ORIGINAL ARTICLE

Clinical Significance of the Detection of Antinuclear Antibodies in Patients with Acute Hepatitis A

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Background/Aims: The findings of several recent studies suggest that antinuclear antibodies (ANAs) are frequently detected in patients with acute hepatitis A (AHA). However, the clinical significance of a positive ANA test remains uncertain. This study was performed to evaluate the clinical significance of ANAs in AHA patients. **Methods:** All patients admitted with AHA were consecutively enrolled in this study. An ANA assay was performed by indirect immunofluorescence during hospitalization. ANA positivity was defined as an ANA titer ≥1:80. The peak international normalized ratio (INR), peak alanine aminotransferase (ALT) and peak bilirubin levels were assessed over the duration of the hospitalization, and the incidence of AHA complications was evaluated. **Results:** A total of 422 patients were enrolled in this study (age, 31±7 years), of which 260 (61.6%) were men. ANAs were detected in 179 AHA patients (42.4%). The proportion of ANA-positive patients varied significantly with AHA status on the day of the ANA assay (4.7% during the prodromal period vs 52.1% during the icteric or recovery period, p<0.001) and sex (56.2% in women vs 33.8% in men, p<0.001). The ANAs became undetectable in all ANA-positive patients within 3 months. The incidence of complications, including mortality, fulminant hepatic failure, renal dysfunction, relapse, and cholestatic hepatitis, did not differ significantly between ANA-positive and ANA-negative patients. **Conclusions:** ANAs were detected frequently and transiently in patients with AHA, especially after their peak-ALT day. The presence of ANAs may not be associated with the clinical outcome of AHA, but simply with AHA status on the ANA assay day. **(Gut Liver 2011;5:340-347)**

Key Words: Autoimmune; Hepatitis A; Clinical outcome; Complication

INTRODUCTION

Antinuclear antibody (ANA), one of the non-organ-specific autoantibodies, is widely used in screening for and monitoring of autoimmune hepatitis and other autoimmune disorders. However, ANA is detectable under conditions not related to autoimmune disorders, such as bacterial or viral infections.[1,2] Furthermore, ANA-positive serum is found in about 5% of healthy populations.[3]

Positive ANA tests, based on multiple reports, have been reported in 7% to 63% of patients with chronic hepatitis C.[4-10] Although various studies have attempted to define the clinical significance of ANA in these patients, this significance remains to be clearly defined. Some authors suggest that ANA-positive serum in patients with chronic hepatitis C is associated with a more severe disease state,[5-8] while others failed to find any clinical significance.[9,10]

Currently, acute hepatitis A (AHA) is the most common cause of acute hepatitis in Korea.[11] AHA is a self-limiting disease, and so the symptoms of most patients resolve without any complications. However, serious complications including fulminant hepatic failure or renal dysfunction could develop in some patients. Meanwhile, several studies have suggested that transient ANA detection is not rare during the course of AHA.[12,13] In addition, several authors have reported cases of autoimmune hepatitis triggered by AHA.[14-19] However, the precise role of ANA-results in the clinical outcomes of AHA has yet to be fully elucidated. Therefore, this study was performed to elucidate the role of ANA-positive results in the clinical outcomes of AHA.

MATERIALS AND METHODS

1. Patients

All patients with AHA who were admitted with AHA to the participating hospitals (Korea University Anam Hospital and Korea University Guro Hospital, Seoul, Korea) between September 2007 and August 2009 were consecutively enrolled in this study. AHA was diagnosed when patients were found to be positive for the hepatitis A virus IgM antibody and had a serum alanine aminotransferase (ALT) level of ≥400 IU/L. Patients were hospitalized if they suffered from general weakness and/or poor oral intake because of severe nausea and/or anorexia.

