

DERMATOLOGIC DISORDERS ASSOCIATED VIRAL HEPATITIS IN EGYPT

SOMAIA F. MAHMOUD, MD*
IBRAHIM M. ABD EL HAFEZ, MD*
HALA A. AGINAH, MD**
HOSSAM E L. ABD EL LATIF, MD***

ABSTRACT

SUBJECTIVE:

Viral hepatitis can present with a wide variety of cutaneous manifestations. Of all bloodborne infections, hepatitis has the greatest chance for accidental transmission through breaks in the skin during surgical procedures, needle pricks., etc.

OBJECTIVE :

The aim of this work is to study the cutaneous manifestations of viral hepatitis in Egypt. Also to booster the dermatologist awareness of the various associations, so that an early diagnosis of and precautions against such a serious disorder could be undertaken.

Patients and Methods :

Hepatitis patients were taken at random from the inpatient and outpatient clinics of the university hospitals and liver institute in Egypt. The patients had complete history taking, physical and dermatological examination. Hepatitis serology, blood chemistry for liver functions, lipids, diabetes, and kidney function, skin biopsy, bacterial and mycological culture were done for the patients as indicated.

Results :

900 hepatitis patients (520 males, 380 females) were examined. Of them, 500 had Hepatitis C virus (HCV) and 400 had Hepatitis B virus (HBV) infection. 60% were patients residing in rural regions, and 55.5% were workers and farmers infested with *Bilharzia*. 15% gave different histories of blood transfusion, (27.7%) I.V. drug administration specially for *Bilharziasis*, and 5.5% were in contact with other hepatitis patients. Skin manifestations of liver disease as a whole comprised 48.1% of the total, and 6.1% had skin manifestations of hepatitis. 80% had

skin manifestations with HCV, and 20% with HBV infection. The most prevalent diseases were lichen planus, urticaria, erythema multiforme, psoriasis, leucocytoclastic vasculitis, and erythema nodosum.

Conclusion :

Viral hepatitis is a prevalent infectious disease in Egypt, the commonest types being HCV and HBV most probably as a result of repeated I.V. treatment of *Bilharziasis* patients. Male workers outnumbered females. Skin diseases occurred more with HCV patients. Not all types of the reported skin associations were found in this study, and there has not been a previous report about the prevalence of associated skin disorders in Egypt for comparison.

However, a wider scale study is required for a more precise evaluation. Dermatologists should be aware of the various cutaneous associations of such a serious disease.

INTRODUCTION :

Viral hepatitis is a systemic disease primarily involving the liver, resulting in clinical illness which is characterized by fever, jaundice and gastrointestinal symptoms such as nausea and vomiting. ⁽¹⁾

Of all blood borne infectious diseases, hepatitis has the greatest chance for accidental transmission through trauma in the skin during surgical procedures, needle pricks, etc. Hepatitis can also present with a wide variety of cutaneous manifestations. Hence dermatologist awareness of this is mandatory for taking precautions, and for prompt and early diagnosis. ⁽²⁾

While in the U S A, the annual incidence of acute viral hepatitis was 2.5% ⁽³⁾, in Egypt, hepatitis is a more prevalent disease and the reported annual incidence was 9.2% for hepatitis C (HCV) ⁽⁴⁾, and 10% for hepatitis B virus (HBV) ⁽⁵⁾

The aim of this work is to study the dermatologic disorders associated with viral hepatitis in Egypt, which, to our knowledge, has not been done before, and also to booster the dermatologist awareness to the cutaneous manifestations, so that an early diagnosis of, and precautions against such a serious disorder could be undertaken.

PATIENTS AND METHODS :

Hepatitis patients enrolled in this study were taken at random from the hepatitis inpatient and the outpatient clinics of Benha university hospitals, and of the Liver Institute of El Menoufia University in Egypt.

