, Thrombocytopenia, Cholelithiasis, Gall bladder stone, Weight loss, Hepatomegaly, Weakness, Bronchial Asthma, CAD (Coronary Artery Disease), Low Hemoglobin in causation of HCV infection or HCC.

It has been reported that tobacco use can increase the viability and replication of HCV and speed up the progression of HCC by increasing the expression of DDX3 helicase, which is one of the TSE-upregulating genes found in tobacco smoke extract. HCV is

an enveloped virus like HIV; both are equally susceptible to lipid peroxidation [7]. We estimate that two lipid peroxidation byproducts, HNE (4-Hydroxy-2-Nonenal) and MDA (malondialdehyde), can interact with HCV viral proteins and alter their way of functioning. Non-structural proteins that are crucial for viral replication NS3, NS5A and NS5B could be affected. These oxidative changes may influence viral pathogenesis or impair the ability of the host to generate an effective immune response, which could lead to liver damage and persistent infection.

Cigarette Smoking can cause oxidative stress, weaken immune system and provide resistance to insulin. All of these could increase the risk of developing Hepatocellular carcinoma or HCC as a result of HCV infection [8]. Thus it can be predicted that the core protein causes inflammation and fibrosis in the liver, both of which are accelerated by oxidative stress, therefore speeding up the progression of liver disease and the formation of hepatocellular carcinoma, HCC.

Use of alcohol and its subsequent breakdown in the liver can produce free radicals that lead to oxidative stress and are a primary cause of alcohol-related hepatic cells destruction, which could worsen this virus-induced oxidative stress [9]. An HCV infection itself may cause oxidative stress, which allows the virus survive in the body. It can be inferred that the HCV core protein causes ROS production by promoting mitochondrial malfunction and Endoplasmic Reticulum (ER) stress, both of which leads to oxidative stress in the hepatocytes. Along with NS3/4A protease contributes to oxidative stress by disrupting the liver's redox balance and causing cell damage.

Ascites associated with Hepatitis c virus is a serious condition that can occur in the advanced stages of chronic hepatitis c infection, typically due to virus-induced liver cirrhosis, which leads to portal hypertension and fluid leakage into the abdominal cavity [10]. It can be inferred that as cirrhosis develops, the liver's ability to produce albumin decreases. This causes decreased serum albumin levels, which decreases plasma oncotic pressure and fluid leaks into the abdominal cavity.

Some cases of Hematemesis were also seen. When Hepatitis c virus causes liver cirrhosis, the resulting portal hypertension dilates and weakens esophageal varices, making them more prone to rupture and bleeding as pressure in the portal vein increases [11]. The Chronic HCV infection causes liver inflammation, fibrosis and eventually cirrhosis. Cirrhosis causes resistance to blood flow in the liver, resulting in high pressure in the portal vein. Genotype 1a and 1b is related with an increased risk of developing cirrhosis and HCC.

Few cases of Cataract were observed. HCV can cause severe oxidative stress within the eye lens (Convex), triggering a process of free radical generation, oxidized material accumulation and resulting into cataract development [12]. We infer that HCV proteins such as Core, NS3/4A protease and NS5A can cause cataract formation by processes likely oxidative stress, inflammation, apoptosis and Endoplasmic reticulum stress. These molecular pathways disturb the normal function of lens cells, resulting in protein aggregation, cellular damage and leads to cataract formation.

HCV infection may contribute to T2DM by causing hepatic steatosis as seen in the study. A study has been reported in Huh-7 hepatocytes wherein serine-phosphorylation of IRS-1(Insulin receptor substrate-1) was seen to increase and inhibit insulin signaling. TNF-$\alpha$ has been associated with decreased GLUT4 mRNA expression in muscle and adipose tissues, as well as lower expression of IRS-1 and PPARs (Peroxisome proliferator-activated receptor). HCV causes direct insulin signaling alterations. Hepatic fibrosis and cirrhosis are not the primary factors contributing to glucose intolerance and frank diabetes in HCV patients [13]. It can be inferred that NS5A non-structural protein particularly of HCV genotype has been demonstrated to inhibit AKT (a major kinase in the insulin signaling pathway), which is responsible for GLUT4 translocation. This inhibitor could inhibit GLUT-4 mediated glucose absorption, contributing to insulin resistance.

