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Dermatology

Cutaneous Manifestations of Hepatitis C Virus Infection: A Comprehensive Study

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Abstract **Review Article**

Background: Hepatitis C virus (HCV) infection is a global health problem that is mainly associated with hepatic consequences. However, extrahepatic manifestations of HCV infection, including a variety of skin disorders, are also common. Different dermatological conditions can manifest in various ways using the underlying genetic mutations. ***Objective:*** To assess the spectrum and prevalence of cutaneous manifestations in chronic HCV infection and evaluate their relationship to the stage of hepatic dysfunction. Methods: Cross-sectional clinical study was conducted from September 2024 to February 2025, in a tertiary care hospital. A systematic evaluation for dermatological manifestations through clinical examination, laboratory investigations, and histopathological analysis where required was performed on forty-five consecutive patients with a diagnosis of chronic HCV infection. Statistical analysis was conducted with SPSS version 25.0. ***Results:*** The most common cutaneous manifestations encountered were mixed cryoglobulinemia (37.8%), lichen planus (24.4%), and porphyria cutanea tarda (15.6%) among others. The severity of liver dysfunction was significantly associated with the prevalence of these skin conditions ($p < 0.05$). Most of the affected patients were middle-aged (31–50 years). ***Conclusion:*** cutaneous manifestations are frequent in patients with HCV infection and correlate with hepatic disease severity. Incorporating dermatological assessment into HCV management pathways could facilitate early diagnosis and improve patient care.

Keywords: Hepatitis C, Cutaneous diseases, Mixed cryoglobulinemia, Lichen planus, Dermatological assessment.

INTRODUCTION

Hepatitis C virus (HCV) is a global public health problem, with approximately 58 million HCV-infected individuals worldwide, with a significant burden in the WHO Eastern Mediterranean Region [24]. Although HCV is traditionally recognized for its hepatic-related outcomes, such as hepatitis, fibrosis, cirrhosis and carcinoma of the liver [6], HCV is also associated with multiple extrahepatic diseases, such as dermatological conditions [3]. These skin diseases, including mixed cryoglobulinemia, lichen planus, and porphyria cutanea tarda, frequently represent early warning sign of HCV infection, enabling early diagnosis and intervention [4]. This prospective, hospital-based study was done from September 2024 to February 2025 in a tertiary care hospital to analyse the pattern and prevalence of cutaneous disorders in 45 patients with chronic HCV infection and their association with severity of hepatic dysfunction.

Epidemiology and Clinical Spectrum of Cutaneous Lesions

The study demonstrated a high frequency of skin lesions in HCV-associated patients, with mixed cryoglobulinaemia being the most frequent presentation among the cases, around 37.8% [3, 13]. This rapidly progressive disorder is characterized by deposition of immune complexes in small to medium-sized vessels, and presents with vasculitic features, including palpable purpura [13]. Lichen planus, present in 24.4% of subjects, was considered to be a manifestation of an autoimmune response to viral antigens with a painful mucocutaneous lesions [8]. Porphyria cutanea tarda (PCT), which was reported in 15.6% of the cohort, is related to the decreased activity of hepatic uroporphyrinogen decarboxylase and presents with photosensitive bullous lesions [5]. Necrolytic acral erythema (8.9%), Raynaud's phenomenon (6.7%), jaundice (20.0%), pruritus (26.7%), easy bruising (22.2%), and spider angiomas (13.3%) were less frequently observed [2, 9].

Demographic and Clinical Features

We enrolled 45 patients (men, 64.4%; mean age, 47.6 ± 12.3 years). Of these patients, 66.7% had liver cirrhosis, and 31.1% had previously undergone antiviral therapy [11]. The highest incidence of cutaneous lesions (51.1%) occurred in the middle aged (31–50 years) group, potentially because of chronicity of

HCV and late diagnosis [6]. In terms of gender, mixed cryogobulinemia presented with only a little male predominance (41.4%) rather than lichen planus (31.3%), with similar gender distribution [7].

Associated with liver dysfunction

There was a marked association ($p < 0.05$) that was found between the severity of liver disease and the cutaneous findings [3]. Most patients with mild liver function were associated with pruritus and easy bruising, followed by patients with the moderate liver function as having lichen planus and jaundice. Advanced liver involvement was related to complicated disease including mixed cryoglobulinemia, PCT, and spider angiomas 11. This association highlights the systemic character of HCV infection, as long-term liver injury leads to worsening immune dysregulation and vascular fragility contributing to the severity of cutaneous manifestations [13].

