

CHRONIC HEPATITIS “C”;

A DERMATOLOGIC PERSPECTIVE

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ABSTRACT.....OBJECTIVE: To find spectrum of various dermatological manifestations during hepatitis “C” virus infection in local population of hyderabad. **METHODS:** This descriptive study was conducted in medicine department of Isra University Hospital Hyderabad from January 2011 to June 2012. A total of 325 anti-HCV positive patients were enrolled. All patients were subjected to detailed history, careful clinical examination of skin by a dermatologist to diagnose skin disease. All data was analyzed using statistical package SPSS 14.0. **RESULTS:** A total of 325 HCV positive patients (61% males and 39% females) were enrolled in this study. Mean age was 43 (SD +10 years), ranging from 15 to 78 years. About 41% had one or more dermatologic manifestations. Pruritis was the leading manifestation found in 11% , lichen planus (oral and cutaneous) was next to be found in 6.7% patients and hyperpigmentation in 5.2% patients. Urticaria (acute & chronic) was next counting in 5.23%. Jaundice, alopecia and vitiligo were seen in 4.9% each. Dry skin and interferon injection site erythema were observed in 4.6% patients each. Cutaneous vasculitis was noticed in 3.6% each, while photosensitivity, psoriasis and Raynaud's phenomenon were seen in 1.8%, 2.5%, 1.5% patients respectively. **CONCLUSION:** Dermatological manifestations are very common in patients with chronic HCV infection and when confronted with a suspected skin lesion, patient should be screened for it. Epidemiological studies are essential to determine the real prevalence of other dermatoses during course of HCV infection.

Key words: Hepatitis C virus infection, dermatological manifestations, pruritis, lichen planus, urticaria.

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INTRODUCTION

Hepatitis C virus (HCV) infection is a major public health challenge globally. It affects 170 million people worldwide¹, while in Pakistan estimated prevalence rate ranges from 6-20%^{2,3}. HCV is a major cause of both acute and chronic hepatitis and hepatocellular carcinoma worldwide. Most HCV infected patients are asymptomatic and may remain undiagnosed for longer periods³.

HCV infection is associated with various extrahepatic manifestations involving kidneys, bones, muscles, nerves, gastrointestinal tract and skin³. Dermatological manifestations constitute an important proportion of extrahepatic signs related to HCV infections^{4,5}. Cutaneous manifestations appear to be mostly due to deposition of circulating immune complexes in skin or tissue deposition of specific T lymphocytes. In most cases, the details of pathogenesis of these disorders remain uncertain⁶. Cutaneous manifestations of chronic HCV may be

arbitrarily divided into three groups: often associated (mixed cryoglobulinemia, porphyria cutanea tarda, leukocytoclastic vasculitis, livedo reticularis); associated (lichen planus, sjogren's syndrome, urticaria, pruritus, polyarteritis nodosa) and uncommonly associated (erythema nodosum, erythema multiforme, vitiligo, psoriasis, unilateral nevoid teleangiectasia, pyoderma gangrenosum, behcet's syndrome, mooren corneal ulcer, granuloma annulare, disseminated superficial actinic prokeratosis) conditions⁷. The cutaneous features are not only cause of morbidity but provide an indirect clue for underlying disease. Such an observation leads to early detection and initiation of therapy. Accurate and timely diagnosis of HCV is critical to prevent the life threatening complications⁸.

Since local data regarding dermatological manifestations associated with HCV infection is scarce and large number of chronic liver disease patients being admitted in hyderabad, hence we

conducted this study to determine spectrum of various dermatological manifestations in patients of HCV.

MATERIAL & METHODS

This descriptive study was conducted in medicine department of Isra University Hospital Hyderabad from January 2011 to June 2012. A total of 325 anti-HCV positive patients were enrolled. Informed and written consent was taken from study participants. The local ethical committee of the institute had approved study protocol.

