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Clinical study of autoimmune hepatitis: A single center study at National Liver Institute

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***Abstract*---**Introduction: Autoimmune hepatitis (AIH) is an infrequent liver insult with notorious comorbidities, in which autoimmune-mediated relativities against hepatocytes are thought to play a crucial role. Aim: to delineate updated demographics of AIH. Methods: This study was conducted retrospectively. Assessment included demographic, laboratory, radiological, and histopathological characteristics (if feasible). Results: The mean age of the studied cases was 34.63 ± 12.76 years with minimum 19 years and maximum 65 years with female predominance as There were 15 males (26.3%) and 42 females (73.7%). 15.8% of cases had AIH associated DM, 2.2% with autoimmune thyroiditis, and 1.5% with Crohn's disease. Conclusion: AIH is a prevalent liver disease.

Keywords---autoimmune, Crohn's disease, liver biopsy, hepatitis.

Introduction

Autoimmune hepatitis (AIH) is a chronic liver disease in which autoimmune-mediated relativities against hepatocytes are thought to play a crucial role (1). The point prevalence of AIH is reported to be 10 to 25 per 100,000 population in European countries, and 5 to 25 in the Asia-Pacific region (2). The male-to-female ratio of the population with AIH is considered to have changed over time, indicating a relative increase in the number of male patients. In Japan, the male-to-female ratio was 1:7 in 2004 and 1:4 in 2016 (3).

AIH is multifactorial and involves the interaction of both genetic background and environmental triggers; accordingly, environmental insult in genetically susceptible individuals may result in aberrant immunological reactions and lead to autoimmune-mediated injury to hepatocytes (4). The diagnostic criteria for AIH were created as a diagnostic scoring system by the International AIH Group in 1993 and revised in 1999 (4). This study aimed to delineate the prevalence, age and sex distribution of autoimmune hepatitis.

Patients and methods

This observational study was conducted on Egyptian patients having confirmed diagnosis of autoimmune hepatitis. The study was conducted retrospectively from April 2017 to March 2018 Patients were recruited from patient records.
Inclusion criteria: Any case with confirmed diagnosis of autoimmune hepatitis by clinical (jaundice& abdominal distension), laboratory (elevations of serum transaminases, detectable autoantibodies and elevated serum IgG), or -whenever feasible- histopathological evidences of autoimmune hepatitis (5).
Exclusion criteria: Patients with evidence of viral hepatitis or drug induced nonimmune hepatitis (not fulfilled criteria of DIAIH which meeting established international criteria AIH, hypergammaglobulinemia, autoantibodies and typical liver biopsy), patients younger than 18 years and any case with incomplete data.

Methods

In the retrospective group, the all required data in concern was meticulously collected from the patient's records along with contact with cases whenever possible for the one year (from 2017 to 2018).

All studied patients were subjected to the following: History taking and clinical examination: Demographic characteristics (age, sex). Smoking indices. Presence of medical systemic disorders (diabetes mellitus, and hypertension). The diagnosis of AIH was made according to Simplified International scoring system and Revised Original International Scoring System for the diagnosis of AIH. Both the definite and probable categories of AIH patients were included in the study (tables V, VI). Remission: is defined as resolution of the laboratory indices (normal serum ALT or AST, c-globulin and IgG levels). Relapse: is defined as recurrence of symptoms, increase serum AST level >_ 3-fold normal and/ or reappearance of interface

hepatitis. Treatment failure: is defined as deterioration despite compliance with therapy and may be observed within 3-6 weeks. Incomplete response: is defined as insufficient remission criteria after 3 years.
Laboratory investigations: Liver function tests: serum bilirubin total and direct, aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin alkaline phosphatase (ALK), gamma glutamyl transferase (GGT), prothrombin activity, and international normalized ratio (INR). Renal function tests: serum urea and creatinine.

