

Autoimmune Hepatitis Markers in Association with Chronic Viral Hepatitis Type B and C

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Abstract

Circulating auto-antibodies have gained great significance for the diagnosis of autoimmune hepatitis (AIH) and various autoantibodies have been reported in patients infected by chronic viral hepatitis. Enzyme linked immunosorbent assay (ELISA) was used to assess these autoantibodies in the sera of 116 seropositive hepatitis B & C virus patients admitted to Baghdad Teaching Hospital from March 2009 to the end of December 2009. The presence of autoantibodies against cell nuclei (ANA), smooth muscle (SMA), liver- cytosol type-1 (anti LC1) and liver kidney microsome type1 (anti LKM-1) for all the affected patients' sera was measured. Antinuclear antibodies (ANA) results showed that 18 (16%) of cases revealed seropositive results, while anti-smooth muscle antibodies (SMA) results showed only two (2%) seropositive results both of which are of HCV patients. Results of anti LC-1 autoantibodies and anti LKM1 autoantibodies showed seropositivity in 6 (5%) and 8 (7%) cases, respectively, all of which are of HCV type. The current study suggest that chronic HCV infection can mimic autoimmune chronic active hepatitis; and special care must be held in patients who are unresponsive to immunosuppressive treatment, as HCV may be the role here.

Introduction

The presentations of autoimmune hepatitis (i.e., clinical, biochemical, histological, and serological) are each highly diverse, explaining why criteria committees have experienced such difficulty in defining the disease (1). The determination of autoantibodies against soluble liver antigen, pancreas antigen (SLA/LP) is a new and important component of autoimmune diseases of the liver (2). Circulating autoantibodies have gained great significance for the diagnosis of autoimmune hepatitis (AIH). Besides antibodies against SLA/LP, the following auto-antibodies are associated with AIH: antibodies against cell nuclei (ANA), nDNA, smooth muscle (SMA, with the most important target antigen being F-actin), liver-kidney microsomes (LKM-1, target antigen: cytochrome p450 IID6) and granulocytes (pANCA: perinuclear anti- neutrophil cytoplasmic antibodies) (3). Some authors classify AIH in accordance with the autoantibody status: subtype I (antibodies against ANA, SMA), subtype II (antibodies against LKM1, LC-1) and subtype III (antibodies against SLA/LP) (4, 5). Various autoantibodies have been reported in patients chronically infected by hepatitis C virus. 2% to 10% of these patients have anti-liver-kidney microsome type 1 (anti-LKM1) autoantibodies. In type 2 autoimmune hepatitis, anti-LKM1 auto- antibodies are frequently associated with anti-liver-

cytosol type 1 (anti-LC1) autoantibodies (6). Autoantibodies against cell nuclei (ANA) and against smooth muscle (SMA) are frequent in AIH. But also occur in 10% to 20% of patients with chronic viral hepatitis and in other diseases. As oppose to all other auto-antibodies, antibodies against SLA/LP are highly specific for AIH and have not been described in viral hepatitis (7, 8).

Materials & Methods

A cross sectional hospital based study was held in Baghdad Teaching Hospital-Teaching Laboratories from March 2009 until the end of December 2009. One hundred sixteen (116) cases of seropositive hepatitis B and C patients were included, all were screened and tested using simple immunodiffusion strip test (Figure 1), then confirmed by using quantitative Enzyme Linked immunosorbent (ELISA) assay-Sandwich method (Figure 2). Seventy seven (77) of them were hepatitis B virus seropositive while (31) were hepatitis C virus seropositive and only (8) were having both B and C types. Using quantitative Enzyme Linked immunosorbent (ELISA) assay-Sandwich method, we measure the presence of autoantibodies against cell nuclei (ANA), smooth muscle (SMA), liver- cytosol type-1 (anti LC1) and liver kidney microsome type1 (anti LKM-1) for all the affected patients' sera. Data were collected and statistically analyzed.



Fig (1): the strip tests used for screening the seropositive hepatitis virus patients (Left shows negative results while right shows positive results)



Fig (2): the ELISA kit used for confirming the seropositive patients (dark-orange colored wells suggest positive results)

Results

Among 116 patients with chronic viral hepatitis, 52 were males and 64 were

females, distributed on different age groups as shown in table (1).

Table (1):- Illustrating the age group and sex distribution of chronic viral hepatitis of group B & C.

| <i>Sex</i> | <i><10 yr</i> | <i>10-19 yr</i> | <i>20-29 yr</i> | <i>30-39 yr</i> | <i>40-49 yr</i> | <i>50-59 yr</i> | <i>> 60 yr</i> | <i>Total</i> |
|--------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-------------------|--------------|
| Male | 7 | 15 | 12 | 10 | 4 | 1 | 3 | 52 |
| Female | 9 | 21 | 10 | 13 | 6 | 3 | 2 | 64 |
| Total | 16 | 36 | 22 | 23 | 10 | 4 | 5 | 116 |

Antinuclear antibodies (ANA) results showed that among the total 116 hepatitis patients, 18 patients (16%) revealed seropositive results, 16 of them (14%) were hepatitis C virus (HCV) seropositive cases (3 patients were of mixed infections with both B

and C types) and only two cases were of hepatitis B virus (HBV) patients. Anti- smooth muscle antibodies (SMA) results showed only 2 (2%) seropositive results both of which are of HCV patients, as shown in figure (3).