INCLUSION CRITERIA

Hepatitis C positive patients of all ages and both sexes were examined. Patients with chronic HCV infection without any clinical or radiological evidence of liver cirrhosis were included in study. Hepatitis C was diagnosed on the presence of anti-HCV antibodies in blood and confirmed by HCV-RNA PCR.

EXCLUSION CRITERIA

Anti-HCV positive patients who also have concomitant HBV infection or suspicion of liver disease due to any other viral etiology or any other cause were excluded from study. Similarly patients suffering from chronic systemic diseases such as diabetes mellitus, chronic renal failure, rheumatoid arthritis or other autoimmune diseases, were also excluded.

Patients fulfilling the inclusion and exclusion criteria were subjected to detailed history, careful clinical examination of skin by a dermatologist (especially for oral mucosa, skin and its appendages) to diagnose skin disease. Relevant laboratory investigations (like complete blood count, liver function tests, abdominal ultrasound) were carried out. Frequencies of various dermatologic manifestations associated with HCV infection were noted and analyzed.

Data were recorded on a specially designed proforma. All data were analyzed using statistical package SPSS 14.0. Descriptive statistics were used. Mean +

standard deviation was calculated for age. Frequencies and percentages for various variables were calculated.

RESULTS

A total of 325 HCV positive patients were enrolled in this descriptive study. Male patients were 199(61%) and female 126(39%). Mean age was 43 (SD+10 years), ranging from 15 to 78 years. A small fraction of patients 76(23%) were using anti-viral therapy, while rest 249(77%) without antiviral therapy. About 133(41%) had one or more dermatologic manifestations.

Pruritis was the leading manifestation found in 36(11%). Lichen planus (oral and cutaneous) was next found in 22(6.7%) patients. Hyperpigmentation was seen in 18(5.5%) patients. Urticaria was next counting 17(5.23%). Jaundice, alopecia and vitiligo were seen in 16(4.6%) each. Dry skin and interferon injection site erythema was observed in 15(4.9%) patients each, Cutaneous vasculitis was noticed in 12(3.6%), while photosensitivity, psoriasis and Raynaud's phenomenon were seen in 6(1.8%), 8(2.5%), 5(1.5%) patients respectively.

Signs	Number of Patients	Percentage
Pruritis	36	11.00%
Hyperpigmentation	18	5.05%
Lichen Planus	22	6.06%
Urticaria	17	5.23%
Jaundice	16	4.9%
Alopecia	16	4.9%
Vitiligo	16	4.9%
Dry Skin	15	4.6%
Injection Site Erythema	15	4.6%
Vasculitis	12	3.6%
Photosensitivity	06	1.8%
Psoriasis	08	2.6%
Raynaud Phenomenon	06	1.8%

Table-II. Dermatologic manifestations in HCV (n = 133)

Characteristics	Frequency	Percentage
Mean age + SD (Range)	43.0 + 10.0 (15 to 78)	
Gender		
Male	199	61%
Female	126	39%
Therapy		
With Antiviral	76	23%
Without Antiviral	249	77%

Table-I. Baseline Characteristics of HCV +ve Patients (n=325)

DISCUSSION

Hepatitis "C" is the most common cause of chronic liver disease worldwide. The course is usually sub-clinical and usually present with nonhepatic symptoms. At least 40% to 70% HCV patients develop extrahepatic manifestation⁹. Demographic profile of patients in our study reveals a preponderance of males which in our opinion is true representation of chronic HCV infection in our population. Similar finding were reported by Devis et al¹⁰ and Ejaz et al¹¹, while a study from Turkey by Soyulu et al¹² found female dominance. Extrahepatic manifestations of HCV are numerous¹³, cutaneous symptoms or findings relevant to HCV infection manifest in 20-40% of patients presenting to dermatologists and in a significant percentage (15-20%) of general patients. HCV is suggested and must appear in the differential diagnosis of these patients to avoid missing this important but occult factor in clinical disease in appropriate setting. All of which should be regarded as early markers of a potentially fatal chronic liver disease¹⁴. In our study one or more mucocutaneous manifestations were exhibited in 41% HCV patients, matching studies by Cacoub et al¹⁵ and Raslan et al¹⁶, while Paoletti et al¹⁷ reported cutaneous signs in 80% HCV patients.