Day 0, defined as the day of acute hepatitis-associated symptom onset, was determined by a thorough patient history. Blood tests, including serum ALT and bilirubin (BIL), and international normalized ratio (INR), were performed for each patient every 2 to 3 days until peak levels of all parameters were identified. The course of AHA was divided into three periods as follows:[20]

1) The prodromal period, defined as the period before serum ALT levels peaked (peak-ALT day). The serum levels of both ALT and BIL increased during this phase.

2) The icteric period, defined as the period after the peak-ALT day and before the day that serum BIL levels peaked (peak-BIL day). The serum ALT levels decreased but serum BIL levels continued to increase during in this phase.

3) The recovery period, defined as the period after the peak-BIL day. The serum levels of both ALT and BIL decreased in this phase, but had not recovered to below the upper limit of normal.

Hospitalization day was considered as the peak-ALT day in patients who were hospitalized during the icteric or recovery periods, and as the peak-BIL day in patients who visited our hospitals during the recovery period.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by our Institutional Review Board. Written informed consent to participate was obtained from each enrolled patient.

2. ANA assay

ANA assays were performed by indirect immunofluorescence on Hep-2 cells during patient hospitalization. ANA-positive serum was defined as ANA titers ≥1:80 because detection of low ANA titer is apparent even in the healthy population.[3] In ANA-positive patients, further ANA tests were performed every month until levels decreased to <1:80.

3. Clinical outcome of AHA

To evaluate whether the ANA data were associated with the clinical outcomes of AHA, peak serum ALT and BIL levels, peak INR, and the incidence of mortality or liver transplantation, fulminant hepatic failure, renal dysfunction, severe renal dysfunction requiring dialysis, relapse, and cholestatic hepatitis

were evaluated. Serum ALT levels on the day of hospitalization were considered peak ALT levels in patients who were admitted during the icteric or recovery periods, and serum BIL levels on the hospitalization day were considered the peak BIL level in patients who visited our hospitals during the recovery period. Fulminant hepatic failure was defined as the development of encephalopathy, evidence of significant liver injury, and severe, prolonged prothrombin time without previous liver disease. Relapse was defined as a biphasic or second peak of serum ALT elevation after complete or partial resolution of the first ALT peak.[21] Cholestatic hepatitis was defined as a persistent elevation in serum BIL >2.5 mg/dL for more than 2 months after illness onset. Renal dysfunction was defined as a serum creatinine level >1.5 mg/dL.

4. Statistics

Statistical analyses were performed using the SPSS version 13.0 (SPSS, Chicago, IL, USA). Data are expressed as mean±standard deviation (SD), or percentage values. Student's t-test and the χ^2-test were used to compare group continuous and categorical variables, respectively. Binary logistic regression analysis was performed to identify those factors significantly associated with the ANA data. The level of statistical significance was set at $p<0.05$ (two-sided).

RESULTS

1. Baseline characteristics

Table 1 presents the baseline characteristics for the 422 patients (age, 31±7 years; 61.6% men) who were admitted to our hospitals for treatment of AHA. Serum ALT level, BIL level, and INR on the day of hospitalization were 2,980±2,058 IU/L, 4.6±3.5 mg/dL, and 1.3±0.4, respectively. Patients visited our hospitals at 5±3 days after day 0. The AHA status on the day of hospitalization was the prodromal period in 122 patients (28.9%), the icteric period in 146 patients (34.6%), and the recovery period in 154 patients (36.5%).

Patients were hospitalized for 9±6 days. The serum ALT level, BIL level, and INR reached peak values of 3,508±2,130 IU/L, 7.4±4.4 mg/dL, and 1.4±0.6, respectively, at 6±2, 10±5, and 6±3 days after day 0. Fulminant hepatic failure developed in 10 patients (2.4%), and 7 patients (1.7%) died during hospitalization (n=6) or received liver transplantation for fulminant hepatic failure (n=1). Renal dysfunction developed in 30 patients (7.1%) and dialysis was needed in 13 (3.1%). Relapse and cholestatic hepatitis were noted in 3 (0.7%) and 22 (5.2%) patients, respectively.

