Japanese Journal of Gastroenterology and Hepatology[R] ISSN 2435-1210|Volume 11

Case Report Open Access

Uncommon Extrahepatic Manifestations in Hcv

Parveen Malhotra, Chitrakshi Bhardwaj, Shivanshu Kaushik, Himanshu, Rajasvi Khuranna, Rahul Siwach, Pranav Malhotra and Anuj Sharma

Department of Medical Gastroenterology, PGIMS, Rohtak Haryana and VMMC & Safdarjung Hospital, New Delhi, India

***Corresponding author:**

Parveen Malhotra,
128/19, Civil Hospital Road, Rohtak, Haryana, India

Received: 03 Dec 2025
Accepted: 15 Dec 2025
Published: 31 Dec 2025
J Short Name: JJGH

Keywords:

Hepatitis B; Dry Mouth; Oral Ulcers; Diabetes Mellitus; Hypothyroidism; Lichen Planus; Aplastic Anemia; Rheumatoid Factor

Citation:

Parveen Malhotra, Uncommon Extrahepatic Manifestations in Hcv. Japanese Jour of Gastro and Hepatology® 2025; V11(1): 1-4

1. Abstract

1.1. Introduction

Approximately 130-170 million people, or 3% of the world's population, are chronically infected with the hepatitis C virus (HCV). It is a major public health problem, with an estimated 3-4 million people infected each year worldwide. Extrahepatic manifestations of HCV are conditions affecting organs outside the liver, most of which are immune-mediated. These can include cryoglobulinemia, various skin disorders like porphyria cutanea tarda and lichen planus, kidney diseases, type 2 diabetes, lymphomas, and cardiovascular issues. Successful HCV treatment with direct-acting antivirals can improve or prevent these complications, making antiviral therapy an urgent consideration for patients with these manifestations.

1.2. Aim of Study

To estimate prevalence of Extrahepatic manifestations of Chronic HCV infection in respect to Dermatological, Haematological, Endocrinological and Dental involvement at tertiary care centre of Northern India.

Material and Methods- This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over one year, from 01.11.2024 to 31.10.2025, during which 1000 confirmed hepatitis C patients were evaluated for Dermatological, Haematological, Endocrinological and Dental involvement or problems. All hepatitis B patients were confirmed on HbsAg on Enzyme linked immunosorbent assay (ELISA) test and HCV RNA Quantitative on Polymerase chain reaction test (PCR).

1.3. Observation and Results

On prospective analysis of 1000 confirmed hepatitis C patients, males were 680 (68%) and females were 320 (32%). Out of total pool of 1000 HBV patients, 81 patients (8.1%) were having dental involvement in form of dry mouth and oral ulcers. Out of these total 81, 43 patients (53.08%) were having dry mouth and 38 patients (46.92%) were having complaints of oral ulcers. In total pool of 1000 HBV patients, 72 patients (7.2%) were diabetics, 20 patients (2%) were having hypothyroidism and 50 patients (5%) were hypertensive. Lichen Planus and aplastic anaemia was not seen in any patient. Rheumatoid Factor positivity was seen in 270 patients (27%).

1.4. Conclusion

The hepatitis C patients need to be evaluated not only from hepatic point of view but also its extra hepatic impact, of which dermatological, haematological, endocrinological, dental and musculoskeletal system are integral part. In Northern India, as per our observations, rheumatoid factor positivity, dry mouth, oral ulcers and diabetes mellitus are more commonly seen than aplastic anaemia or lichen planus which are almost negligible but these findings require confirmation on large scale studies.

