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Original Research Article

A Study of the Liver Involvement in Autoimmune Diseases

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Conflict of interest: Nil

Abstract

Background: There has been evidence of significant regional variation in the prevalence and clinical symptoms of autoimmune hepatitis (AIH). In India, it is regarded as a sporadic cause of liver disease. The goal of the current investigation was to ascertain the prevalence, clinical, biochemical, and histological characteristics of AIH in patients visiting our tertiary care teaching hospital in south India.

Methods: All patients underwent thorough physical examinations, with specific emphasis dedicated to checking for symptoms of liver illness such as icterus, edema, hepatosplenomegaly, and ascites, as well as characteristics of autoimmune phenomena such as alopecia and vitiligo. LFT, ESR, and whole blood count were standard lab tests. Prothrombin time was one of the measures used to assess liver function. Immunological markers were detected by using the immunofluorescence approach, and rheumatoid factor (RF) and antinuclear antibody (ANA) were measured.

Results: Out of n=40 cases included in this study n=20 cases out of n=29 cases of Rheumatoid Arthritis suffering from systemic conditions which included 13/29 cases of diabetes mellitus and 7/29 suffering of thyroid disorders. Similarly, in the cases of systemic lupus erythematosus, we found n=2/11 cases with diabetes mellitus and n=/11 cases of thyroid diseases. The mean Globulin level was 3.1 gm/dl, Elevated globulin (> 3.4 gm %) was seen in n=19 cases. The AST range (8 to 48 U/L) estimation was found to be elevated in n=15 cases and ALT (7 to 55 U/L) was found to be elevated in n=22 cases and ALP *(*44–147 IU/l) was found to be elevated in n=23 cases.

Conclusion: Autoimmune diseases like SLE and Rheumatoid arthritis are the major causes of liver dysfunction in autoimmune diseases. Clinical presentation may be nonspecific with myalgia, arthralgia, and chronic fatigue syndrome. Diabetes and thyroid diseases are mostly associated disorders. Serological markers of autoimmunity are positive in most cases. The presence of multiple markers is probably proportional to activity. A small minority of patients present with decompensated liver disease and signs of portal hypertension, with varices and ascites.

Keywords: Autoimmune liver diseases, Systemic Erythematosus, Ascites, Hepatitis.

Introduction

Liver involvement is very common in cases of autoimmune diseases and Still and Wishart published the first findings of a connection between liver illness and arthritis in 1897. [1] and 1903, respectively. [2] Thereafter, several attempts to induce jaundice to reduce joint discomfort were made. [3] The conclusion of the search for the "active agent" in this jaundice-induced reaction was the corticosteroid hormone metabolism was abnormal in these circumstances. First reports of a remarkable response to corticosteroid treatment in rheumatoid arthritis followed. [4] Rheumatoid arthritis and other connective tissue illnesses include impaired liver function, which has been linked to the systemic character of the underlying disease process. [5] Numerous case series of patients with autoimmune disorders with subclinical and symptomatic liver impairment was documented. [6, 7] Terminology has been clarified throughout the past 25 years, going from lupoid hepatitis to chronic active hepatitis to autoimmune hepatitis. New prospects for understanding the genetic and molecular foundation of autoimmune liver disease have emerged because of the explosion of knowledge in the domains of genetics and molecular biology. Autoimmune hepatitis is an unresolved inflammation of the liver of unknown cause characterized by the presence of interface hepatitis, portal plasma cell infiltration, hypergammaglobulinemia, and autoantibodies. [8] In 5 to 9.7% of PBC patients, rheumatoid arthritis is present. Rheumatoid factor is positive in 64% of cases, the majority of which had asymptomatic joint erosions. 10% of individuals have symptoms of arthritis. 72% of people experience the sicca complex of dry mouth and eyes. Scleroderma and CREST syndrome affects 17% of individuals, whereas 12% of patients have Raynaud's phenomenon. In white people from northern Europe, the incidence of autoimmune hepatitis is 1.9 cases per 100,000 people per year, and the point prevalence is 16.9 instances per 100,000 people per year. [9] Less than 1 case per 100,000 people is reported to occur in India each year. [10] The illness is underdiagnosed in the elderly and affects all age groups with equal frequency. Additionally, it is a diagnosis that should be established in babies. Patients make up 78% of the population, and the female-to-male ratio is 3.5. Comparatively more women than males have concomitant immunological disorders when they have autoimmune hepatitis. This illness is characterized by fluttering arthritis, which is caused by hypercholesterolemia. In 35–38% of individuals, digital clubbing and hypertrophic osteoarthropathy have been found. [11] Autoimmune hepatitis is commonly associated with arthralgia, or stiffness in big joints. In 95% and 84% of patients, respectively, rheumatoid factor and ANA are positive. [11] Less frequent symptoms include effusion and joint edema. Autoimmune hepatitis is an emerging condition in our country however, due importance has not been given as compared to chronic hepatitis. The current study aimed to detect liver involvement in cases of autoimmune diseases presented to our tertiary care teaching institute in South India.