Pathophysiological Mechanisms

The pathogenesis of HCV-related dermatological features is complicated. Leucocytoclastic vasculitis occurs due to the deposition of the immune complex in mixed cryoglobulinemia [13]. Lichen planus is thought to result from an autoimmune reaction to chronic viral antigens in predisposed individuals [8]. PCT is a failure of hepatic enzymes, in particular uroporphyrinogen decarboxylase, and is induced by HCV-mediated oxidative stress [5]. Necrolytic acral erythema, which is rarer, is associated with nutritional deficiencies and improves with zinc replacement [10]. These pathways illuminate the relationship between chronic inflammation, immune dysfunction, and metabolic alterations in HCV-related dermatoses [13].

Clinical Implications

The high frequency of dermatoses in HCV associated patients underline the necessity of a standard dermatologic examination in the management of HCV [9]. Rapid identification of skin lesions facilitates the diagnosis of HCV, especially in middle-aged individuals in whom the infection is often detected late [4]. Furthermore, the introduction of direct anti-viral agents (DAAs) has changed the management of an HCV infection, but dermatologic side effects may persist or even exacerbate so that there is still a need for dermatologic after care during treatment [1]. The incorporation of dermatology into multidisciplinary HCV care can improve the quality of life of patients, as well as provide a clinical index of disease activity [14].

Limitations of the Study

The study has limitations, in spite of its insights. That study was conducted at a single center; thus the sample size of 45 patients is small for generalizability [7]. Being a tertiary care hospital, selecting population may led to bias thus excluding those with milder form of HCV or coming from rural areas [2]. Cross-sectional nature does not permit the determination of temporal relationships and the response to antiviral therapy for skin findings [11]. Furthermore, the use of clinical diagnosis, with biopsies being taken selectively, may result in possible misclassification of atypical dermatoses [9]. Incompletely controlled confounders like nutritional status or comorbidities could have influenced the results [13].

Future Directions

These are preliminary findings that require larger, multicentre prospective studies to verify and investigate the effect of DAAs on skin manifestations [1]. Including control groups and evaluating nutrition and comorbidity factors would enhance causal inference [7]. In addition, studying sex-related immune responses and hormonal effects might explain the gender related differences in cutaneous disease [13]. Improved screening programmes focusing on the middle aged may enhance early detection of HCV and thereby lessen the burden of extrahepatic manifestations [4].

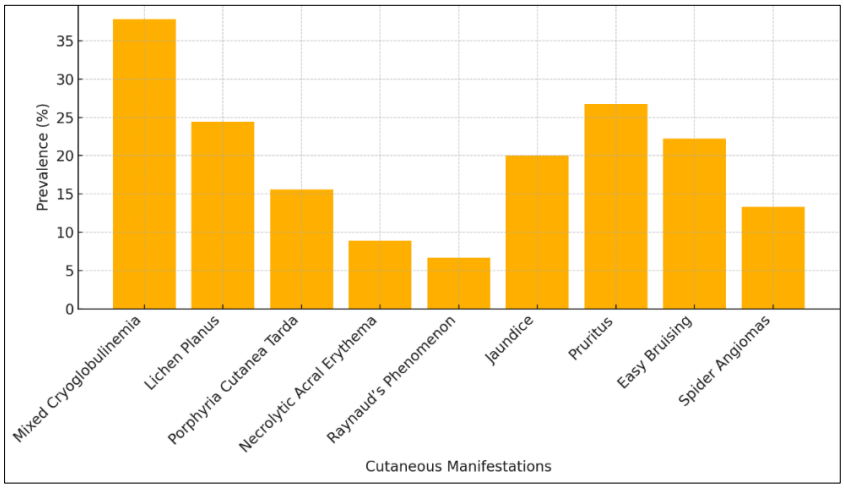

Figure 1: Bar Chart Showing Prevalence of Cutaneous Manifestations in HCV Patients

Figure 1 illustrates the prevalence of various cutaneous manifestations observed among patients with chronic HCV infection. The bar chart highlights that mixed cryoglobulinemia (37.8%) was the most common manifestation, followed by lichen planus (24.4%), porphyria cutanea tarda (15.6%), pruritus (26.7%), easy bruising (22.2%), jaundice (20.0%), and spider angiomas (13.3%). Less common conditions included necrolytic acral erythema (8.9%) and Raynaud's phenomenon (6.7%). The graphical presentation emphasizes the predominance of immune-complex and autoimmune-mediated dermatological complications in HCV patients