2. Results of ANA testing

Patients were hospitalized at 5±3 days after day 0 and tested for ANA at 6±3 days after day 0 (1±1 days after hospitalization). The AHA status on the day of the ANA assay (ANA-assay

Table 1. Baseline Characteristics of Patients with AHA Relative to the ANA Results

Characteristic	All (n=422)	ANA-negative (n=243)	ANA-positive (n=179)	p-value
Age, yr	31.1±6.5	30.9±6.1	31.3±7.1	0.563
Males, n (%)	260 (61.6)	172 (70.8)	88 (49.2)	<0.001
HBsAg positivity, n (%)	15 (3.6)	9 (3.7)	6 (3.4)	0.847
The course of AHA at the initial ANA-assay day				<0.001
Prodromal period, n (%)	86 (20.4)	82 (33.7)	4 (2.2)	
Icteric period, n (%)	176 (41.7)	89 (36.6)	87 (48.6)	
Recovery period, n (%)	160 (37.9)	72 (29.6)	88 (49.2)	
ALT level on ANA-assay day, IU/L	2,766±1,899	3,011±2,020	2,471±1,670	0.003
BIL level on ANA-assay day, mg/dL	4.9±3.4	4.0±3.0	6.0±3.5	<0.001
INR on ANA-assay day	1.3±0.4	1.3±0.4	1.3±0.4	0.462
Peak ALT level, IU/L	3,508±2,130	3,739±2,172	3,195±2,037	0.009
Peak BIL level, mg/dL	7.4±4.4	7.2±4.5	7.8±4.3	0.146
Peak INR	1.4±0.6	1.4±0.6	1.4±0.5	0.393
Duration of hospitalization, day	9±6	9±6	9±5	0.493

AHA, acute hepatitis A; ANA, antinuclear antibody; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; BIL, bilirubin; INR, international normalized ratio.

day) was the prodromal period in 86 patients (20.4%), the icteric period in 176 patients (41.7%), and the recovery period in 160 patients (37.9%).

Of all AHA patients, 179 were observed as ANA-positive (42.4%). ANA titers were negative in 162 patients (38.4%), 1:40 in 81 patients (19.2%), 1:80 in 94 patients (22.3%), 1:160 in 76 patients (18.0%), 1:320 in 7 patients (1.7%), and 1:640 in 2 patients (0.5%). The proportion of ANA-positive patients varied significantly with AHA status on the ANA-assay day; it was significantly lower in the prodromal period (4 of 86 patients, 4.7%) than in the icteric (87 of 176 patients, 49.4%; p<0.001) and recovery (88 of 160 patients, 55.0%; p<0.001) periods, while it did not differ between the icteric period and recovery period (p=0.308, Fig. 1).

Therefore, all patients were classified into two groups according to their AHA status on the ANA-assay day. Group I was consisted of patients who underwent ANA testing during the prodromal period (i.e., before the peak-ALT day); and group II was comprised of patients who underwent ANA testing during the icteric or recovery periods (i.e., after the peak-ALT day). The distribution of titers differed significantly between groups I and II (p<0.001, Fig. 2). ANA-positive results were more frequent among women (91 of 162 women, 56.2%) than men (88 of 260 men, 33.8%; p<0.001). Serum BIL levels on the ANA-assay day were significantly higher in ANA-positive than in ANA-negative patients (6.0±3.5 mg/dL vs 4.0±3.0 mg/dL, respectively; p=0.003) and in serum ALT level on the ANA-assay day (2,471±1,670 IU/L vs 3,011±2,020 IU/L, respectively; p=0.003). Peak serum levels of ALT (3,195±2,037 IU/L vs 3,739±2,172 IU/L, respectively; p=0.009) were significantly lower in ANA-positive than in ANA-negative patients. However, peak serum BIL levels
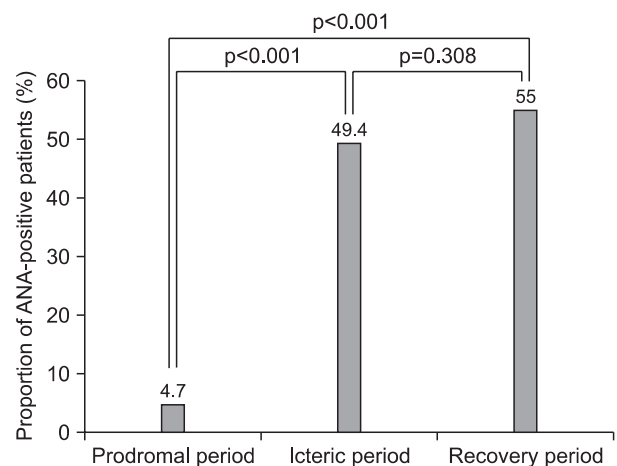