Material and Methods

This prospective study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study. Written consent was taken from all the participants after explaining the nature of the study in the local language.

Inclusion criteria

1. Newly detected cases of systemic lupus erythematosus [SLE]

2. Newly detected cases of Rheumatoid arthritis based on American Rheumatological Association (ARA) criteria.
3. Aged 18 years and above
4. Positive serological tests for (RF/ ANA)
5. Males and females

Exclusion criteria

1. Cases of metabolic liver diseases
2. Acute febrile illnesses
3. Positive of HBsAg anti HCV
4. Alcoholic liver diseases
5. Unwilling to participate in the study

All patients underwent thorough physical examinations, with specific emphasis dedicated to checking for symptoms of liver illness such as icterus, edema, hepatosplenomegaly, and ascites, as well as characteristics of autoimmune phenomena such as alopecia and vitiligo. In addition to complaints of liver involvement, connective tissue involvement, and related endocrine involvement, the demographic profile and clinical history were documented. The use of herbal and alternative medications was looked for in the pertinent drug history. Liver Function Tests (LFT), ESR, and whole blood count were standard lab tests. Prothrombin time was one of the measures used to assess liver function. Immunological markers were detected by using the immunofluorescence approach, and rheumatoid factor (RF) and antinuclear antibody (ANA) were measured. An ultrasound of the abdomen was part of the imaging. We measured the spleen and liver sizes, the portal vein diameter, the existence of collaterals, and the amount of free fluid. When necessary, an upper GI endoscopy was performed to check for signs of portal hypertension.

Statistical analysis: All the available data was uploaded on an MS Excel spreadsheet and analyzed by using SPSS version 19 in windows format. For continuous variables mean, percentage, and standard deviations were used. For categorical variables, the chi-square test was used to detect the significance.

Results

A total of n=40 subjects satisfying the inclusion criteria were enrolled into the study. The age ranged from 18 years to 60 years. Most of the cases in the study belonged to the age group 21 – 30 years with 32.5% of all cases followed by the age group 41 – 50 years with 25% of cases the details have been depicted in table 1. Out of the n=40 cases n=30(75%) were females and n=10(25%) were males. The male-to-female ratio was 3: 1. The mean duration of illness before presentation to the hospital was 6.0 ± 1.5 months the range was 1 – 12 months. Of the n=40 patients enrolled in the study, n=11 (27.5%) cases were diagnosed to have SLE, whereas n=29(72.5%) had features of Rheumatoid arthritis.

Table 1: Demographic profile of the cases included in the study

Age (years)	SLE	RA	Total (%)
18 – 20	6	1	07 (17.5)
21 – 30	4	9	13 (32.5)
31 – 40	0	7	07 (17.5)
41 – 50	1	9	10 (25.0)
51 – 60	0	3	02 (5.0)
Total	11(27.5)	29(72.5)	40 (100.0)

Overall, the frequent presentation was with nonspecific symptoms of arthralgia, myalgia, and loss of appetite. Most of the patients presented with chronic fatigue syndrome. N=22(55%) cases reported had fatigue, n=34 (88%) had arthralgia and n=30 (75%) had myalgia. Jaundice and GI bleeding were less frequent. A detailed description has been given in table 2.

