

Autoimmune hepatitis: Clinical characteristics and predictors of biochemical response to treatment

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ABSTRACT

Background and Objectives: Autoimmune hepatitis (AIH) is an important cause of chronic liver disease. Aim of this study was to evaluate the clinical characteristics and factors predicting response to treatment in patients with AIH. **Methods:** In this prospective observational study, all patients diagnosed with AIH from 2017 to 2019 were included. Biochemical response to the treatment was checked three months after the start of the treatment. Response was considered good if transaminases normalized, or poor if either remained persistently elevated or improved partially. **Results:** Of the total 56 patients, 41 (73.2%) were females. Mean age was 29.5 (± 16.9) years. About half (53.6%; $n = 30$) the patients were aged < 25 years and majority [47 (83.9%)] were cirrhotic. Autoimmune serology was negative in 20 (35.7%). Seronegativity was associated with severe necroinflammation ($P = 0.015$) and esophageal varices ($P = 0.021$). Response to treatment was good in 34 (60.7%). Bivariate analysis showed that good response to treatment was associated with pre-treatment serum IgG level > 20 g/L ($P = 0.024$), presence of pseudorosettes on histopathology ($P = 0.029$) and three months post-immunosuppression serum total bilirubin < 2mg/dL ($P < 0.001$). Multivariate logistic regression analysis showed that only pre-treatment serum IgG >20 g/L ($P = 0.038$) and post-treatment serum total bilirubin <2 mg/dL ($P = 0.004$) were independent predictors of good response to treatment. **Conclusion:** Majority of AIH patients in our study were young and cirrhotic. A negative autoimmune serology does not rule out AIH and liver biopsy may be required to confirm the diagnosis. Seronegative AIH rapidly progresses to advanced liver disease. Response to treatment is good with pre-treatment IgG > 20g/L and post-treatment total bilirubin < 2 mg/dL.

Key words: autoimmune hepatitis, treatment response, clinical characteristics

INTRODUCTION

Autoimmune hepatitis (AIH) is an important cause of chronic liver disease. It has a global distribution, affects all ages and both genders, and has genetic predispositions that can differ between races and between age groups within races.^[1] Highest incidence and prevalence have been reported in Alaskan natives and New Zealand populations, while low in Brunei Darussalam.^[2] It is a chronic, progressive liver disease that is triggered by immunologic, environmental and genetic factors resulting in T cell activity against hepatocyte antigens. Histologically, it is characterized by the presence of portal

lymphoplasmacytic infiltration, interface hepatitis and lobulitis.^[3]

Treatment of AIH consists of steroids and various immunosuppressive agents including azathioprine, mycophenolate mofetil or tacrolimus. A biochemical remission is achieved with such agents in about 80–90% of the cases within two years.^[4] About 15% patients experience an incomplete response, while 9% develop treatment failure with steroids.^[5] Cirrhosis develops in 7%–40% of treated patients, depending on the frequencies of relapse, treatment failure and incomplete response.^[6] Response to treatment may vary from patient to patient depending upon various

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factors related to host (*e.g.*, age, gender, race, body mass index, treatment compliance), immunologic factors (serum immunoglobulin G titer, anti-nuclear antibody titer, HLA genotype), disease type (type I *vs.* II AIH, seropositive *vs.* seronegative disease), baseline liver histology (degree of liver fibrosis, severity of inflammation), and the type of treatment employed (number and type of immunosuppressants used). Knowledge about clinical characteristics that have a significant impact on treatment outcome provides useful information to the concerned physician in the tailoring of management strategies of patients with AIH.^[7,8]

Poor response to treatment in patients with AIH may lead to cirrhosis and its life threatening complications. It is, therefore, essential to study those patients and the disease related characteristics that adversely affect the treatment outcome so that careful monitoring of such patients can be performed and alternative treatment strategies be anticipated. Significant research has been done in this regard in various parts of the world^[9,10]; however, very little effort has been made in our set up. The purpose of this study, therefore, was to determine the clinical characteristics of patients with autoimmune hepatitis and also to identify the factors affecting the biochemical response to the treatment.

PATIENTS AND METHODS

This prospective observational cohort study was performed at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation from January 2017 to June 2019. The study was performed in accordance with the declaration of Helsinki and approval was obtained from the institutional ethical review committee (ERC). All consecutive patients, of both gender and any age who were diagnosed as having autoimmune hepatitis were included in the study. Informed consent was taken from all such patients. Those patients who had any other co-existing liver disease that could result in derangement of liver enzymes like viral hepatitis, non-alcoholic fatty liver disease and veno-occlusive liver disease were excluded.

