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Original Article

Hepatitis C seropositivity in patients with acute and chronic urticaria

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Abstract

Background Hepatitis C virus (HCV) infection is associated with many dermatologic manifestations. Urticarial vasculitis and urticaria with mixed cryoglobulinemia are well known associations. Ordinary urticaria with short-lived wheals may also be one of the cutaneous signs of HCV infection.

Objective To find out the prevalence of hepatitis C seropositivity in patients with acute and chronic urticaria.

Patients and methods Forty eight consecutive patients (32 females and 16 males) with ages ranging from 12 to 60 years, presenting with acute or chronic urticaria were included in the study. Fifty age- and sex-matched controls were also included. All cases were tested for anti-HCV antibodies by the ELISA method. Other investigations included complete blood examination, liver function tests and hepatitis B surface antigen. An odds ratio of ≥2 was considered significant.

Results Anti-HCV antibodies were positive in 6 patients (12.5%) and in 3 controls (6%). Hepatitis B surface antigen was positive in 2 patients (4.1%) both of whom were anti HCV negative. Odds ratio was calculated to be >2 which was statistically significant (p <0.05).

Conclusion There is a statistically significant association between hepatitis C virus infection and acute and chronic urticaria in our population.

Key words
Hepatitis C virus, urticaria

Introduction

Infection with hepatitis C virus (HCV) may have effects not only on the liver but also non-hepatic tissues and may be associated with many unrelated diseases and morbid conditions.[1] During the past decade several dermatological manifestations of HCV infection have been noted although all have not been proved.[2] Urticaria is among one of them.[3] Often the dermatosis is the only clinical evidence of underlying HCV infection. Since early detection of hepatitis C may result in a more favourable response to therapy it is important that physicians be aware of these dermatologic manifestations.

Urticaria has a spectrum of diverse clinical presentatations and causes.[4] Urticarial vasculitis is a form of small vessel vasculitis which may present with both urticaria and arthritis. It has recognized association with HCV infection.[5] The more common ordinary urticaria without vasculitis, characterized by short-lived wheals, however, has also been reported as an extra-hepatic manifestation of HCV infection.[6]

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The objective of our study was to look for an association between ordinary acute and chronic urticaria and HCV infection in a population in which HCV infection is on the rise. Hepatitis C virus seropositivity was evaluated in patients with acute and chronic urticaria and compared with age- and sex-matched controls from the general population.

Patients and methods

This study was conducted at department of dermatology, Lahore General Hospital, Lahore from March to September, 2007. Forty eight consecutive patients with typical urticaria were enrolled in the study. Inclusion criteria were patients of any age and both sexes with typical urticaria (evanescent wheals lasting not more than 24 hours at one time). Both acute (duration less than 6 weeks) and chronic (duration more than 6 weeks) urticaria patients were included. Patients on drugs known to cause urticaria, with known liver disease and with urticarial vasculitis (lesions remaining for more than 24 hours at a time) were excluded from the study.

After taking informed consent all cases were recorded on a standard proforma. Detailed history and clinical examination were carried out. The investigations carried out in these patients apart from anti-HCV antibody by the ELISA method, included complete blood counts, liver function tests and hepatitis B surface antigen.

Fifty age- and sex-matched individuals during the same time period were included as controls. None of the controls had history of urticaria, or hepatitis. The only investigation carried out in the control group was anti-HCV antibody test by the ELISA technique.

Table 1 Demographic data of patients and controls

	Patients (n=48)	*Controls (n=50)*
Females	32	32
Males	16	18
Age range (yrs)	12-60	19-55
Mean age (yrs)	31.6	32.4

Table 2 HCV seropositivity in patients of urticaria and controls

	Patients (n=48)	*Controls (n=50)*
Anti-HCV positive	6	3
Anti-HCV negative	42	47
Total	48	50

Odds ratio=2.25, $p<0.05$

Results

The demographic data of patients and controls is shown in **Table 1**. Majority of the patients were females (66.6%). The mean age was 31.6 years with ages ranging from 12 to 60 years. Out of 48 patients 45 had chronic urticaria and 3 had acute urticaria. Anti-HCV antibody was positive in 6 patients (12.5%) and in 3 controls (6%). Anti-HCV antibody was positive in 1 out of 3 patients of acute urticaria and 5 out of 45 patients of chronic urticaria. Hepatitis B surface antigen was positive in 2 patients (4.1%), both of whom were anti-HCV negative. Liver function tests and blood counts were normal in all patients.