Table 2: Symptoms recorded in the cases of the study

Symptoms	Frequency	Percentage
Fatigue	22	55.0
Anorexia	12	30.0
Myalgia	30	75.0
Arthralgia	34	85.0
Jaundice	05	12.5
GI bleed	03	07.5

Note: some cases had multiple symptoms

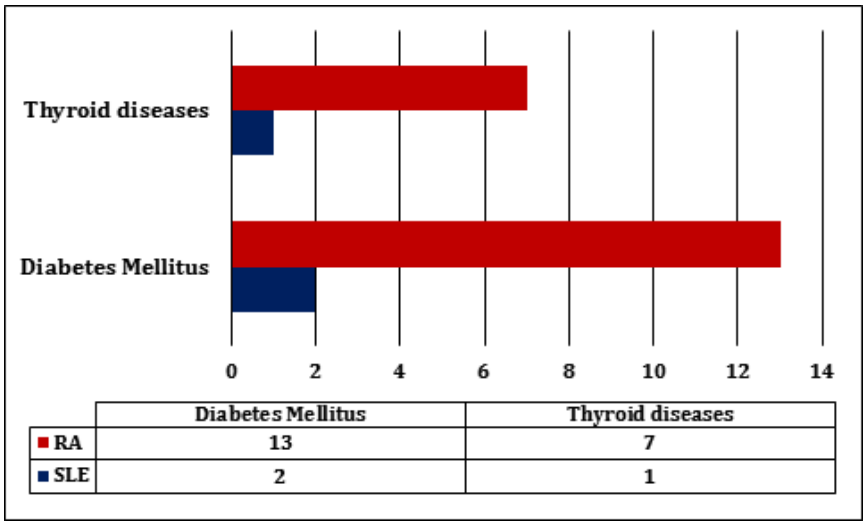

Figure 1: Associated systemic conditions recorded in the cases of the study

In this study, we found n=20 cases out of n=29 cases of Rheumatoid Arthritis suffering from systemic conditions which included 13/29 cases of diabetes mellitus and 7/29 suffering of thyroid disorders. Similarly, in the cases of systemic lupus erythematosus, we found n=2/11 cases with diabetes mellitus and n=/11 cases of thyroid diseases. The details have been depicted in figure 1.

N=31/40(77.5%) gave a history of drug intakes recently, out of which NSAID drugs were commonly used in 21 cases. N=9 cases used drugs from other systems of medicine which included ayurveda, homeopathy, and Siddha however, the nature of the drugs could not be ascertained.

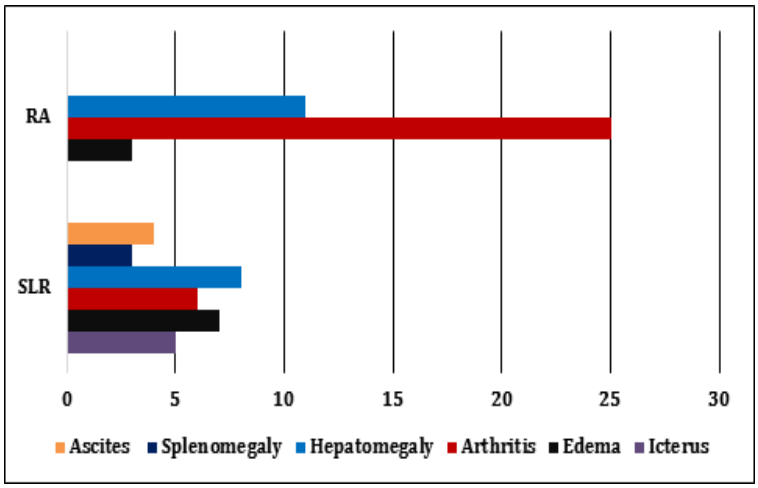

Figure 2: Incidence and distribution of physical signs among the cases of the study

There were few clinical indicators of liver illness, such as dilated veins, fluttering tremors, and spider nevi. Alopecia, arthritis, and edema were frequent symptoms. In 47.5% of all the cases, hepatomegaly was seen. Jaundice, splenomegaly, and ascites are a few uncommon yet common symptoms of liver dysfunction in SLE patients. Physical signs of decompensated chronic liver disease and portal hypertension were seen in n=2/11 SLE (18.18%) patients as well.