2. Introduction

Globally Viral hepatitis is now recognized as a major public health challenge as it caused 1.34 million deaths in 2015, a number comparable to deaths caused by tuberculosis and higher than those caused by HIV]1]. It is estimated that 325 million people worldwide are living with chronic HBV or HCV infection [2]. Viral hepatitis is increasingly being recognized as a public health problem in India. It is known that chronic hepatitis C (CHC) can lead to cirrhosis and hepatocellular carcinoma. The main site of HCV replication is in hepatocytes, which explains the significant liver damage that it causes. However, it is well known that the virus is not hepatotoxic, and the majority of the injury in the liver is caused by a cell-mediated immune reaction against infected liver cells. Similarly, immune abnormalities resulting in autoimmunity may be involved in the development of extrahepatic manifestations (EMs). EMs of CHC can be classified by the affected organ, system, or pathological mechanism. However, the strength of accessible evidence linking them to CHC varies [3]. The clinical presentation of patients with CHC range from subclinical cases to very serious immunological

diseases. Indeed, sometimes, autoimmune manifestations linked to HCV infection led to the diagnosis of HCV infection [4].

2.1. Aim of Study

To estimate prevalence of Extrahepatic manifestations of Chronic HCV infection in respect to Dermatological, Haematological, Endocrinological and Dental involvement at tertiary care centre of Northern India.

2.2. Material and Methods

This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over one year, from 01.11.2024 to 31.10.2025, during which 1000 confirmed hepatitis C patients were evaluated for Dermatological, Haematological, Endocrinological and Dental involvement or problems. All hepatitis B patients were confirmed on HbsAg on Enzyme linked immunosorbent assay (ELISA) test and HCV RNA Quantitative on Polymerase chain reaction test (PCR).

2.3. Observation and Results

On prospective analysis of 1000 confirmed hepatitis C patients, males were 650 (65%) and females were 350 (35%). Out of total pool of 1000 HCV patients, 106 patients (10.6%) were having dental involvement in form of dry mouth and oral ulcers. Out of these total 106, 53 patients (5.3%) were having dry mouth and 53 patients (5.3%) were having complaints of oral ulcers. In total pool of 1000 HCV patients, 90 patients (9%) were diabetics, 53 patients (5.3%) were having hypothyroidism. Lichen Planus was seen only in 1 patient (0.1%) and aplastic anaemia was not seen in any patient. Rheumatoid Factor positivity was seen in 500 patients (50%). The majority of patients having extrahepatic manifestations were males and in between 40-50 yrs of age group which is in accordance with their representation in total pool of patients. Except for Diabetes mellitus which was seen maximally in patients with significant fibrosis and cirrhosis, others were seen in majority of patients who were not having significant fibrosis or cirrhosis.