Fig. 1. Proportion of antinuclear antibody (ANA)-positive patients with acute hepatitis A according to AHA status on the ANA assay day. AHA, acute hepatitis A.

(7.8±4.3 mg/dL vs 7.2±4.5 mg/dL; p=0.146) did not differ between ANA-positive and ANA-negative patients (Table 1).

Multivariate analysis revealed that testing for ANA during the icteric or recovery periods (β, 3.218; odds ratio [OR], 24.971; 95% confidence interval [CI], 7.869 to 79.237; p<0.001], being female (β, 1.319; OR, 3.741; 95% CI, 2.263 to 6.186; p<0.001), higher serum ALT (β, 0.000; OR, 1.000; 95% CI, 0.999 to 1.000; p<0.001) and BIL levels (β, 0.171; OR, 1.186; 95% CI, 1.092 to 1.289; p<0.001) on the ANA-assay day, and a higher peak ALT level (β, 0.000; OR, 1.000; 95% CI, 1.000 to 1.001; p=0.006) were significantly associated with ANA-positive status.

3. Subgroup analysis with patients admitted during the prodromal phase

ANA results were significantly associated with AHA status on the ANA-assay day, sex, and also with serum ALT and BIL levels on the ANA-assay day and peak ALT level. However, the peak ALT level in group II patients could not be considered their true peak level. In addition, serum ALT and BIL levels on the ANA-assay day might simply reflect AHA status. Therefore, to exclude these potentially confounding factors, a subgroup analysis with 122 patients who were hospitalized during the prodromal period was performed. The age of this subgroup was 31.5±5.6 years, and 86 (70.5%) were men. Hepatitis B surface antigen was present in 4 patients (3.3%). The ALT level, BIL level, and INR were 2,230±2,168 IU/L, 2.0±1.6 mg/dL, and 1.3±0.4 at baseline, respectively, and peaked to 4,114±2,428 IU/L, 7.8±5.2 mg/dL, and 1.6±0.8, respectively, at 5±2, 11±6, and 5±3 days after day 0.