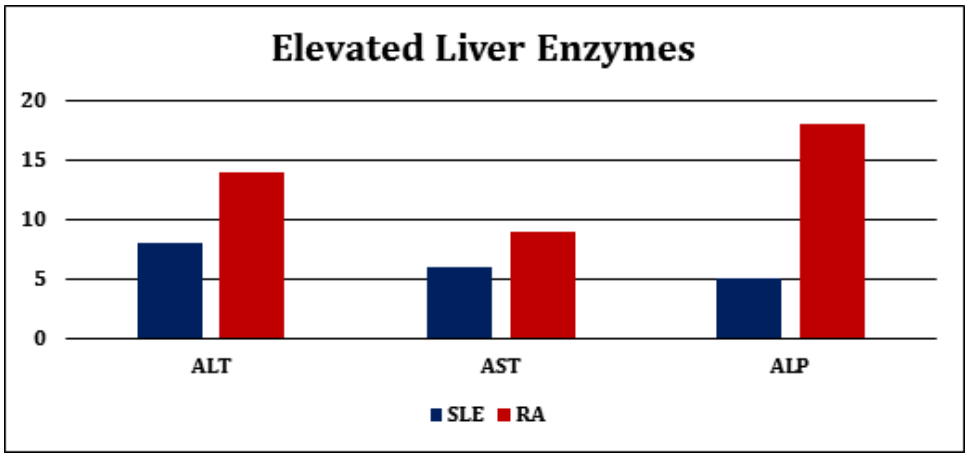

Figure 3: Distribution of Elevated liver enzymes in the patients of the study

Anemia and elevated acute phase reactants like sedimentation rate and C reactive protein were frequently seen. Mean Hb was 10.2 gm% whereas mean ESR was 61 mm at 1 hr. Modestly elevated bilirubin up to 4.5 mg% was seen in 5 patients (12.5%), of which 2 had decompensated liver disease. Mean albumin was 3 gm/ dL, and low albumin (< 2.5g %) was seen in 7 cases. The mean Globulin level was 3.1 gm/dl, Elevated globulin (> 3.4 gm %) was seen in n=19 cases. The AST range (8 to 48 U/L) estimation was found to be elevated in n=15 cases and ALT (7 to 55 U/L) was found to be elevated in n=22 cases and ALP (*44–147 IU/l)* was found to be elevated in n=23 cases. The distribution of the elevated liver enzymes in both groups of cases has been depicted in figure 3. Immunological markers, Antinuclear antibodies (ANA) were positive in n=16 (40%) cases, and Rheumatoid factor (RF) in n=30 (75%) patients. Both were positive in n=4(10%) of patients.

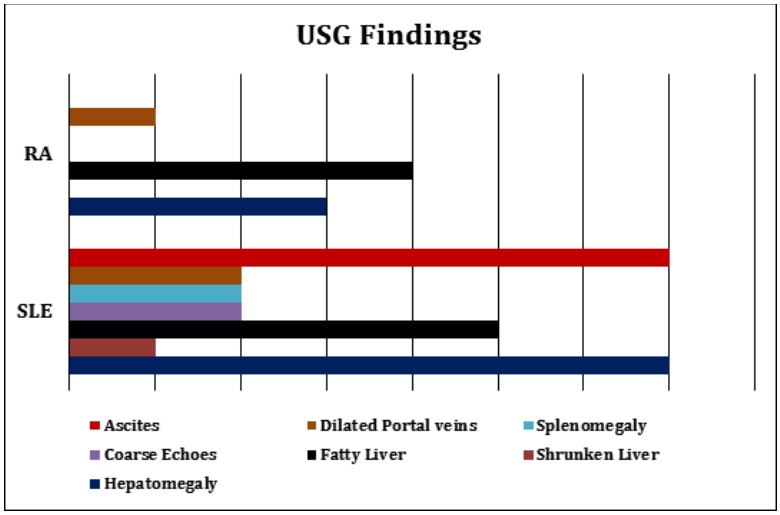

Figure 4: Distribution of ultrasound findings in both the group of cases in the study

Hepatomegaly was found in n=10/40 (25%) of cases followed by ascites in n=7/40 (17.5%) cases and fatty liver in n=9(22.5%) of cases. The n=2 SLE cases with decompensated liver disease had dilated portal vein diameter (> 1.3 cm) and Splenomegaly. All the sonogram findings were more common in SLE than in Rheumatoid arthritis. Splenomegaly, coarse echoes, ascites, and shrunken liver were exclusively seen in SLE details have been depicted in figure 4.