Complete blood count: (hemoglobin concentration, total leucocytic count, platelet counts): HCV antibodies by third generation enzyme immunoassay, and if positive; Polymerase chain reaction (PCR) of HCV. Hepatitis B surface antigen (HBsAg), anti-hepatitis B core (HBc)-IgG, anti-HBc-IgM, anti-EBV-IgM, anti-CMV-IgM, Antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA) antimitochondrial antibody (AMA) perinuclear anti-neutrophil cytoplasmic antigen (p-ANCA) and anti-liver-kidney microsomal antibody (anti-LKM-1) and Serum IgG. Imaging: Abdominal ultrasonography. Histopathological examination of liver biopsies: whenever feasible.

Results

The mean age of the studied cases was 33.93 ± 10.53 years with minimum 20 years and maximum 52 years with female predominance as There were 4 males (26.7%) and 11 females (73.3%) As shown in table (1). In table (2), as regarding laboratory data the mean AST level of the studied cases was 411.53 ± 410.19 with minimum 27 and maximum 1158, the mean ALT level of the studied cases was 300.88± SD 400.95 with minimum 27 to maximum 1158 IU. As shown in table (3), Anti smooth muscle antibodies was present in 87.7% of studied cases, antinuclear antibodies was present in 89.5% of studied group (95.2% of prospective group was positive while 73.3% of retrospective group was positive), anti-liver kidney microsomal 1 was present in 7% of studied cases, anti-mitochondrial antibodies was present in 3.5%.

Table (1): Age and sex distribution cases

	Retrospective (n = 15)	
	No.	%
Gender		
Male	4	26.7
Female	11	73.3
Age (years)		
Min. – Max.	20.0 – 52.0	
Mean ± SD.	33.93 ± 10.53	
Median (IQR)	32.0 (26.0 – 39.5)	

IQR: Inter quartile range
SD: Standard deviation
*Continuous data expressed as mean ± SD and median (range). N: number
* Categorical data expressed as Number (%)

Table (2): AST and ALT in cases

	Retrospective (n = 15)
AST(U/L)(0-35) Min. – Max. Mean ± SD. Median (IQR)	 27.0 – 1158.0 411.53 ± 410.19 179.0 (68.5 – 797.0)
ALT(U/L)(0-35) Min. – Max. Mean ± SD. Median (IQR)	 13.0 – 1405.0 453.40 ± 495.45 299.0 (46.5 – 761.0)

IQR: Inter quartile range
SD: Standard deviation
ALT: alanine transferase, AST: aspartate transferase

Table (3): presence of autoantibodies in cases

	Retrospective (n = 15)	
	No.	%
ASMA	10	66.7
ANA	11	73.3
Anti LKM1	1	6.7
AMA	0	0.0

ASMA: anti smooth muscle antibodies ANA: antinuclear antibodies
Anti LKM1: anti liver kidney microsomal 1 AMA: anti mitochondrial antibodies

Table (4): positive viral hepatitis markers (HCV, HBV, HAV) in both studied groups

	Retrospective (n = 15)	
	No.	%
Viral markers (hepatitis c)	1	6.7

HCV: hepatitis c virus, HBV: hepatitis b virus, HAV: hepatitis A virus,

As shown in table 4, All of cases was negative for HBV and HAV While 5.3% of studied cases was HCV positive (3 cases was positive, 2 in prospective group and 1 in retrospective group).

Table (5): Ultrasonography data of both studied groups

u/s	Total (n = 57)		Prospective (n = 42)		Retrospective (n = 15)	
	No.	%	No.	%	No.	%
Cirrhotic liver	53	93.0	40	95.2	13	86.6
Fatty liver	2	3.5	1	2.4	1	6.7
Mild liver fibrosis	2	3.5	1	2.4	1	6.7

As shown in table 5, as regarding ultrasonography cirrhotic liver was present in 93% of studied cases, Fatty liver was present in 3.5% of cases and mild liver fibrosis was present in3.5% of cases.

Discussion

Despite these advancements, many questions remain unanswered in the management of AIH, such as the actual national and international prevalence and incidence rates, the optimal timing for withdrawing or stopping treatment, and whether some patients can maintain good health without treatment. Unfortunately, there is currently no comprehensive study in Egypt that has examined the prevalence, characteristics, and clinical scenarios of AIH in Egyptian patients.