The ANA assay was performed 4±2 days after day 0 and at -1±2 days from the peak-ALT day. The AHA status on the ANA-assay day was the prodromal period in 86 patients (70.5%, group I) and the icteric period in 36 (29.5%, group II). ANA-positive results were found in 25 patients (20.5%). The prevalence of ANA-positive results did not differ significantly between men (12 of 76 men, 15.8%) and women (13 of 46 women, 28.3%; p=0.098). ANA-positive patients occurred more frequently in group II (21 of 36 patients, 58.3%) than in group I (4 of 86 patients, 4.7%; p<0.001). Serum BIL levels (2.7±2.2 mg/dL vs 3.9±2.1 mg/dL, p=0.018) on the ANA-assay day differed significantly between ANA-negative and ANA-positive patients, while serum ALT level on the ANA-assay day and peak ALT and BIL levels did not differ (Table 2). Only the results of ANA assays performed during the icteric or recovery periods were significantly associated with the ANA data according to multivariate analysis (β, 3.357; OR, 38.700; 95% CI, 8.622 to 95.535; p<0.001).
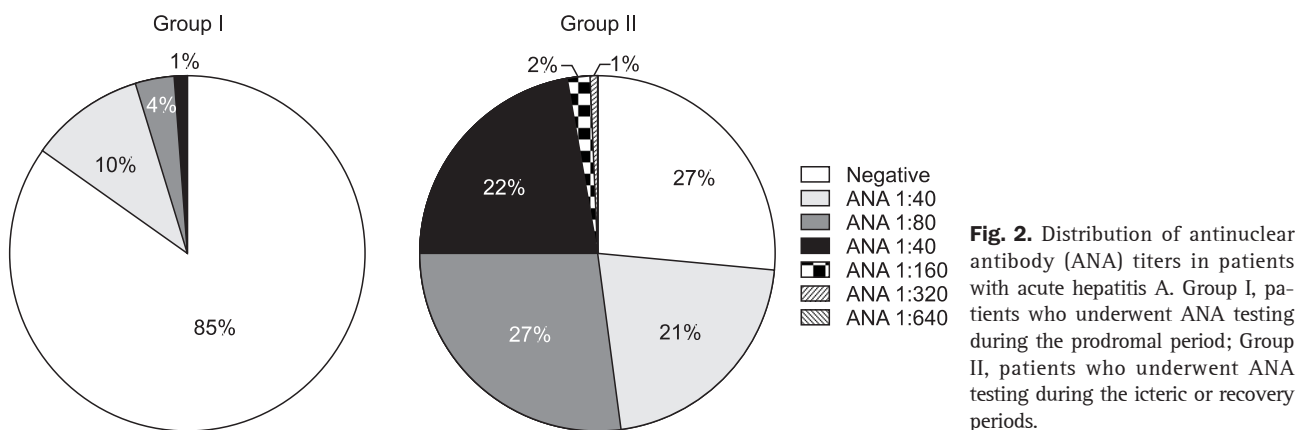

Fig. 2. Distribution of antinuclear antibody (ANA) titers in patients with acute hepatitis A. Group I, patients who underwent ANA testing during the prodromal period; Group II, patients who underwent ANA testing during the icteric or recovery periods.

Table 2. Baseline Characteristics and Clinical Outcomes of Patients with AHA Who Visited Hospitals during the Prodromal Phase Relative to the ANA Results

| Characteristic	ANA-negative (n=97)	ANA-positive (n=25)	p-value*	p-value[†]
Age, yr	31.1±5.5	33.1±5.9	0.119	
Male, n (%)	64 (66.0)	12 (48.0)	0.098	
HBsAg positivity, n (%)	3 (3.1)	1 (4.0)	0.820	
ANA assay during the prodromal period, n (%)	82 (84.5)	4 (16.0)	<0.001	<0.001
Results on the ANA-assay day				
Serum ALT level, IU/L	2,655±1,960	3,026±2,239	0.415	
Serum BIL level, mg/dL	2.7±2.2	3.9±2.1	0.018	0.827
INR	1.4±0.5	1.4±0.6	0.828	
Peak values of				
Serum ALT level, IU/L	4,065±2,283	4,301±2,971	0.667	
Serum BIL level, mg/dL	7.8±5.1	7.8±5.7	0.991	
INR	1.6±0.9	1.5±0.5	0.480	

HBsAg, hepatitis B surface antigen; ANA, antinuclear antibody; ALT, alanine aminotransferase; BIL, bilirubin; INR, international normalized ratio.
*Univariate analysis; [†]Multivariate analysis.