(*) Dermatology Department, Benha faculty of Medicine, Zagazig University, Egypt

(**) Pathology Department, Benha faculty of Medicine, Zagazig University, Egypt

(***) Department of Internal Medicine, Liver Institute, El Menoufia University, Egypt

Address for correspondence :

Dr. Somaia Fathy Mahmoud,
4, Nasser Khessro st., 7th zone, Madinat nasr, Cairo Egypt.

Full history was taken for each patient as regards personal history, complaint, present history of hepatitis and its possible route of transmission, present history of skin lesions, past history of previous condition or medication, and a family history as regards hepatitis and a similar skin disorder.

Each patient had complete physical examination for the signs of hepatitis, and dermatological examination for the presence of associated skin disorders. The following investigations were performed.

Hepatitis serology :

Blood chemistry for liver functions, diabetes, lipids and kidney functions.

Skin biopsy was taken as indicated. Paraffin embedded sections were stained with Haematoxylin and Eosin stain.

KOH preparation, mycological and bacterial culture as indicated.

The patients were given palliative therapy. No one had a specific interferon therapy.

RESULTS :

A total of 900 patients (520 males, 380 females) were examined. 500 patients had HCV (370 males, 130 females), and 400 (150 males, 250 females) had HBV. 135 (15%) gave a past history of blood transfusion, 250 (27.7%) had a history of repeated I.V. drug administration, and 50 (5.5%) had exposure to hepatitis patients. 99 patients (11%) had a family history of hepatitis.

Hepatitis patients coming from rural areas were 540 (60%) and from urban areas were 360 (40%). 500 patients (55.5%) were workers and farmers.

Of the studied group, 200 patients (22.2%) had hepatitis of less than 6 months duration, and 700 (77.8%) were old hepatitis cases.

The mean age (35.5 + 11.9) and the hepatitis duration in years (3.1 + 1.2) for HBV patients who were not significantly different from HCV patients [age (44.6 + 12.33); duration (3.2 + 0.7)].

Skin disorders with the liver disease :

433 patients (48.1%) had different skin manifestations that developed after the occurrence of hepatitis. For simplicity, the patients were classified into three groups, A,B,C, (table 1):

A- 362 patients presenting with the current skin manifestations of liver disease in general.

B- 55 patients with dermatological diseases associated with viral hepatitis.

C- 16 patients having infections.

55 patients (6.1%) of the total were of group (B); 44(80%) had HCV and 11(20%) had HBV infection. The diagnosis was based on the clinical data and the histopathological examination of H&E stained sections. Erythema multiforme patients presented with symmetrical erythematous maculopapular rash on the trunk and the extensor surface of both upper and lower limbs. They were of the mixed type histopathologically. Of the 21 patients with lichen planus, 6 had erosive oral mucosal involvement. Four patients had the chronic form of erythema nodosum and presented with unilateral large erythematous plaque with central clearing on the shin of their lower limbs. Leucocytoclastic vasculitis patients presented with multiple purpuric and erythematous maculopapular and nodular rash on the extremities. Psoriasis vulgaris occurred in 5 patients. The rash affected both elbows, knees, and the back. 15 patients had chronic urticaria with a mean duration of 1.5 years.

The mean age (41.1 + 11.6) and the mean duration (3.07 + 2.64) in years in HBV patients with group (B) were not significantly different from HCV patients who had a mean of (44.7 + 12.3) for age and (3.35 + 2.31) for the duration ($t_{1.007}$, 0.35, $P > 0.05$) respectively.

Table (2) summarizes the skin diseases found in association with hepatitis patients in relation to age, sex, type of hepatitis, and the duration.

Results of serological investigations :

HBsAg was +ve in 400 patients (44.4%) of them 11 (2.8%) had associated dermatological diseases. HCVAb was +ve in 500 patients (55.6%) of them 44(8.8%) had associated skin diseases.

All the patients had elevation of serum bilirubin, liver enzymes SGOT, SGPT, and alkaline phosphatase, but the differences between the two types of hepatitis were not significant ($t_{0.903}$, $t_{0.605}$, $t_{0.1001}$, $t_{0.837}$, $P > 0.05$) respectively.