2.4. Discussion

The EHM associated with HCV can be organ specific like ocular, thyroid, dermatological, renal or pulmonary. They can be autoimmune related like cryoglobulinemia or rheumatoid arthritis. The metabolic EHM are diabetes mellitus and insulin resistance whereas neoplasm is of B cell lymphomas. The cardiovascular EHM are stroke or acute myocardial infarction whereas neuropsychiatric ones are of cognitive impairment and depression. Fatigue comes under general EHM. Several clinical studies have suggested an association between chronic HCV infection, Insulin resistance (IR) and diabetes mellitus (DM) by demonstrating that patients with CHC have an increased risk for developing DM compared with uninfected individuals [5]. The epidemiological observations found that type 2 diabetes mellitus (T2DM) developed in 14.5-33% of patients with CHC [6,7]. The broad range of these findings may be the result of various factors, including age, ethnicity, body mass index, the prevalence of diabetes, viral load, and HCV genotype. Antonelli et al [8]. Reported that the prevalence of T2DM was higher in patients with HCV-related cirrhosis than in those with cirrhosis resulting from other liver diseases. In addition, White et al [9], Showed that CHC was associated with an increased risk of T2DM in comparison to uninfected and hepatitis B virus (HBV)-infected controls. HCV-associated IR correlated with poor outcomes by accelerating the progression of hepatic fibrosis and the development of hepatocellular carcinoma, in addition to reducing sustained virologic response (SVR) rates [10]. In our total pool of 1000 HCV patients, 9% patients had diabetes mellitus which is in alignment with other previous literature. As expected, it is more common than seen in 7% of HBV patients. Thyroid dysfunction, including chronic thyroiditis, hypothyroidism and hyperthyroidism, has been associated with HCV infection [11]. An autoimmune mechanism has been proposed because of the prevalence of antithyroid autoantibodies from 4% to 15% [12]. However, the role of HCV remains unclear. Patients with CHC are more likely to have increased levels of serum anti-thioperoxides and anti-thyroglobulin autoantibody than the general population, possibly due to the activation of helper T-cells [13]. The development of thyroid disease was described in 11% of male HCV patients in one study, that was responsive to the treatment and reversible [14]. In our study group 5.3% had hypothyroidism and all of them were having hypothyroidism. It was more than seen in 2% of HBV patients, in a study done by our group. Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease characterized by chronic and destructive arthritis [15]. Patients infected with Hepatitis C Virus (HCV) often present with rheumatic symptoms, but its link to rheumatoid arthritis (RA) remains unclear. Although RA pathogenesis is incompletely understood, chronic viral infections may be one of the triggers for its onset [16]. In one study on hepatitis C patients, RF was positive in 46.7%, anti-CCP was positive in 3.3%, and anti-MCV was positive in 30% of the group [17]. There are studies suggesting a significant correlation with disease activity [18] while some others did not find any correlation [19]. The rheumatoid factor is one of the highest prevalent autoantibodies in patients with HCV and present in 50-80% of cases [20] and same 50% was observed in our Study group, which had a good number of 500 patients. It is much higher than 26.80% seen in HBV patients [21]. Aplastic anaemia can be associated with HCV, although it is rare and its exact role is not fully understood. The connection is not typically a direct viral infection of the bone marrow, but rather an immune-mediated response triggered by the infection that attacks the bone marrow stem cells. Hepatitis-associated aplastic anaemia (HAAA) is an uncommon but distinct variant of aplastic anaemia in which pancytopenia appears two to three months after an acute attack of hepatitis. HAAA occurs most frequently in young male children and is lethal if leave untreated. The ethology of this syndrome is proposed to be attributed to various hepatitis and non-hepatitis viruses. Several hepatitis viruses such as HAV, HBV, HCV, HDV, HEV and HGV have been associated with this set of symptoms [22] It has also been reported that HCV is not generally implicated as a causative agent of hepatitis preceding aplastic anaemia [23]. In our study group of 1000 HCV patients, there was not even one patient of aplastic anaemia, this is in alignment with previous studies which also prove that asso-

ciation of aplastic anaemia with HCV is rare phenomenon. It is exactly on same lines in HBV patients, as reported by our group in an anther study, where no patient developed aplastic anaemia. Oral manifestations in Hepatitis C Virus (HCV) infection include dry mouth (xerostomia), oral lichen planus (OLP), candidiasis, and gingivitis. It can also cause bleeding gums, atrophic tongue, and an increased risk for oral cancer. Some of these symptoms are related to the liver dysfunction caused by HCV, while others are a direct or indirect effect of the virus. The oral mucosal signs and symptoms were generally more frequent among HCV compared to healthy controls. The frequency was statistically significant higher in HCV patients regarding xerostomia (40%), altered taste (24%) and oral lichen planus (20%), but insignificant regarding atrophic tongue (18%), oral pigmentation (14%) and pallor (10%). The presence of HCV was significantly associated with increased odds of xerostomia (P = 0.028, OR=4.3), oral pigmentations (P = 0.013, OR=12.6) and atrophic tongue (P = 0.039, OR=7.8). While other predictors had no significant effects on any of oral findings. (24) Oral lichen planus is a chronic inflammatory dermatosis that affects the mucous membrane of the oral cavity. The cause of lichen planus is not completely understood, but genetics and immunity may be involved [25]. Chitturi and al in India have suggested in 2014 that altered cytokine secretion induced by HCV infection may predispose to subsequent development of OLP [26]. A meta-analysis conducted by Shengyuan in 2009 based on studies carried out in different countries concluded that there is a statistically significant association between HCV infection and OLP. In fact, compared with controls, patients affected by OLP showed a higher prevalence of HCV exposure, and those infected by HCV had a higher risk of being affected by the OLP [27]. In our study group also 5.30% had history of oral ulcers and same number 5.30 % had complaints of dry mouth. It is comparatively less than reported in other studies. One reason can be predominance of younger age group non-cirrhotic patients. It is more than seen in HBV patients, as reported by our group in an anther study. In our total pool of 1000 HCV patients, only one patient had findings of lichen planus in mouth.