The HCV core protein has also been found to be more common in the kidney tubules of HCV infected patients. Hepatitis c virus, HCV activates certain enzymes such as Caspase 3, 8 and as well as 9 in the cells of the kidney tubules, which affects their ability to function properly and triggers cell death (Apoptosis). As the kidney tubule cells get damaged crystals quickly form on their surface. These crystals are taken up by the cells and gradually they can combine and grow into kidney stones [14]. We predict that HCV infection typically affects the liver, but it can also cause damage to the kidneys. Non-structural proteins such as NS3 and NS4A as well as NS5A damage mitochondrial integrity, resulting in membrane potential loss and the leakage of

mitochondrial content like cytochrome C (pro-apoptotic proteins) into the cytoplasm and further activate caspases, which are important mediators of apoptosis and inflammation.

Thrombocytopenia: The Hepatitis c virus not only produces an immunological reaction by producing antiplatelet antibodies, but also directly suppress bone marrow, leading to thrombocytopenia. Chronic HCV infection causes liver fibrosis and cirrhosis, resulting in portal hypertension, hypersplenism, platelet sequestration this leads to thrombopoietin production and endothelial dysfunction. These all factors can contribute to thrombocytopenia [15]. In HCV infection, inflammatory cytokines such as TNF-$\alpha$ (Tumour Necrosis Factor) and IL-6 (Interleukin-6) are increased, leading to liver inflammation and fibrosis and leads to rise in pressure in portal vein which produce spleen enlargement. We predict that HCV can directly impact the bone marrow which produces platelets. Proteins like NS3/4A and core may block megakaryocyte development and maturation, resulting in reduced platelet formation.

*Cholelithiasis (Gall Bladder Stone)*

Gallbladder dysfunction and altered bile composition leads to Gallstone development in Chronic Hepatic C patients. Chronic hemolysis induced by hypersplenism, hypoestrogenism changes in biliary lipid proportions, poor hepatic bile salt synthesis and transport and unconjugated bilirubin all contribute to gallstone formation in patients with Chronic liver disease, CLD. Direct HCV infection of the gallbladder could play a significant impact in gallstone development. Chronic HCV infection damages the bile ducts, increasing the chances of intrahepatic cholangiocarcinoma. HCV core protein may also cause malignant transformation of human biliary epithelial cells [16]. HCV proteins mainly Core and NS3 protein have an effect on hepatic lipid metabolism. The HCV core protein can directly impact liver cells, causing a buildup of free fatty acids and lipids in the liver known as Hepatic steatosis. It can be predicted that A lipid imbalance in the liver can alter the composition of bile, contributing to a situation in which cholesterol precipitates and forms stones. The liver's failure to effectively metabolize lipids and cholesterol may contribute to the production of gallstone.

*Weight Loss*

Weight loss in patients with chronic HCV may be associated with the enhancement of fibrosis and it will reduce hepatic steatosis due to considerable drop in hepatic stellate cells, even in these thin patients with HCV genotype 3 [17]. We infer that few viral proteins like core, NS3 and NS5A might result in muscle catabolism, a disease known as cachexia. This is characterized by weight loss, muscle mass loss and anemia and is frequently observed in chronic liver illness such as cirrhosis and severe HCV infection.