Blood urea was elevated in 2 patients, creatinine in 4, cholesterol in 10, F.B.S. in 26 including 5 patients with lichen planus.

The serological tests in respect to the associated skin diseases were not statistically significant, table⁽³⁾.

DISCUSSION:

From the present work, HCV infection was the most prevalent type of hepatitis. Males outnumbered

females and hepatitis was more common among residents of rural regions which could imply the low socioeconomic standard as an indirect factor.

The occurrence of hepatitis was more among workers and farmers, being more at risk of acquiring different infections necessitating I.V. drug administration, during indulging in their outdoor working activities. Also farmers are more prone to hepatitis owing to the frequent bilharzial infestations, and its therapeutic medications including frequent I.V. drug administration. On the other hand, an appreciable number of patients gave different histories of blood transfusion, hence the importance of hepatitis screening of the blood donors.

The dermatological manifestations of hepatitis are variable with the different types of hepatitis. However, the commonest cutaneous manifestations include: lichen planus, serum sickness like prodrome, urticaria, erythema nodosum, recurrent papular eruption of trunk and upper extremities, Gianotti-Crosti syndrome, cutaneous vasculitis, polyarteritis nodosa, mixed cryoglobulinaemia, pyoderma gangrenosum, dermatomyositis like syndrome, porphyria cutanea tarda, scarlatiniform eruption⁽²⁾, nodular prurigo⁶, necrolytic acral erythema⁽⁷⁾, and unilateral naevoid telangiectasia⁽⁸⁾.

This is in conjunction with the current dermatologic manifestations associated with liver disease such as jaundice, pruritus, hyperpigmentation, linea distensae, evascular changes, gynaecomastia, and hair and nail changes⁽⁹⁾.

In this study, nearly half of the patients presented with different skin manifestations of liver disease which would show the dermatological importance in the diagnosis. Skin diseases associated with viral hepatitis accounted to 6.1% of the total and was more with HCV infection. The most prevalent dermatoses were lichen planus, urticaria, erythema multiform, psoriasis, leucocytoclastic vasculitis, and erythema nodosum respectively.

Several authors reported a high prevalence of chronic liver disease in patients with lichen planus⁽¹⁰⁾ and HCV was generally the cause of the liver

disease⁽¹¹⁾. The prevalence of HCV markers in patients with lichen planus was reported to be 50%⁽¹²⁾ and in another report was 33.3%⁽¹³⁾ in Egypt, 4% in eastern France and 38% in Spain⁽¹⁰⁾. HBV infected patients have at least twice the risk of developing lichen planus than in general population⁽¹⁴⁾. In this study, lichen planus was the commonest associated dermatoses, more with HCV, and represented 38.1% of skin diseases associated with viral hepatitis.

There has been a report of interferone induced psoriasis in a patient with HCV infection⁽¹⁵⁾. In this study, more cases of psoriasis were reported. The psoriatic patients were not on interferone therapy. However, Psoriasis being common in Egypt, it is difficult to ascertain whether its occurrence was due to liver disease or a mere coincidence.

The occurrence of necrolytic acral erythema with HCV infection has been previously reported in Egypt^(7,12), however, no clinical case was found in this study.

Reports are lacking about the prevalence of infection among hepatitis patients. In this study, some patients had recurrent bacterial and fungal infections. Yet more studies are required before considering such association, bearing in mind that most of the patients had low socioeconomic status.

Not all dermatological diseases associated with viral hepatitis were included in this study. In spite of being a random study, all the patients were either of HBV or HCV infection, so the dermatological associations with other types of hepatitis are lacking. It also implies that HCV and HBV infection are the predominant types of hepatitis. Further wider scale study is required for a more precise evaluation, bearing in mind that there has not been a previous report about the prevalence of associated skin disorders in Egypt for comparison.

Dermatologists should be aware of the different skin manifestations of liver disease and of the different associations with viral hepatitis, so that an early diagnosis and precautionary measures of such a serious disorder could be undertaken.