Table 3. Regression Analysis of the Relationship between ANA Results and the Incidence of AHA Complications

Complication	β	OR (95% CI)	p-value*
Death or liver transplantation	0.670	1.954 (0.287–13.302)	0.494
Fulminant hepatic failure	0.317	1.373 (0.284–6.653)	0.693
Renal dysfunction	−0.158	0.854 (0.364–2.005)	0.717
Severe renal dysfunction	−0.462	0.630 (0.158–2.518)	0.513
Relapse	1.963	7.120 (0.317–159.685)	0.216
Cholestatic hepatitis	0.943	2.568 (0.945–6.975)	0.064

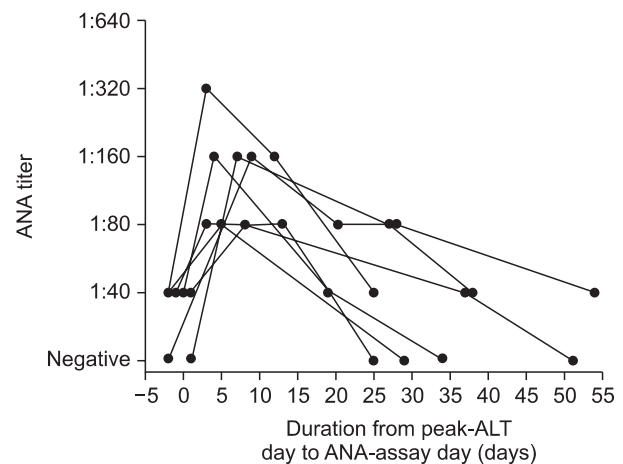OR, odds ratio; CI, confidence interval.
*Adjusted for sex and AHA status.
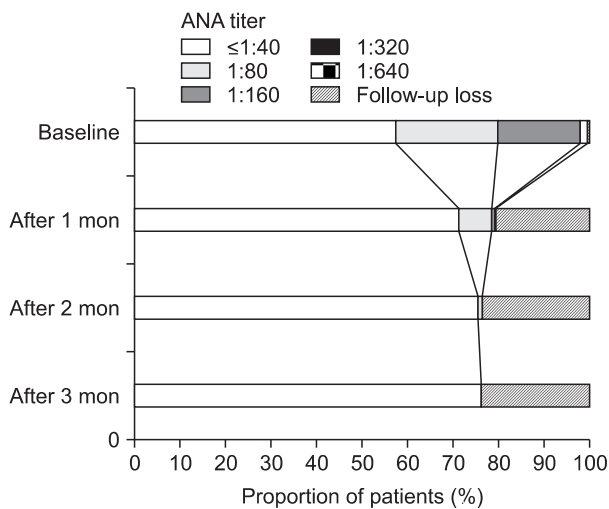
Fig. 3. Change in the distribution of antinuclear antibody (ANA) titers in patients with acute hepatitis A during a 3-month follow-up period.

Fig. 4. Antinuclear antibody (ANA) assay findings during the course of acute hepatitis A in seven patients whose baseline ANA titers are ≤1:40.
ALT, alanine aminotransferase.

4. Effect of ANA-positive status on the incidence of AHA complications

The incidence of death or liver transplantation (1.6% vs 1.7%, p=0.981), fulminant hepatic failure (2.5% vs 2.2%, p=0.876), renal dysfunction (8.2% vs 5.6%, p=0.296), severe renal dysfunction requiring dialysis (4.1% vs 1.7%, p=0.152), relapse (0.4% vs 1.1%, p=0.391), and cholestatic hepatitis (4.1% vs 6.7%, p=0.232) did not differ between ANA-negative and ANA-positive patients. Since ANA results were significantly associated with sex and AHA status on the ANA-assay day, regression analysis was performed to evaluate the relationship between ANA findings and the clinical outcome of AHA adjusted for sex and AHA status on the ANA-assay day. There was no significant relationship found between ANA-positive results and any clinical outcome (Table 3).