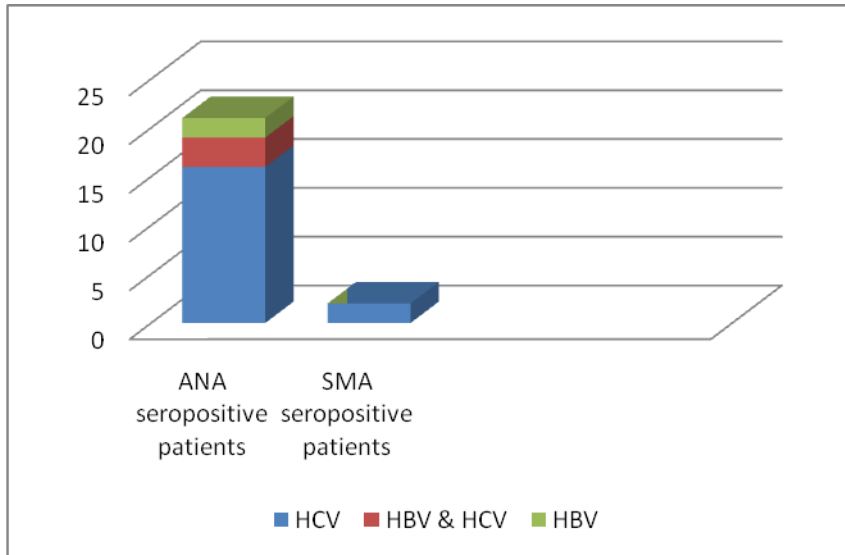


Fig (3):- shows the distribution of seropositive ANA and SMA patients among the total patients with chronic viral hepatitis.

The current study showed only 6 cases (5%) of HCV seropositive patients with anti LC-1 autoantibodies. While the anti LKM1 autoantibodies were positive in 8 HCV seropositive patients

(7%), four of them were also positive for ANA autoantibodies, as shown in figure (4). No HBV cases were positive for anti LKM1 or LC-1 autoantibodies.

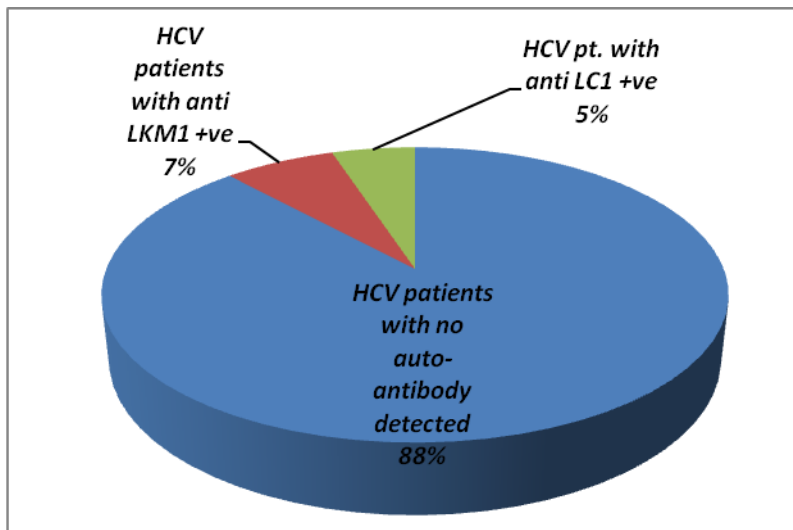


Fig (4):- shows the distribution of anti- LKM1 seropositive cases among the HCV patients.

Discussion

Anti nuclear antibodies (ANA) are a specific class of autoantibodies that have the capability of binding and destroying certain structures within the nucleus of the cells (9). The prevalence of antinuclear antibody (ANA) has been documented in patients with hepatitis C virus (HCV) infection (10). In current study, about 19% of HCV seropositive cases were also having ANA autoantibodies, which is near to what Peng *et al* (10) and Pawlotsky *et al* (11) have found. Several studies from Europe have observed a relationship between hepatitis C virus infection and anti-liver/kidney microsome-1 (anti-LKM1) positive chronic hepatitis. It has been suggested that hepatitis C may induce an autoimmune phenomenon that leads to the development of a specific type (type II anti-LKM1 positive) autoimmune chronic hepatitis (12). In current study, 7% and 9% of chronic active hepatitis cases were seropositive for anti LC-1 and LKM1 autoantibodies, respectively, all of which are of HCV patients. This goes with what Reddy *et al* (12), Gerotto *et al* (13) and Beland *et al* (14) found. Kitazawa *et al* (15) stated that Anti-LKM1 may be able to recognize simultaneously at least two antigenic sites on the CYP2D6 protein, and reactivities against individual epitopes may differ according to HCV infectivity status. The current study conclude that chronic HCV infection can mimic type 1, as well as type 2, autoimmune chronic active hepatitis; and special care must be held in patients who are unresponsive to immunosuppressive treatment, as HCV may be the role here.

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