*Hepatomegaly*

Hepatomegaly can be caused by fat infiltrating the liver. Steatosis may result into liver enlargement in HCV patients. HCV can cause fat deposition in the liver and genotype 3 is linked with steatosis in the chronic HCV patients, most likely by promoting the production the production of lipid-rich VLDL (Very-low density lipoprotein) which facilitates maturation of HCV precursors by activating HCV replication and therefore contributing to steatosis [18]. We infer that HCV genotype 3 is thought to have a direct influence on lipid metabolism. Its infections cause more severe insulin resistance and increased fatty acid production, which contributes to greater rates of hepatic steatosis.

*Weakness*

The causes of the higher frequency of decreased muscle mass among chronic HCV infected patients remain unknown. Previous research has shown that individuals with cirrhosis are more likely to be underweight. These studies shown that hepatic decompensation probably produced by ascites-induced intestinal edema, disrupts absorption of macronutrients and metabolism, eventually resulting in malnutrition. In addition, the emergence of hepatic encephalopathy is typically associated with decreased in oral intake, especially protein-rich diet, which may worsen malnutrition [19]. It can be inferred that the HCV core protein has been found to cause mitochondrial dysfunction and oxidative stress in liver cells and likely muscle cells. This disruption may interfere with the production of energy in muscles, resulting in weakness.

*Bronchial Asthma*

Chronic HCV infection may modify airway inflammation, making asthmatic patients more likely to develop severe asthma. According to this study, HCV Core protein has been found to directly increase interleukin-8 expression and production in human fibroblasts. HCV core protein's direct pro-inflammatory activity may harm the airway in infected patients as interleukin-8 is a

critical inflammatory mediator that causes neutrophilic inflammation and bronchoconstriction [20]. It can be inferred that HCV proteins, especially the structural protein Core can stimulate cellular signaling pathway NF-kB (Nuclear factor kappa B) that enhance the expression of IL-8 in various tissues, including lung epithelial cells and liver. This leads to neutrophil recruitment and inflammation.

*Coronary Artery Disease (CAD)*

Hepatic steatosis has been associated to elevated inflammatory and endothelial dysfunction markers. This characteristic suggests a probable reason for an elevated risk of CAD in at least a subset of HCV-infected patients. Because inflammation and thrombosis are critical factors in the development of CAD and HCV infection is related with changes in inflammatory markers, this may represent a shared pathway that increases CAD risk. Lower lipid levels in HCV- infected individuals are considered to be produced by HCV particles binding to various lipid fractions, impaired hepatocyte assembly of very-low density lipoprotein due to microsomal transfer protein inhibition and HCV entrance into hepatocytes via LDL-C receptors [21]. We infer that HCV proteins namely Core, NS3, NS4A protease, NS5A as well as NS5B polymerase might directly influence lipid metabolism and increase the risk of atherosclerosis. The HCV core protein has been proven to have a direct effect on lipid metabolism. It can cause lipid accumulation in liver cells, which contributes to Non-Alcoholic Fatty Liver Disease (NAFLD). This condition increases the risk of atherosclerosis and cardiovascular events, such as Myocardial infarction.

*Low Hemoglobin*

Oxidative stress in severe liver cirrhosis is indicated by elevated levels of lipid peroxides and lipid hydroperoxides in red blood cells (RBCs), due to an imbalance between free radicals and antioxidant systems. This causes lipid peroxidation of phospholipid fatty acids, forming short, ionized, unsaturated fatty molecules and leads to earlier hemolysis in the RBCs of liver cirrhotic patients [22]. It can be concluded that hemolytic anemia was observed may be due to broken down of carbonic acid present in the RBC into H+ and bicarbonate ion. Bicarbonate ion is released across RBC membrane into plasma then their defined channel but H+ ions cannot come out. Now from plasma when patient chloride level increases, these chloride ions after entering into RBC through channels may form HCl into higher concentration and leads to Acidosis of Hb molecule.