The patients were treated with both steroids and immunosuppressive agents, or either one of these, according to the AASLD guidelines for autoimmune hepatitis.^[11] The various clinical features, before start of the treatment, were recorded including demographics (age, gender, socioeconomic status, body mass index), baseline blood test reports (complete blood picture, liver function tests, ALT/AST ratio, serum albumin, renal function tests, *etc.*), immunology profile (serum autoimmune profile, including serum anti-nuclear antibody [ANA] test report and titer, serum IgG level, *etc.*), abdominal imaging (features

of chronic liver disease on ultrasound abdomen), upper gastrointestinal (GI) endoscopy findings (presence of esophageal varices or portal hypertensive gastropathy), and histologic features on liver biopsy (grading and staging according to The Ishak Modified HAI score,^[12] presence or absence of pseudorosettes). These patients were initially followed up regularly at two weekly intervals for first 6 weeks and then three weekly for the next 6 weeks. The pre-treatment liver function tests were compared with those after 3 months to determine the biochemical response to treatment. The liver biopsy was only performed before the start of the treatment and was not repeated after 3 months of treatment. All those patients whose hepatic transaminases dropped down to normal (*i.e.*, < 40 U/L) after 3 months of treatment were categorized as good responders, while those whose transaminases remained high or were only partially improved after 3 months of treatment were considered as poor responders.

Statistical analysis

All data were analyzed using SPSS 20. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. Chi square and Fisher exact test was used to identify the clinical factors associated with seronegativity and also to identify clinical parameters associated with good response to treatment. Multivariate analysis was then performed to identify independent predictors of response to treatment using logistic regression analysis. A *P* value of less than 0.05 was considered as statistically significant. Odds ratio and confidence interval for predictors of response to treatment were calculated.

RESULTS

Clinical presentation

Of the total 56 patients, 41 (73.2%) were females and 15 (26.8%) were males (Table 1). Mean age was 29.5 (\pm 16.9) years. The ages ranged from 5–72 years. The mean body mass index (BMI) was 22.6 (\pm 3.62) kg/m², ranging from 14.6 to 34.1 kg/m². Ten (17.8%) patients had a BMI of more than 25 kg/m². About half the patients 53.6% (*n* = 30) were < 25 years of age, while 73.2% (*n* = 41) were less than 40 years old. Among the total 56 patients, majority [47 (83.9%)] were cirrhotic. Among the cirrhotic patients, 22 (46.8%) had compensated cirrhosis, while 25 (53.2%) had decompensated cirrhosis. Esophageal varices were present in 34 (60.7%) patients; ascites in 25 (44.6%) patients; while both esophageal varices and ascites were present in 19 (33.9%) patients. In two patients, the disease was triggered by viral hepatitis (hepatitis E virus infection) and in one patient by the antibiotic nitrofurantoin. Seven (12.5%) patients had overlap syndrome (AIH with primary biliary cholangitis [PBC] in 4 and AIH with primary sclerosing

Table 1: Characteristics of patients with autoimmune hepatitis (n = 56)

Clinical characteristics		Number (n)	Percentage (%)
Gender	Females	41	73.2
	Males	15	26.8
Age group	Age < 25	30	53.6
	Age > 40	15	26.8
Autoimmune serology	Positive	36	64.3
	Negative	20	35.7
Types of AIH*	Type I	34	94.4
	Type II	02	5.6
Cirrhosis presentation	Yes	47	83.9
	No	9	16.1
Response to treatment	Good	34	60.7
	Poor	22	39.3

* Among the seropositive patients

cholangitis [PSC] in 3) and 4 (7.1%) had systemic lupus erythematosus [SLE] associated AIH. Treatment was initiated with weight based steroids (prednisone) and azathioprine in all patients. Due to inadequate response or intolerability to azathioprine, 15 patients were switched to mycophenolate mofetil or tacrolimus. Response to the treatment was good in 34 (60.7%) and poor in the remaining 22 (39.3%) patients.