Odds ratio was calculated which was greater than 2 (**Table 2**). This showed that there was a statistically significant difference in HCV seropositivity in urticaria patients and the control population ($p<0.05$).

Discussion

The hepatitis C virus is an RNA virus that is a major cause of acute and chronic hepatitis. It is contracted chiefly through parenteral exposure to infected material.[7] Although the incidence of transfusion-associated hepatitis C infection has declined significantly since the practice of blood screening, this change has little impact on overall disease incidence.[8] In developed countries, prevalence rates of seropositivity are generally less than 3% whereas they may be as high as 10 to 30% in certain endemic areas e.g. in Egypt.[9] Its incidence is alarmingly on the rise in Pakistan. According to various studies the prevalence of hepatitis C seropositivity in the general Pakistani population is between 4-7%.[10,11]

Both acute and chronic hepatitis C are asymptomatic in most patients. Chronic hepatitis C is associated with numerous extra-hepatic manifestations among which skin disorders are quite common.[12] Often, the dermatosis is the only clinical evidence of the underlying disease and many of these patients are first seen by dermatologists. Some of the skin disorders have well-established associations with hepatitis C infection, like porphyria cutanea tarda (PCT), cutaneous necrotising vasculitis, mixed cryoglobulinemia and lichen planus.[13,14,15] Others have weak associations which need to be studied further.

Urticaria has diverse clinical presentations and causes. Clinically, it is classified into ordinary urticaria, physical urticarias, contact urticaria, urticarial vasculitis and angioedema.[4] Although, urticarial vasculitis and urticaria as part of mixed cryoglobulinemia are well-known to occur with HCV infection, the association of ordinary urticaria remains unclear.[5,16,17]

The objective of our study was to evaluate association of acute and chronic ordinary urticaria with hepatitis C virus infection. That is why we excluded patients with urticarial vasculitis. Our study showed that in the control population the anti-HCV antibody was positive in 6 %. This figure is in accordance with the previously known prevalence in the general Pakistani population i.e. 4-7%.[11] The percentage of hepatitis C sero-positivity in urticaria patients was twice that of controls i.e. 12.5%. The results are statistically significant (odds ratio>2, $p<0.05$). Our results are in accordance with some similar previous studies. A Japanese study by Kanazawa *et al*. in 1996, showed a statistically significant association between urticaria and hepatitis C.[18] HCV genotypes determined in these patients were 2/1b in majority. Ahmed *et al.* in 2003 found that 13.4 % of urticaria patients were positive for anti-HCV antibodies, although they did not include a control group.[19] These results were close to our figure of 12.5%. However, both these studies did not exclude urticarial vasculitis patients like us.

Many researchers, however, refute this association. Cribier *et al*. in 1999 in France demonstrated that hepatitis C rates in urticaria patients were similar to those of general population.[20] The reason for high seropositivity in our population might be the difference in HCV genotypes prevalent in our community. Different genotypes may differ in their immunogenic potential. HCV genotypes mainly found in our part of the world are 3a/b and 2/a/b/c.[7] There may be a genetic predisposition in patients with

chronic urticaria for high reactivity to HCV. HLA-DRB1*04, HLA-DQB1*0302, HLADRB1*15, and HLA-DQB1*06 are known to have genetic predisposition for developing chronic urticaria.[21] Hepatitis C virus infection may act as a predisposing factor along with others in patients who are already genetically predisposed. This may explain the difference in results between Asian and European studies. Whether the prevalence of HCV in urticaria in other geographical areas is similar remains to be seen.

Conclusion

According to our study there was a statistically significant association between hepatitis C and acute or chronic urticaria in our population in which hepatitis C infection is on the rise. We therefore recommend screening for hepatitis C infections of all patients presenting with acute or chronic urticaria. This may be effective in early detection of a potentially fatal disease.

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Authors Declaration

Authors are requested to send a letter of undertaking signed by all authors along with the submitted manuscript that:

The material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the *Journal of Pakistan Association of Dermatologists.*