Discussion

The overall results of the current study are in concordance with other similar studies done in this field with few differences. This could be due to variations in genetic, geographical, and racial differences in the population studied. The unique aspect of the current study was we could examine the issue of autoimmune liver disease at an early stage because of the study's distinctive viewpoint. It offers a chance to understand the diverse natural history and hepatic symptoms of autoimmune disorders. Angela Hilton et al., [12] studied liver abnormalities in patients with joint symptoms of varied etiology. Thirty patients suffering from SLE, Rheumatoid arthritis, Gout, and other disorders were evaluated with routine liver function tests, immunology, and histology. They did not exclude any patients with alcoholic or viral hepatitis. They found the commonest abnormality was elevated transaminase (ALT) seen in 19 patients (63%), low serum albumin in 6 patients (20%), and elevated serum globulin in 16 cases (53%). This is comparable to the results of our study, where 29 patients (58%) had elevated ALT, and 8 (16%) had low albumin. In the current study, we found Modestly elevated bilirubin up to 4.5 mg% was seen in 5 patients (12.5%), of which 2 had decompensated liver disease. Mean albumin was 3 gm/ dL, and low albumin (< 2.5g %) was seen in 7 cases. The mean Globulin level was 3.1 gm/dl, Elevated globulin (> 3.4 gm %) was seen in n=19 cases. The AST range (8 to 48 U/L) estimation was found to be elevated in n=15 cases and ALT (7 to 55 U/L) was found to be elevated in n=22 cases and ALP (*44–147 IU/l)* was found to be elevated in n=23 cases. Cockel R et al., [13] found liver abnormalities in n=57 patients with SLE. Elevated transaminases were seen in 56% of cases. Of great interest to us is the finding that three of their patients had fatty liver compared to the four of our SLE patients who also had fatty liver. This gives the impression that autoimmune liver disease probably passes through a phase of fatty liver, like that seen in alcoholics, before causing Cirrhosis. The importance of this finding lies in the fact that these individuals can be identified as being at high risk for the development of Cirrhosis, hence requiring aggressive therapy and surveillance. Matsumoto T et al., [14] and Rothfield NF et al., [15] noted comparable anomalies in SLE patients. Of 520 SLE patients, only 3.8% had jaundice, according to Dubois EL., et al., [16] In the study by Koffman (46) it was found that 12% of SLE patients had jaundice. This is related to our study's low incidence of jaundice (6 cases/12%). Choudhuri et al., [10] in a similar study found autoimmune liver diseases formed 1.7% of all liver diseases. The most common manifestations were splenomegaly in 13 instances (34%), tiredness, edema, and hepatomegaly in 17 cases (44%), and jaundice in 21 cases (55%). These observations were similar to the observations found in the current study (figure 2). They found most prevalent related extrahepatic disorders were thyroiditis and diabetes in concordance with the observations of the current study. The mean duration of illness before presentation to the hospital was 6.0 ± 1.5 months the range was 1 – 12 months. Although tiredness, fluctuating jaundice, and arthralgia are the typical symptoms of autoimmune hepatitis, a significant number of patients lack any overt liver disease symptoms or appear suddenly, as was the case in 25% of cases, according to western

research. [17] In general, alkaline phosphatase and bilirubin levels are higher, whereas aminotransferases are more dramatically elevated. However, in rare instances of AIH, a cholestatic picture with elevated levels of conjugated bilirubin and alkaline phosphatase is seen. The typical first treatment for AIH is steroid monotherapy or combination therapy with prednisolone and azathioprine. Elderly patients, those with osteoporosis, diabetes, hypertension, obesity, and mental illnesses are the greatest candidates for combination therapy. In patients with hematological problems and young people with concerns about fertility, monotherapy with steroids is preferable. A hydrophilic bile acid with immunomodulatory properties is ursodeoxycholic acid. Small, uncontrolled studies conducted over two years revealed clinical and biochemical improvement as well as a decline in histological abnormalities. [18] The majority of cases in this study received prednisolone monotherapy and a few cases in combination with azathioprine depending on the age. [18]

Conclusion

The important findings of the current study were There is a female predominance; the majority of cases are young women with cases of autoimmune hepatitis. Autoimmune diseases like SLE and Rheumatoid arthritis are the major causes of liver dysfunction in autoimmune diseases. Clinical presentation may be nonspecific with myalgia, arthralgia, and chronic fatigue syndrome. Diabetes and thyroid diseases are mostly associated disorders. Serological markers of autoimmunity are positive in most cases. The presence of multiple markers is probably proportional to activity. A small minority of patients present with decompensated liver disease and signs of portal hypertension, with varices and ascites. In our country, there is a delay in diagnosis due to a lack of clinical suspicion of autoimmune liver disease causing chronic liver diseases. Therefore, earlier diagnosis, treatment, and supportive management are required to prevent complications.

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