Figure 1: Showing Lichen Planus in Oral Cavity in HCV Patient.

Table 1: Showing Sex and Geographical Distribution in HCV Patients.

Total HBV Patients	Males	Females	Rural Background	Urban Background
1000	650 (65%)	350 (35%)	670 (67%)	330 (33%)

Table 2: Showing Extrahepatic Parameters Distribution in HCV Patients.

Total HBV Patients	Dry Mouth/Eyes	Oral Ulcers	Diabetes Mellitus	R A Factor Positivity	Hypothyroidism	Lichen Planus	Aplastic Anemia
1000	53 (5.3%)	53(5.3%)	90 (9%)	500(50%)	53 (5.3%)	1(0.1%)	0 (0%)

3. Conclusion

The hepatitis C patients need to be evaluated not only from hepatic point of view but also its extra hepatic impact, of which dermatological, haematological, endocrinological, dental and musculoskeletal system are integral part. This approach will help in decreasing morbidity and mortality associated with HCV. In Northern India, as per our observations, rheumatoid factor positivity, dry mouth, oral ulcers and diabetes mellitus are more commonly seen than aplastic anaemia or lichen planus which are almost negligible but these findings require confirmation on large scale studies.

4. Limitations of Study

The limitation of our study was almost negligible representation of acute hepatitis C patients and children, as certain extrahepatic manifestations are predominantly seen in them. Hence, large scale studies having equal representations from above two groups will be able to give clear picture of extrahepatic manifestations of HCV.