Biochemistry

Laboratory tests showed that the mean pre-treatment total bilirubin, ALT and AST were 2.27 mg/dL, 121 U/L and 174 U/L, respectively. The mean pre-treatment platelet count and albumin were 154,000 per mm³ and 2.9 gm/dL, respectively. After three months of treatment with immunosuppressive agents, the mean total bilirubin, ALT and AST were 1.73 mg/dL, 53 U/L and 69 U/L, respectively.

Immunology

Among the patients diagnosed with AIH, positive autoimmune serology was found to be present in 36 (64.3%) patients, while a significant proportion, *that is*, 20 (35.7%) patients had a negative autoimmune serology and were subsequently diagnosed to have AIH based on the compatible liver histology. Among the 36 patients with positive serology, 34 (94.4%) patients had type I AIH (*i.e.*, positive serum anti-nuclear antibody [ANA] or anti-smooth muscle antibody [ASMA]) while 2 (5.6%) had type II AIH (*i.e.*, positive serum anti liver kidney microsomal antibody [anti LKM]). None of the patients was found to have anti soluble liver antigen [Anti SLA] antibody. Among the seropositive AIH patients, serum ANA titer was low (dilutions of \leq 1:80) in majority of cases, *that is*, 21 (58.3%), while high (dilutions of $>$ 1:80) in 15 (41.6%) patients. Serum IgG was $>$ 20 g/L in 40 (71.4%) patients and $>$ 25g/L in 27 (48.2%) patients.

Histology

Histological analysis showed that portal tract inflammation was mild to moderate in 29 (51.8%), while severe in 27 (48.2%) patients. The histology activity index (HAI) scoring of necroinflammation (grade) of $>$ 6/18 was present in 16 (28.6%) and a fibrosis (stage) $>$ 4/6 in 47 (83.9%) patients (stage of 4/6 in 4 [7.1%], 5/6 in 13 [23.2%], while stage 6/6 in 30 [53.6%] patients). Pseudorosettes (pseudoductular appearance of hepatocytes) were found to be present in 15 (26.8%) patients.

Associations of seronegative AIH

Since a significant proportion of patients had negative autoimmune serology, an analysis was performed to identify the clinical factors associated with seronegative AIH and these were found to be the presence of severe portal tract inflammation ($P = 0.015$) and esophageal varices ($P = 0.021$) (Table 2).

Predictors of good response

Bivariate analysis showed that good response to treatment was associated with pre-treatment serum IgG level $>$ 20 g/L ($P = 0.024$), presence of pseudorosettes on histopathology ($P = 0.029$) and three months post-immunosuppression serum total bilirubin $<$ 2 mg/dL ($P < 0.001$). However, multivariate logistic regression analysis showed that only pre-treatment serum IgG $>$ 20 g/L ($P = 0.038$) and three months post-treatment serum total bilirubin $<$ 2 mg/dL ($P = 0.004$) were independent predictors of good response to treatment (Table 3).

DISCUSSION

Our study showed that majority of the patients with AIH were females; and that more than half of them were under the age of 25 years. These findings are similar to

Table 2: Clinical factors associated with seronegative autoimmune hepatitis (Bivariate analysis, $n = 56$)

Clinical variable		Negative serology	Positive serology	Odds ratio	Confidence interval	P-value
Age (years)	< 40	16	25	1.76	0.48–6.49	0.533
	> 40	4	11			
Gender	Females	14	27	0.78	0.23–2.63	0.686
	Males	6	9			
BMI (kg/m ²)	< 25	17	28	1.62	0.38–6.95	0.728
	> 25	3	8			
Serum IgG (g/L)	> 20	16	24	2.00	0.55–7.31	0.365
	< 20	4	12			
Portal inflammation severity	Severe	14	13	4.13	1.28–13.35	0.015
	Mild-Mod	6	23			
Rosettes (liver biopsy)	Present	5	10	0.87	0.25–3.01	0.822
	Absent	15	26			
Overlap syndrome	Present	2	5	0.69	0.12–3.92	1.000
	Absent	18	31			
Cirrhosis (liver biopsy)	Present	19	28	5.43	0.63–47.02	0.136
	Absent	1	8			
CTP score	A	7	15	1.33	0.43–4.12	0.625
	B or C	13	21			
Esophageal varices	Yes	17	19	5.07	1.26–20.37	0.021
	No	3	17			
Ascites	Yes	11	14	1.92	0.64–5.81	0.245
	No	9	22			
Serum Albumin (gm/dL)	< 2.8	9	16	1.02	0.34–3.07	0.968
	> 2.8	11	20			
Pre-Tx Total bilirubin (mg/dL)	< 2	10	21	1.40	0.47–4.20	0.548
	> 2	10	15			
Post-Tx* Total bilirubin (mg/dL)	< 2	16	29	0.966	0.25–3.81	1.000
	> 2	4	7			