This study aimed to address these knowledge gaps by determining the prevalence, age, and gender distribution of AIH in Egypt and by elucidating various clinical scenarios related to disease presentation, clinical course, and treatment response. This study was conducted retrospectively from April 2017 to March. The study revealed that AIH in Egypt predominantly affects females, with a mean age of 34.63 years.

Coincidingly, Fallatah et al, (6) found that among 33 patients with AIH, the mean age at presentation was 32.3 years, with a female predominance of 75.7%. Similarly, Mogahed et al, (7) reported in their study that among 34 AIH patients, 22 were females (64.7%) with a female-to-male ratio of 1.8:1. Furthermore, Aljumah et al, (8) found that the mean age of acute-onset AIH patients at presentation was 33.8±1.5 years, with a female-to-male ratio of 1.4:1. Additionally, Koay et al, (9) noted a female predominance in a ratio of 5.7:1.

These demographic insights provide a foundational understanding of the study's patient population, and confirming what is settled about AIH female sex predilection. Many theories had been suggested to explain this feminine preference of AIH including hormonal, chromosomal, microchimerism, and microbiota (10). However, no definite theory had been eventually adopted.

AIH is a complex condition with many facets, and this study provides valuable insights into its prevalence and clinical characteristics in Egypt. The findings from this research contribute to our understanding of AIH and may inform more effective management strategies in the future. A noteworthy proportion (15.8%) of patients had a history of diabetes mellitus (DM). Some patients presented with

both DM and hypertension (HTN) (3.5%). A small subset (5.3%) had a history of smoking. Understanding these comorbidities is vital for evaluating their potential influence on the study outcomes and patient prognosis.

Coincidentally, AIH frequently co-occurs with other disorders. In our current study, we found that 5.3% of patients had autoimmune thyroiditis, 5.3% had an overlap with primary sclerosing cholangitis (PSC), 3.5% had an overlap with primary biliary cholangitis (PBC), 3.5% had contact dermatitis, while 1.8% had scleroderma, and 1.8% had myasthenia gravis. This information is valuable for identifying the presence of autoimmune diseases that may affect the study's results and patient outcomes.

Consistently, Mogahed et al, (7) reported the occurrence of concomitant autoimmune diseases in 14.7% of cases. They observed that 4 patients had systemic lupus erythematosus, one had ulcerative colitis, and one had thyroiditis, with a positive family history of autoimmune diseases in 5.8%. Both Fallatah et al, (10) and Aljumah et al, (8) documented that diabetes mellitus was the most prevalent comorbidity with AIH.

Additionally, Buechter et al, (11) reported autoimmune thyroiditis as the most common concomitant autoimmune disease affecting AIH patients (11.96%), with PBC in 6.17% and PSC in 2.24%. They also observed that 7.10% of patients suffered from concomitant rheumatic diseases, including 22 cases of rheumatoid arthritis and 16 cases of Sjögren's syndrome. Furthermore, 4.86% of patients had inflammatory bowel diseases, encompassing 18 cases of ulcerative colitis and 12 cases of Crohn's disease. In line with these findings, Tamimi et al, (12) discovered associated autoimmune disorders in six patients, with individual patients exhibiting Hashimoto's thyroiditis, vitiligo and psoriasis, rheumatoid arthritis, celiac disease, ulcerative colitis, and Sjögren's syndrome.

A small percentage (5.3%) of patients tested positive for hepatitis C viral markers. This information is vital for assessing the role of viral hepatitis in the liver condition of the study subjects. In conclusion, this study highlights the specific characteristics and challenges in managing AIH in Egypt. Early recognition, diagnosis, and treatment of AIH are crucial to prevent complications like cirrhosis and reduce the need for liver transplantation in treatable cases. Collaboration and the collection of national data can further enhance our understanding of AIH in Egypt, leading to improved patient outcomes care.

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