References

1. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. WHO. 2015
2. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd ed. WHO. 2016
3. Virovic Jukic L, Kralj D. Smolic M, Vcev A, Wu GY, editors. Extrahepatic Manifestations of Hepatitis C Virus Infection. Update on hepatitis C. Intech Open. 2017; 111-124.
4. Flores-Chávez A, Carrion JA, Forns X, Ramos-Casals M. Extrahepatic manifestations associated with Chronic Hepatitis C Virus Infection. Rev Esp Sanid Penit. 2017; 19: 87-97.
5. Wang CS, Wang ST, Yao WJ, Chang TT, Chou P. Hepatitis C virus infection and the development of type 2 diabetes in a community-based longitudinal study. Am J Epidemiol. 2007; 166: 196-203.
6. Zein CO, Levy C, Basu A, Zein NN. Chronic hepatitis C and type II diabetes mellitus: a prospective cross-sectional study. Am J Gastroenterol. 2005; 100: 48-55.
7. Lecube A, Hernández C, Genescà J, Simó R. Glucose abnormalities in patients with hepatitis C virus infection: Epidemiology and pathogenesis. Diabetes Care. 2006; 29: 1140-1149.
8. Antonelli A, Ferri C, Fallahi P, Sebastiani M, Nesti C. Type 2 diabetes in hepatitis C-related mixed cryoglobulinemia patients. Rheumatology (Oxford) 2004; 43: 238-240.
9. White DL, Ratziu V, El-Serag HB. Hepatitis C infection and risk of diabetes: a systematic review and meta-analysis. J Hepatol. 2008; 49: 831-844.
10. Hsu YC, Lin JT, Ho HJ, Kao YH, Huang YT, Hsiao NW. Antiviral treatment for hepatitis C virus infection is associated with improved renal and cardiovascular outcomes in diabetic patients. Hepatology. 2014; 59: 1293-1302.
11. Mao XR, Zhang LT, Chen H, Xiao P, Zhang YC. Possible factors affecting thyroid dysfunction in hepatitis C virus-infected untreated patients. Exp Ther Med. 2014; 8: 133-140.
12. Broussolle C, Steineur MP, Bailly F, Zoulim F, Trépo C. Hepatitis C virus infection and thyroid diseases. Rev Med Interne. 1999; 20: 766-773.
13. Fallahi P, Ferrari SM, Giuggioli D, Manfredi A, Mancusi C. Thyroid involvement in hepatitis C - associated mixed cryoglobulinemia. Hormones (Athens) 2014; 13: 16-23.
14. Bini EJ, Mehandru S. Incidence of thyroid dysfunction during interferon alfa-2b and ribavirin therapy in men with chronic hepatitis C: a prospective cohort study. Arch Intern Med. 2004; 164: 2371-2376.
15. Weyand CM, Goronzy JJ. The immunology of rheumatoid arthritis. Nat Immunol. 2021; 22(1): 10-8.
16. Ferucci ED, Choromanski TL, Varney DT, Ryan HS, Townshend-Bulson LJ. Prevalence and correlates of hepatitis C virus-associated inflammatory arthritis in a population-based cohort. Semin Arthritis Rheum. 2017; 47(3): 445-50.
17. Ece Kaptanoğlu, Işılay Nadir, Zahir Bakıcı, Emrullah Hayta, Mehmet Türkmen. Differentiation of Rheumatoid Arthritis from HCV Infection: Rheumatoid Factor, Anti-Cyclic Citrullinated Peptide or Anti-Mutated Citrullinated Vimentin? Archives of Rheumatology. 2010; 25(1): 019-023.
18. Wagner E, Skoumal M, Bayer PM, Klaushofer K. Antibody against mutated citrullinated vimentin: a new sensitive marker in the diagnosis of rheumatoid arthritis. Rheumatol Int. 2009; 29: 1315-21.
19. Ursum J, Nielen MM, van Schaardenburg D, van der Horst AR. Antibodies to mutated citrullinated vimentin and disease activity score in early arthritis: a cohort study. Arthritis Res Ther. 2008; 10: R12.
20. Lormeau C, Falgarone G, Roulot D and Boissier MC. Rheumatologic manifestations of chronic hepatitis C infection. Joint Bone Spine. 2006; 73: 633-638.
21. Vani Malhotra, Parveen Malhotra, Harman Singh, Senti, Sandeep Kumar, Rahul Siwach, Pranav Malhotra, Anuj Sharma. Prevalence of Rheumatoid Factor Positivity in Hepatitis B Patients. Positif Journal. 2025.
22. Rauff B, Idrees M, Shah SA, Butt S, Butt AM, Ali L, Hussain A, Irshad-Ur-Rehman, Ali M. Hepatitis associated aplastic anemia: a review. Virol J. 2011; 8: 87.
23. Hibbs JR, Frickhofen N, Rosenfeld SJ, Feinstone SM, Kojima S, Bacigalupo A, Locasciulli A, Tzakis AG, Alter HJ, Young NS. Aplastic anemia and viral hepatitis. Non-A, Non-B, Non-C? JAMA. 1992; 267(15): 2051-2054.
24. Ismail, Radwa M, Elansary, Amira R Ezzatt, Ola M. Hepatitis C Associated Oral Lesions: A Hospital-Based Retrospective Case Control Study in Egypt. Journal of International Oral Health. 2023; 52-58.
25. Salma Adnane, Chaimaa Mahad, Sofia Haitami, Ihsane Ben Yahya. Hepatitis C virus infection and oral lichen planus: A controversial association Advances in Oral and Maxillofacial Surgery. 2022; 100271.
26. RT Chitturi, AS Devy, RM Nirmal, PM Sunil Oral lichen planus: a review of etiopathogenesis, clinical, histological and treatment aspects. J Interdiscipl Med Dent Sci. 2014.
27. L Shengyuan, Y Songpo, W Wen, T Wenjing. Binyou Hepatitis C virus and lichen planus: a reciprocal association determined by a meta-analysis Arch Dermatol. 2009; 1040-1047.