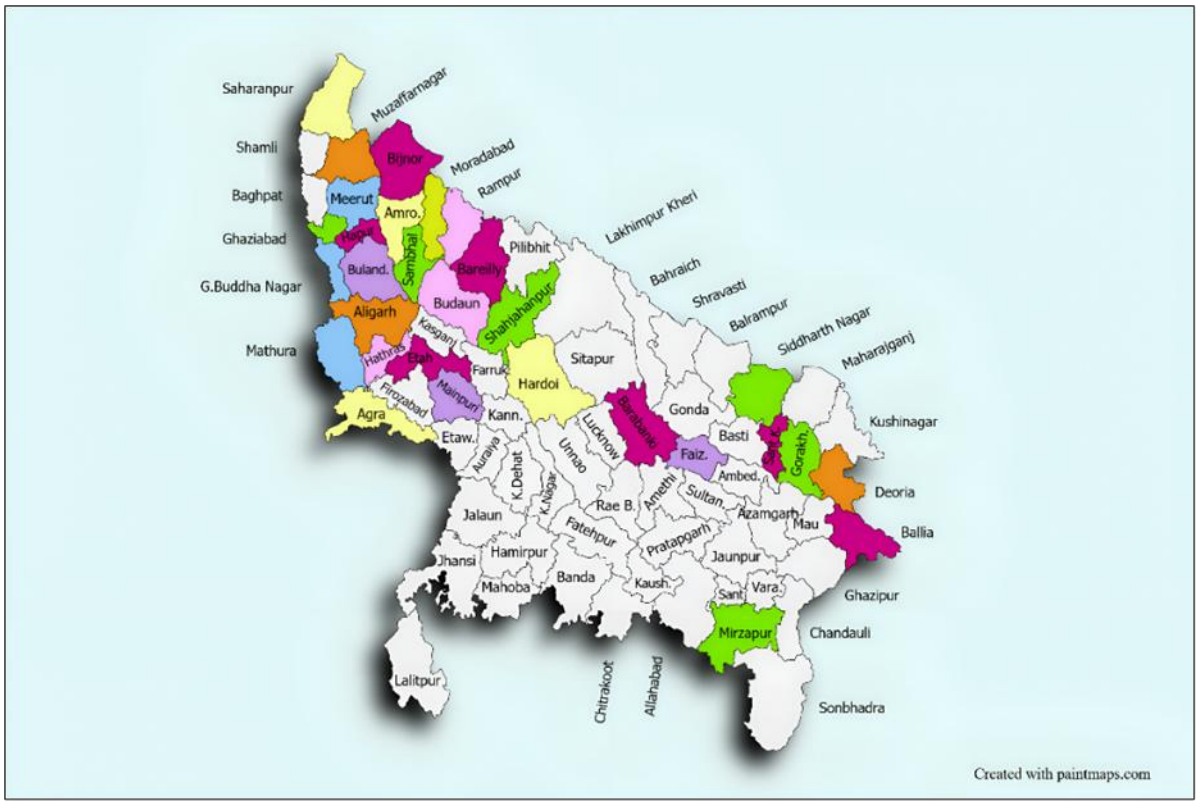


**Figure 1:** Prevalence of Hepatitis C Virus (HCV) among different districts of Uttar Pradesh, India.

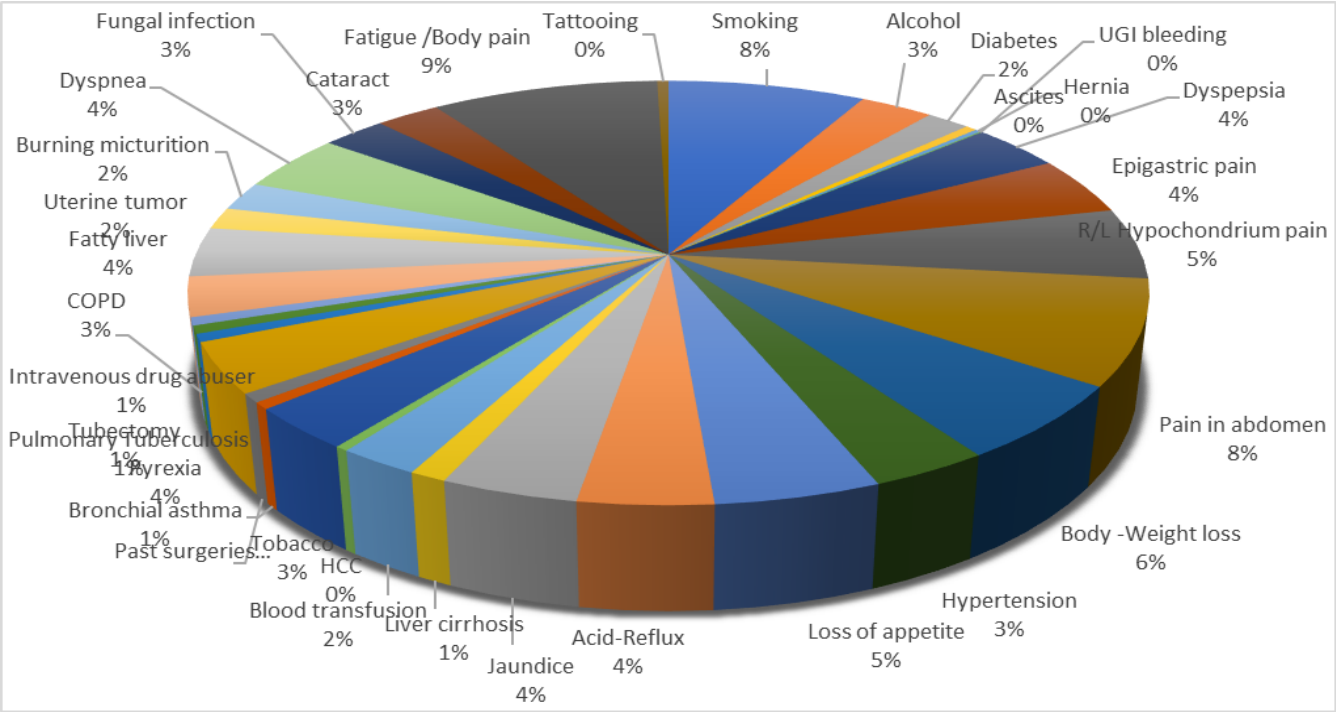


**Figure 2:** Pie chart indicating comorbidities and routine habits in patients of HCV infection.

| S.No | Habits/Co Morbidities | Total Number of Patients | % |
|---|---|---|---|
| 1. | Smoking | 105 | 52.5 |
| 2. | Alcohol | 39 | 19.5 |
| 3. | Diabetes | 23 | 11.5 |
| 4. | Ascites | 6 | 3.0 |
| 5. | Hernia | 3 | 1.5 |
| 6. | UGI bleeding | 1 | 0.5 |
| 7. | Dyspepsia | 48 | 24 |
| 8. | Epigastric pain | 59 | 29.5 |
| 9. | R/L Hypochondrium pain | 72 | 36.0 |
| 10. | Pain in abdomen | 106 | 53 |
| 11. | Body -Weight loss | 77 | 38.5 |
| 12. | Hypertension | 45 | 22.5 |
| 13. | Loss of appetite | 63 | 31.5 |
| 14. | Acid-Reflux | 51 | 25.5 |
| 15. | Jaundice | 52 | 26 |
| 16. | Liver cirrhosis | 14 | 7.0 |
| 17. | Blood transfusion | 31 | 15.5 |
| 18. | HCC | 5 | 2.5 |
| 19. | Tobacco | 43 | 21.5 |
| 20. | Bronchial asthma | 7 | 3.5 |
| 21. | Past surgeries | 9 | 4.5 |
| 22. | Pyrexia | 51 | 25.5 |
| 23. | Tubectomy | 8 | 4.0 |
| 24. | Pulmonary Tuberculosis | 8 | 4.0 |
| 25. | Intravenous drug user | 8 | 4.0 |
| 26. | COPD | 40 | 20 |
| 27. | Fatty liver | 50 | 25.0 |