Several studies have documented a possible link between pruritus and HCV infection. Prevalence of pruritus in HCV infected patients varies from one country to another and epidemiology of HCV differs substantially between countries. Pruritus was associated with nonspecific excoriations, excoriated papules or xerosis¹⁸, the precise mechanism of itch in

liver diseases remains unclear although the presence of bile salts in the skin, histamine and alternative liver metabolites have been proposed as explanations¹⁹.

Pruritus was the leading finding in our study found in 11% HCV positive patients. This fact has been reproduced in many studies, a french study reported in 15% of patients²⁰, a study from Japan was 39%²¹, while in Pakistan a study from Azfar et al²² found 25.9%. The association between HCV infection and lichen planus comes from epidemiological studies that have shown prevalence of antibodies against HCV antigens is higher in patients with lichen planus than in general population²³. Lichen planus may be the first presentation of HCV infection²⁴, especially oral form seems more common²⁵. Although the etiology of HCV-induced lichen planus is unknown, it is probably related to viral replication in lymphocytes²⁶.

We found lichen planus (mucosal & cutaneous) in 6.7% patients. Our results are in concordance with earlier Pakistani studies^{9,11,22}, while a study from France by Cribier et al showed 3.8% and 4% by Raslan et al¹⁶ in Egypt.

The prevalence of chronic urticaria varies from 1% to 5% in the general population²⁷. Doutré et al²⁸ described acute and chronic urticaria in various skin diseases with HCV infection. However Cribier et al²⁹ showed that at least in Europe, HCV rates in cases of chronic urticaria are similar to those of the general population. In patients with HCV, urticaria tends to last longer than typical few hours, is associated with worse liver status and leaves a brown stain³⁰. We found urticaria in 5.23% HCV patients, while Azfar et al²² reported in local study in 2.4% patients.

Vasculitis was found in 3.6% of our patients, which is consistent with finding of Hartmann et al who reported vasculitis of skin in 2%³¹ and by Devis et al¹⁰ 4.2% of HCV-Infected patients. They suggested that immune stimulation of T-cell clones in HCV infection produces

monoclonal macroglobulins with co-affinity to a constituent of HCV and IgG. Potential antigens of relevance include bacteria, viruses, drugs and other chemicals³¹. A generalized hyper-pigmentation was seen in 5.5% of cases matching studies by Azfar et al²² and Raslan et al¹⁶ reported this in 6.2% and 5.3%.

Vitiligo was evident in 4.9% matching 6% from local study by Ejaz et al¹¹. Photosensitivity was noted in 2.5% compare to 7.5% by Azfar et al²² and Reynaud's phenomenon was 1.8% in our study matching 2% in local study by Azfar et al²², while in western study by Cacoub et al¹⁵ it was reported high 6%, probably because of cold weather.

In addition, a variety of skin manifestations may be related to interferon alpha therapy, the most common of which were erythemas at site of injection present in 4.6% patients in our study, while Maticic¹³ found it in 7%. Transient alopecia was documented in 4.9% patients, while Aamir et al³² reported in 64% patients; the reason for such high figure may be due to fact that, this study was being performed on HCV patients on interferon therapy exclusively.

CONCLUSION

Dermatological manifestations are very common in patients with chronic HCV infection and when confronted with a suspected skin lesion, patient should be screened for this notorious infection. Cutaneous manifestations may be the first clinical sign of chronic HCV infection. Epidemiological studies are essential to determine the real prevalence of other dermatoses during the course of HCV infection.

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others, whenever they go.*

Oscar Wilde (1854-1900)