5. Changes in ANA findings after AHA resolution

The ANA assay was repeated 0.8±1.0 times in 179 ANA-positive patients at baseline. A follow-up ANA assay repeated 1 month after symptom onset in 92 of 179 ANA-positive patients (51.4%) revealed a decrease in ANA titer in 89 patients (96.7%),

no change in 1 patient (1.1%), and an increase in 2 patients (9.8%; from 1:80 to 1:160 in 1 patient and from 1:80 to 1:320 in the other). Among the 89 patients with decreased ANA titer after 1 month, the ANA titer was ≤1:40 in 58 patients. An additional ANA assay was repeated the next month in 21 (61.8%) of the 34 patients with an ANA titer ≥1:80 after 1 month, which revealed a decrease in ANA titer in 20 patients (95.2%) with no change in the remaining patient (4.8%). ANA titer was ≥1:80 2 months after the first ANA assay on day 0 in only 3 patients (ANA titers were 1:80 in all 3 patients), but this decreased to ≤1:40 in all 3 patients by 3 months after the first assay on day 0 (Fig. 3).

6. Dynamic changes in ANA titer during the course of AHA in patients with a baseline ANA titer ≤1:40

ANA tests were performed several times every 1 to 2 weeks in seven patients whose baseline ANA titers were ≤1:40 (Fig. 4). Baseline ANA tests were performed at 4±1 days (median, 4 days; range, 2 to 5 days) from day 0 and at -1±1 days (median, -1 day; range, -2 to 1 days) from peak-ALT days. Baseline ANA was negative in 2 patients and 1:40 in 5 patients. In all patients,

ANA-positivity was found in the second ANA assay, which was performed at 10±2 days (median, 10 days; range, 8 to 13 days) after day 0 and at 6±2 days (median, 5 days; range, 3 to 9 days) after peak-ALT day, and then progressively decreased. Peak ANA titer was 1:80 in 3 patients, 1:160 in 3 patients, and 1:320 in 1 patient. ANA titers decreased to ≤1:40 at 37±12 days (median, 35 days; range, 23 to 59 days) after day 0 and at 33±12 days (median, 29 days; range, 19 to 55 days) after the peak-ALT day.

DISCUSSION

The results of several previous studies suggest that ANA can be detected in non-autoimmune conditions such as bacterial or viral infections.[1,2] In addition, ANA positivity was frequently found in patients with AHA.[12,13,22] Therefore, it was not surprising that ANA was frequently detected in patients with AHA in the present study. However, previous studies did not fully elucidate whether transient detection of ANA could be associated with clinical outcomes of AHA. In this context, our results indicate the clinical significance of ANA-positive results in AHA because a large number of patients with various AHA statuses were enrolled. ANA was detected frequently in patients with AHA, especially after the peak-ALT day, and disappeared within 3 months in most cases. In addition, ANA-positivity was not associated with the clinical outcomes of AHA (peak ALT and bilirubin levels, duration of hospitalization, and incidence of complications), but was associated with sex and the course of AHA on the ANA-exam day.

In this study, a significant number of patients was hospitalized during the AHA prodromal period. Patients typically do not know that they have AHA during the prodromal period because symptoms in this period are nonspecific, including fever, chill, nausea, and abdominal pain. However, because of an AHA outbreak in Korea during our study period,[23] interest in AHA increased among the general population and many people visited the hospital to be assessed for the condition if they had a fever or chill. Therefore, AHA patients were diagnosed and hospitalized during the prodromal period.

A recent study found ANA-positive sera in 89% of patients with AHA,[13] which was slightly higher than that found in the present study, even if low ANA titer (1:40) was considered ANA-positive (61.6%). This discrepancy between the two studies may be attributable to differences in patient's AHA status on the ANA-assay day, but information regarding AHA status on the ANA-assay day was not available in the recently published study.[13] If patients who underwent ANA testing during the prodromal period were excluded from this study, the incidence of ANA-positive patients would have been 73.5% (247 of 336 patients). Another discrepancy between these two studies was the sex distribution; 52.5% of all enrolled patients were women in the recent study,[13] while that figure was 38.4% in the present

study. ANA titers were ≥1:40 in 82.1% of women and 67.8% of men among patients who underwent ANA testing during the icteric or recovery periods. Our results suggest that the prevalence of ANA in patients with AHA varies according to the proportion of women in the cohort and to the AHA status on the ANA-assay day.

