

Serum Immunoglobulins Levels in Autoimmune Hepatitis of Iraqi Patients

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Summary:

Background: Autoimmune hepatitis (AIH) is an unresolving inflammation of the liver of unknown cause associated with interface hepatitis on histological examination, hypergammaglobulinemia and presence of circulating autoantibodies. Antibody-mediated tissue injury might be responsible for tissue injury in AIH therefore; a number of studies have been focused on the immunoglobulins in these patients. The aim of the study is to estimate the level of immunoglobulins (IgG, IgA and IgM) in different types of Autoimmune hepatitis (AIH).

Patients and Methods: The study was performed on 73 Iraqi patients with autoimmune hepatitis (AIH), attending the teaching hospital for gastroenterology and liver disease in a period between November 2003 and July 2004. : Anti-soluble liver ANA, SMA, LKM-1, and LC-1 Abs were detected using Enzyme-Linked Immunosorbent Assay (ELISA) technique. Anti-SLA/LP was detected using the Euroline method. Quantitation of serum IgG, IgA and IgM of the study groups were carried by single radial immunodiffusion (SRID) test. Equal volume

Results: Significant differences were observed between AIH patients and healthy control group in the mean level of IgG, IgA and IgM. In addition, level of IgA in the sera of patients with type 2 was lower than those of type 1 and 3.

Conclusion: It was concluded that in patients with AIH, the Immunoglobulin G was significantly higher in type-1, whereas IgA was significantly lower in AIH-2 patients compared to other types of the disease.

Keywords: Autoimmune hepatitis, Immunoglobulin G.

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Introduction:

The importance of humoral factors in immunological response to chronic liver disease has been suggested by various investigators (1,2). The most consistently reported abnormality was found in studies of serum immunoglobulins as well as circulating immune complex (CIC). Serological analysis showed a high level of IgG, IgA and IgM in AIH (3). Moreover, an increase of CIC levels in AIH patients compared to normal control was quietly reported (4, 5). As observed in many studies, auto-reactive antibodies against liver associated antigen present in sera of patients with AIH is significantly higher, which is most likely due to polyclonal and specific activation of B-cells (6,7). Alvarez and associates mentioned that autoantibodies against "self" structure may provide additional information with regard to classification, treatment and prognosis of AIH patients (8).

Patients and Methods:

Patients:

The present study included 73 Arab, Iraqi AIH patients (53 females and 20 males; mean age 35.5 years, ranged between 8-65). Compared with 50 healthy individuals (age and sex matched). Both groups were subjected to serological detection of ANA, SMA, LKM-1, LC-1, and SLA/LP Abs by IIF and Euro line method.

Laboratory investigation: -ANA, SMA, LKM-1, and LC-1 Abs were detected using Enzyme-Linked Immunosorbent Assay (ELISA) technique used human IgG Fc as the antigen coated the microwells plate and isotype-specific horse antibodies coupled to radish peroxidase; result were expressed as the optical density. Anti-SLA/LP was detected using the Euroline method. The test kit contains test strips coated with parallel lines of antigens, which have been purified by affinity chromatography. Euro immune has supplied the above kits company, Germany. Quantitation of serum C3 and C4 of the study groups were carried by single radial immunodiffusion (SRID) test.

Statistical Analysis: It was assessed using ANOVA test and paired (T-test).

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Results:

As it is shown in figure- 1, 49(67%) of patients had type 1 whereas, 16 (22%) had type 2, and 8 (11%) had type 3-AIH.