| | | | |
|---|---|---|---|
| 28. | Uterine tumor | 18 | 9.0 |
| 29. | Burning micturition | 29 | 14.5 |
| 30. | Dyspnea | 58 | 29.0 |
| 31. | Fungal infection | 34 | 17.0 |
| 32. | Cataract | 34 | 17.0 |
| 33. | Fatigue /Body pain | 121 | 60.5 |
| 34. | Tattooing | 6 | 3.0 |

**Table 1:** Percentage indicating comorbidities and routine habits in patients of HCV infection.

| S.No. | Symptoms | Male N=97 (48.5%) | | | Female N=103 (51.5%) | | | Total (n=200) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 20-39 years | 40-59 years | Above 60 years | 20-39 years | 40-59 years | Above 60 years | 20-39 years | 40-59 years | Above 60 years |
| 1. | Smoking | 13 | 23 | 26 | 11 | 18 | 14 | 24 | 41 | 40 |
| 2. | Alcohol | 14 | 15 | 10 | 0 | 0 | 0 | 14 | 15 | 10 |
| 3. | Diabetes | 0 | 6 | 4 | 4 | 6 | 3 | 4 | 12 | 7 |
| 4. | Ascites | 0 | 2 | 1 | 0 | 2 | 1 | 0 | 4 | 2 |
| 5. | Hernia | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 2 |
| 6. | UGI bleeding | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| 7. | Dyspepsia | 5 | 9 | 6 | 7 | 13 | 8 | 12 | 22 | 14 |
| 8. | Epigastric pain | 8 | 11 | 7 | 7 | 18 | 8 | 15 | 29 | 15 |
| 9. | Hypochondrium pain | 9 | 13 | 9 | 11 | 21 | 9 | 20 | 34 | 18 |
| 10. | Pain in abdomen | 10 | 18 | 15 | 17 | 32 | 14 | 27 | 50 | 29 |
| 11. | Body-weight loss | 8 | 20 | 12 | 8 | 23 | 6 | 16 | 43 | 18 |
| 12. | Hypertension | 2 | 9 | 7 | 6 | 16 | 5 | 8 | 25 | 12 |
| 13. | Loss of appetite | 4 | 12 | 14 | 10 | 17 | 6 | 14 | 29 | 20 |
| 14. | Acid-reflux | 5 | 10 | 4 | 6 | 13 | 13 | 11 | 23 | 17 |
| 15. | Jaundice | 7 | 11 | 9 | 6 | 14 | 5 | 13 | 25 | 14 |
| 16. | Liver cirrhosis | 1 | 5 | 3 | 2 | 3 | 0 | 3 | 8 | 3 |
| 17. | Blood transfusion | 2 | 4 | 7 | 7 | 10 | 1 | 9 | 14 | 8 |
| 18. | HCC | 0 | 2 | 1 | 0 | 4 | 0 | 0 | 6 | 1 |
| 19. | Tobacco | 4 | 12 | 8 | 6 | 8 | 5 | 10 | 20 | 13 |
| 20. | Bronchial asthma | 1 | 2 | 2 | 1 | 1 | 0 | 2 | 3 | 2 |
| 21. | Past surgeries | 1 | 3 | 2 | 0 | 1 | 2 | 1 | 4 | 4 |
| 22. | Pyrexia | 7 | 9 | 8 | 7 | 12 | 8 | 14 | 21 | 16 |
| 23. | Tubectomy | 0 | 0 | 0 | 4 | 4 | 0 | 4 | 4 | 0 |
| 24. | Pulmonary Tuberculosis | 2 | 2 | 3 | 1 | 1 | 0 | 3 | 3 | 3 |
| 25. | Intravenous drug user | 4 | 2 | 1 | 0 | 1 | 0 | 4 | 3 | 1 |
| 26. | COPD | 3 | 7 | 11 | 6 | 11 | 2 | 9 | 18 | 13 |
| 27. | Fatty liver | 4 | 12 | 9 | 5 | 11 | 9 | 9 | 23 | 18 |
| 28. | Uterine tumour | 0 | 0 | 0 | 5 | 6 | 7 | 5 | 6 | 7 |
| 29. | Burning micturition | 4 | 4 | 5 | 3 | 10 | 3 | 7 | 14 | 8 |
| 30. | Dyspnea | 9 | 11 | 12 | 5 | 13 | 8 | 14 | 24 | 20 |
| 31. | Fungal infection | 3 | 6 | 6 | 4 | 13 | 2 | 7 | 19 | 8 |
| 32. | Cataract | 4 | 6 | 7 | 4 | 6 | 7 | 8 | 12 | 14 |
| 33. | Fatigue / Body pain | 13 | 21 | 18 | 19 | 37 | 13 | 32 | 58 | 31 |
| 34. | Tattooing | 2 | 2 | 1 | 0 | 1 | 0 | 2 | 3 | 1 |