In non-autoimmune conditions, ANA-positive results have been shown to be associated with sex and age.[3,24-26] Moreover, women in general are two to three times more likely to develop autoimmune diseases.[27] Although the mechanism underlying the relationship between sex and autoimmunity remains unclear, it is believed that hormones such as estrogen may play an important role.[28] Similarly, the etiology of the relationship between age and ANA-positive status is uncertain, but it might reflect a characteristic of the ageing immune system.[10] The age-dependent increase in the frequency of autoimmune antibodies may be attributable to repeated stimulation with bacteria or viruses.[3]

Consistent with previous findings,[3,24-26] ANA-positive results in the present study were more prevalent among women than men, and being female was independently associated with ANA-positive status. However, the difference between the sexes did not reach statistical significance in the subgroup of patients admitted during the prodromal period, which may be explained by the relatively small number of ANA-positive patients (20.5%) and small number of women (37.7%) in this subgroup. In contrast, age did not differ significantly between ANA-positive and ANA-negative patients in this study. In previous studies, an age-dependent variable in ANA-positive status was noted; especially among patients older than 40 to 60 years.[3,25,26] Most of the patients in this study were young (87.7% of patients in the third or fourth decade of life) and only 33 patients (7.8%) were older than 40 years. This narrow age range and the relative youth of our patients might explain the lack of an association between age and ANA-positive results in this study.

It has been reported that ANA was detected in 7% to 35% of patients with chronic hepatitis C.[4-10] However, it is still unclear whether ANA-positive status in chronic hepatitis C is the cause of more severe disease. Some authors suggest that ANA-positive status is associated with higher aminotransferase levels,[5-7] increased severe inflammation,[6] or advanced fibrosis,[8] while others have found no such difference.[9,10] Meanwhile, several studies suggest that ANA-positive status has no clinical impact in patients with AHA because all patients had a favorable course and ANA titer decreased or disappeared within several months.[12,13] Gutiérrez et al.[12] suggested that the presence of ANA is the result of a non-specific immunological response to viral infection. However, due to the small number of enrolled patients and the limited information about their AHA status in these studies, the clinical significance of ANA in AHA could not be confirmed. In our study, the clinical outcomes, including peak ALT and BIL levels, duration of hospitalization, and the incidence of AHA

complications, were analyzed relative to the ANA findings to evaluate the clinical significance of ANA.

Comparisons of peak ALT and BIL levels were analyzed using only patients who were hospitalized during the prodromal period. Since the results of ANA testing were significantly associated with both sex and AHA status on ANA-assay day, the analysis was conducted after adjustment for these two variables. The clinical outcomes of AHA did not differ significantly between ANA-positive and ANA-negative patients. In addition, consistent with the findings of previous studies,[12,13] ANA titer reached ≤1:40 or decreased to negative within 3 months after the onset of AHA in almost all patients with a baseline ANA titer ≥1:80. Therefore, it was concluded that ANA-positive status during AHA is transient and does not have any clinical impact on the course of the disease.

Several authors have reported cases of autoimmune hepatitis triggered by AHA and suggested that AHA actually precipitates autoimmune hepatitis.[14-19] As a potential mechanism, a previous study suggested that T-helper cells reactive to hepatitis A virus antigens exposed on the surface of infected hepatocytes provide help for autoreactive B cells specific for an antigen (the asialoglycoprotein receptor) that is coexpressed on the hepatocyte membrane.[14] In previous cases,[14-19] autoimmune hepatitis developed 2 to 3 months after the onset of AHA, while ANA-positive status disappeared within 3 months after AHA onset in the present study. Our results are consistent with the previous finding that ANA titer decreased or disappeared within several months in all enrolled patients.[12,13]

In conclusion, ANA-positive sera were detected frequently and transiently in patients with AHA, especially after the peak-ALT day. ANA-positive status might not be associated with the clinical outcome of AHA, but simply with AHA status on the ANA-assay day.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

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