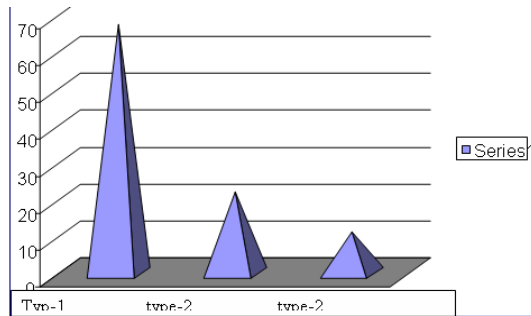


Figure-1: The frequency distribution of AIH types

The autoantibodies (ANA, SMA, LKM-1, LC-1, and SLA/LP) were not detected in healthy control group just in few no. in comparison to AIH patients. Concerning the autoantibodies that present in type 1-AIH, our data revealed that ANA and SMA represent 30.14% and 42.47% respectively, whereas LKM-I, and LC-1 Abs (marker of type 2) exhibit 16.44% and 13.7% respectively, while SLA/LP Abs exhibit 100% of patients with type 3. (Figure-2)

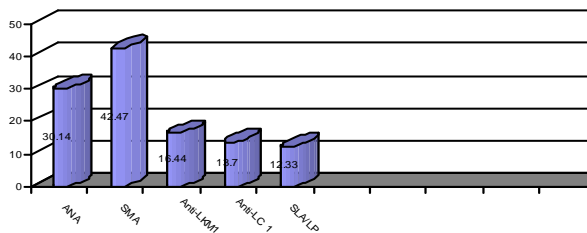


Figure-2: The frequency distribution of autoantibodies among AIH patients

The total level of Igs in the sera of AIH patients and healthy controls were listed in figure-3. The Igs concentration were measured in mg/ml. our result pointed out to a significant changes in the level of IgG , and IgA between three types of AIH and in comparison with healthy subjects . Since a higher value of mean serum IgG level (2447.36 ± 248.95) with significant differences in type 1 patients ($P < 0.001$) compared to that of type 2 and 3 (1340.4 ± 536.0) and (1973.48 ± 264.27) respectively and in comparison to healthy subjects (1169.56 ± 248.32).

On the other hand, the serum IgA level in type 2 patients was significantly lower than those in other types and in healthy control. Furthermore, IgM level was higher than those in healthy control though statistically not significant, while there was no difference in their level between three types of the disease.

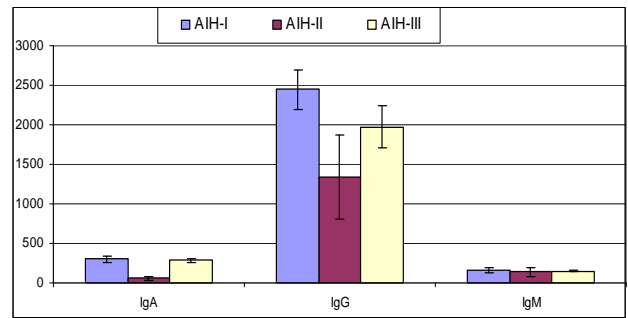


Figure 3: Bar chart showing the immunoglobulins concentration (mg/dl) between 3 types of AIH .

Discussion:

Hypergammaglobulinemia is well accepted to be distinct feature of AIH, thus our result is in agreement with many investigators who collectively cited that serum level of gamma-globulin rises in patients with AIH in comparison to healthy controls (9, 10). Related to this study , it was clear that there were significant differences between AIH sera levels of IgA, IgG, and IgM in comparison with other studying groups (P value < 0.001) except for IgM level (P value > 0.05). The explanation for this finding that the increased synthesis of Abs due to increased number of plasma cell in marrow, and even in liver itself. On the other hand, It should also note that most autoantibodies are not monoclonal rather polyclonal. In general, persistent polyclonal increase in gammaglobulin is though to be related to antigenic stimulation of chronic nature or loss of immunoglobulin regulation (11). Immunoglobulin G was significantly higher in AIH-1 patients, whereas IgA was significantly lower in AIH-2 patients compared to other types of the disease, possible explanation of the above data was since both of them, type1 and type 3, characterized by the presence of many kinds of autoantibodies majority of them are of class IgG which result in elevation of IgG concentration in the patients sera while, type 2 characterized by presence of one or 2 types of autoantibodies so the elevation in the total concentration though it is present but not as high as in type 1 , and 3-AIH which was proved by the electrophoresis picture .On the other hand , IgA concentration is proportionally associated with its consumption due to alternative pathway complement activation which confirmed by decrease level of C4 in type 2-AIH patients sera .

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