**Table 2:** Age wise distribution of habits/co-morbidities observed among patients of HCV.

## Discussion

HCV remains a serious public health concern worldwide, with India, particularly Uttar Pradesh, bearing an enormous burden due to the infection's high incidence. The present study highlights Gautam Buddha Nagar with a population of 147,000 exhibiting the highest prevalence of HCV (39%), followed by Bulandshahr (323,000 population) (19%) and Amroha (288,000 population) (11%) and Sambhal (321,000 population) (6.5%). The key risk factors found here were tobacco use, alcohol intake, loss of body weight, improper medical practices such as infected or used needle sharing or incorrect blood transfusion which were found mostly in the male and female patients in the age group of 40-59 years. In addition to these risk factors, these areas have arsenic-contaminated drinking water as per previous studies.

When we studied all the factors for their possible correlation with HCV proteins, then almost all of these had been documented in the past. Studies have demonstrated that Arsenic exposure increases the production of Reactive Oxygen Species (ROS) and upregulates inflammatory cytokines such as Tumor Necrosis Factor alpha (TNF-$\alpha$) and has been shown to disrupt the function of hepatic stellate cells, which plays an imperative role in liver fibrosis, thus potentiating the liver's susceptibility to the fibrotic and carcinogenic effects of HCV [23]. Arsenic content was higher in these districts of U.P. like Bahraich, Ghazipur, Gorakpur, Bareilly and Chandauli than other districts which is >50 ppb [24].

## Conclusion

We thus conclude the need for a comprehensive strategy involving appropriate healthcare infrastructure in the rural areas, better infection control, knowledge dissemination about HCV and on lifestyle changes, hygiene measures as a step towards reducing the burden of HCV and its progression to severe liver diseases such as HCC in the state of Uttar Pradesh.

## Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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The authors have no acknowledgments to declare.

## Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

## Ethical Statement

The study was approved by the Ethics Committee of Sharda University, India (ID No. SU/SMS&R/76-A/2021/40).

## Informed Consent Statement

Informed consent was obtained from all participants included in the study.

## Authors' Contributions

VJ, BA and AA conceptualized the research work, VJ, BA, RC, AA, JJ, BMS, BS prepared the work plan, RC, AC, KK, MD, BMS, BS, JJ did the Data Collection and Processing; VJ, BA, AA, RC, AC, KK, MD, JJ, BMS and BA conducted the analysis and data Interpretation; RC, AC, KK, MD, PS, JJ did the Literature Search; VJ, BA, RC, AA did the first manuscript writing; VJ, BA, RC, AA, JJ, AC, KK, MD, BMS, BS did the final reviewing of manuscript:

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