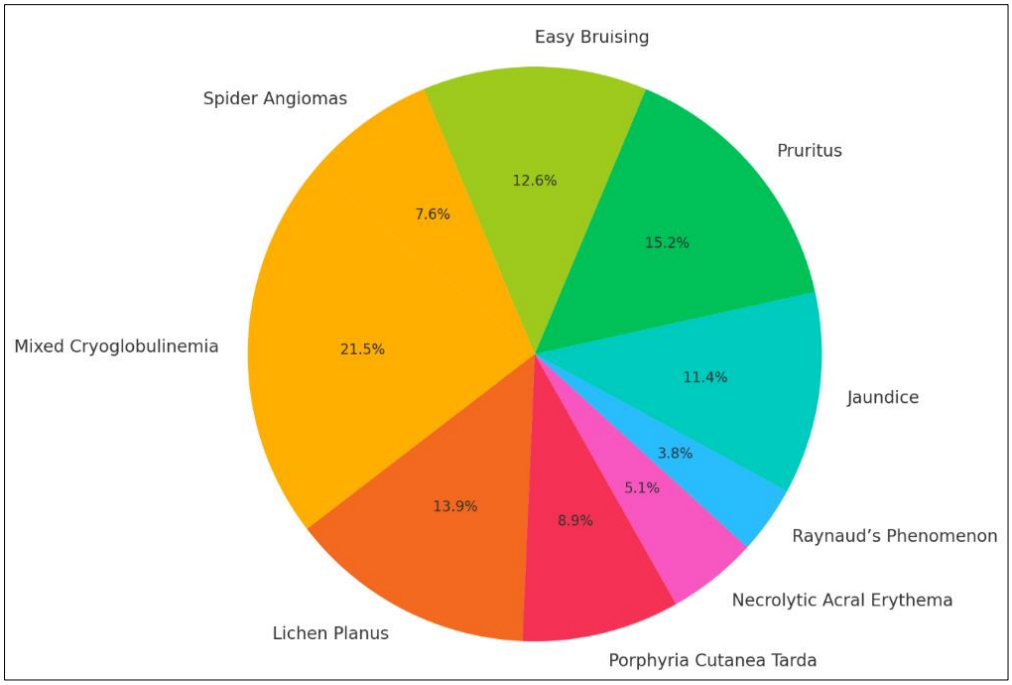

Figure 2: Pie Chart Representing Proportional Distribution of Cutaneous Manifestations

Figure 2 presents the proportional distribution of cutaneous manifestations in HCV patients using a pie chart. The chart visually represents the relative contribution of each condition to the overall disease burden. Mixed cryoglobulinemia, lichen planus, and porphyria cutanea tarda together accounted for the majority of skin manifestations, underscoring their clinical importance. The pie chart also depicts the smaller but significant contributions of pruritus, easy bruising, jaundice, spider angiomas, necrolytic acral erythema, and Raynaud's phenomenon, reflecting the broad spectrum of dermatological involvement in HCV infection

CONCLUSION

This series highlights in particular the substantial burden of cutaneous signs and symptoms of chronic HCV infection with mixed cryoglobulinemia, lichen planus, and porphyria cutanea tarda being the most common [3, 8, 5]. These features strongly associate with the severity of liver disease as a manifestation of the systemic properties of HCV [11]. The clinicians may be able to achieve early diagnosis, effective treatment, and quality of life by incorporating dermatologic examination into HCV care [9, 14]. With HCV taking on new statistical nuances, collaboration among hepatology, dermatology, and infectious disease specialists will be increasingly necessary for the treatment approach to this multi-system illness [2].

These results support a multidisciplinary management of HCV-patients including dermatological and hepatological approaches [16, 18]. Patient quality of life can be enhanced by recognition and treatment of skin-related complications, and these are also clinical indicators of disease progression [20]. Furthermore, this study emphasizes the necessity to diagnose early and start therapy with direct-acting antiviral drugs, which can eliminate the virus and extra-hepatic manifestations, such as cutaneous diseases, may be alleviated [1]. This and other investigations may help educate patients to identify possible dermatologic manifestations of HCV early in their presentation and to seek medical attention promptly, which ultimately would improve care [15].

Despite its relatively narrow scope, the study contributes to the increasing body of evidence on HCV as a multi-organismal infection [14, 17]. Larger, longitudinal, and multicenter trials are needed to study the impact of anti-viral treatment on extracutaneous involvement and pathophysiological process leading to this involvement [19]. In the end, the incorporation of dermatologic care into standard HCV treatment is a promising step that can help with patient-centered care,

QoL, and potential enhancement of thorough therapeutic target pursuit [12, 20].

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