Table (1): Skin Manifestations of liver disease

Type of skin disorder	Skin diseased patients 433 (%)	Total 900 (%)
A) Current Skin manifestations (362)	83.6	40.2
- Nail changes (81)	18.7	9
- Diffuse whitening (32)		
- Clubbing (49)		
- Generalized pruritus (55)	12.7	6.1
- Jaundice (50)	11.5	5.5
- Hyperpigmentation (36)	8.3	4
- diffused muddy (24)		
- melasma like (12)		
- Palmar erythema (30)	6.9	3.3
- Linea distensae (25)	5.8	2.8
- Spider naevi (15)	3.5	1.7
- Dilated umbilical Veins (15)	3.5	1.7
- Gynaecomastia (9)	2.1	1
- Multiple associations of the above (46)	10.6	5.1
B) Diseases associated with viral hepatitis (55)	12.7	6.1
- Lichen planus (21)	4.8	2.3
- Chronic urticaria (15)	3.5	1.7
- Erythema multiform (6)	1.4	0.7
- Psoriasis (5)	1.2	0.6
- Leucocytoclastic Vasculitis (4)	0.9	0.4
- Erythema nodosum (4)	0.9	0.4
C) Infection : (16)	3.7	1.8
- Erysipelas (4)	0.9	0.4
- Tinea Versicolor (7)	1.6	0.8
- Tinea Circinata (5)	1.2	0.6

TABLE (2) SKIN DISEASES ASSOCIATED WITH HEPATITIS IN RELATION TO AGE, SEX, TYPE OF HEPATITIS AND THE DURATION IN YEARS

Skin disease	Sex		Total	Mean age in both sexes	Type of Hepatitis		Mean duration of skin lesions	% Skin Lesions (55)	% Total (900)
	Male	Female			B	C			
Lichen planus	15	6	21	43.9	5	16	0.8	38.1	2.3
Chronic urticaria	12	3	15	39.9	3	12	1.5	27.3	1.7
Erythema multiform	5	1	6	42.8	-	6	0.1	10.9	0.7
Psoriasis	1	4	5	48	1	4	2	9.1	0.6
Leucocytoclastic Vasculitis	2	2	4	31.5	2	2	0.2	7.3	0.4
Erythema nodosum	3	1	4	45.5	-	4	0.6	7.3	0.4
Total	38	17	55		11	44			6.1%

TABLE (3) : SEROLOGICAL TESTS IN RELATION TO SKIN DISEASES ASSOCIATED WITH HEPATITIS

Serological test Skin disease	Total bilirubin X ± S D	S G P T X ± S D	S G O T X ± S D	Alkaline phosphatase X ± S D	Blood Urea X ± S D	Serum Creatinine X ± S D	Cholesterol X ± S D	F . B .S. X ± S D
Lichen Planus	1.57±0.50	50.61 ± 41.34	49.5 ± 46.4	28.9±13.2	23.6±7.1	0.97±0.1	193.6±26.05	109.2±27.5
Urticaria	5.2 ± 10.08	35.53 ± 20.92	37.7 ± 29.9	30.5 ± 29.7	19.1±4.7	14.7±48.7	190.7±58.6	112.0±30.8
Erythema multiform	1.9 ± 0.5	47.5 ± 37.1	50.5 ± 36.2	27.0 ± 15.6	23.0±6.3	0.98±0.1	230.0±47.2	124.2± 29.7
Psoriasis	1.28 ± 0.63	53.0 ± 43.5	59.0 ± 36.6	27.6±8.9	20.4 ± 4.6	0.88±0.1	213.0±25.9	99.0±6.5
Leucocytoclastic vasculitis	2 ± 0.0	55.0 ± 49.5	45.0 ± 21.2	43.0±4.24	27.5±3.5	1.0±0.0	220.0±42.43	102.5±10.6
Erythema nodosum	1.5 ± 0.07	25.0 ± 7.07	51.5±54.5	20.0 ± 7.07	20.0±7.07	1.0±0.0	225.5±102.5	97.5±3.5
P	> 0.05	> 0.05	> 0.05	> 0.05	>0.05	>0.05	> 0.05	>0.05

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