* 3 months after treatment with immunosuppressive therapy.

those observed in our neighboring country India where younger age at diagnosis and female predominance were also noted.^[13] In the study by Gourdas Choudhuri, among the 38 patients with AIH, the mean age was 36.2 years with 89.4% being females.^[13] In our study, the mean age was even younger, *i.e.*, 29.5; and although, female gender was affected most (73.2%), males were a little more common. Also, in our study, majority of the patients (83.9%) had already developed cirrhosis with some of them having decompensated cirrhosis. The fact that cirrhosis at presentation is very common among AIH patients of Pakistani origin, has been reported previously too.^[2] Furthermore, the Indian study by Amarapurkar D showed cirrhosis to be present in as many as 71.2% patients at presentation, indicating similar pattern of presentation in the South Asian countries.^[14] Interestingly, AIH related advanced liver fibrosis has been shown to be more common in South Asia (India, Pakistan) and in the middle East (Iran, Israel, Saudi Arabia)^[15]; and uncommon in the Far East (Japan, Korea) and in the non-Asian countries (*e.g.*, UK, Canada, Italy, Denmark).^[2] The various reasons that can explain the development of cirrhosis at initial presentation in Pakistan include: firstly, lack of clinical suspicion of AIH as a cause of CLD by

the primary physician resulting in progression of disease without treatment; secondly, delay in referral to expert hepatologist because of negative autoimmune serology in a significant proportion of patients; and lastly, poor socioeconomic status and healthcare facilities in the rural settings of several of our patients resulting in hindrance in seeking valuable medical advice. Besides, further studies would be required in the future to study the contribution of unidentified environmental and genetic factors that may play an important role in the relatively rapid progression of the disease in our part of the world.

The Indian study by Amarapurkar D showed that 22 out of 125 (17.6%) AIH patients had a negative autoimmune serology.^[14] However, our study revealed that an even higher proportion of patients (*i.e.*, 35.7%) suffering from AIH had a negative autoimmune serology. The diagnosis of such patients was made on the basis of typical histopathology findings (lymphoplasmacytic portal infiltrates, interface hepatitis, lobulitis and pseudorosettes) and subsequent significant response to treatment with immunosuppressants. This finding is unique to our study and may demonstrate the special characteristics of AIH in the south Asian region. The reason behind the seronegativity with compatible liver

Table 3: Factors predicting response to treatment in patients with autoimmune hepatitis (n = 56)

Bivariate Analysis		Multivariate analysis				
Clinical Variable		Good response	Poor response	Odds Ratio	Confidence Interval	P value
Age (years)	< 40	25	16	0.960	0.28–3.15	0.947
	> 40	9	6			
Gender	Females	25	16	0.960	0.28–3.15	0.947
	Males	9	6			
BMI (kg/m ²)	< 25	27	18	1.167	0.29–4.57	1.000
	> 25	7	18			
Autoimmune serology	Positive	22	14	1.048	0.34–3.20	0.935
	Negative	12	8			
Serum IgG (g/L)	> 20	28	12	0.257	0.08–0.87	0.024
	< 20	6	10			
Portal inflammation severity	Severe	18	9	0.615	0.21–1.82	0.379
	Mild-Mod	16	13			
Rosettes (liver biopsy)	Present	13	2	0.162	0.03–0.81	0.029
	Absent	21	20			
Overlap syndrome	Present	4	3	1.184	0.24–5.29	1.000
	Absent	30	19			
Cirrhosis (liver biopsy)	Present	30	17	2.206	0.52–9.34	0.294
	Absent	4	5			
CTP score	A	12	10	1.528	0.51–4.55	0.447
	B or C	22	12			
Esophageal varices	Yes	22	14	0.955	0.31–2.92	0.935
	No	12	8			
Ascites	Yes	17	8	0.571	0.19–1.71	0.316
	No	17	14			
Serum albumin (gm/dL)	< 2.8	15	10	1.056	0.36–3.10	0.922
	> 2.8	19	12			
Pre-Tx Total bilirubin (mg/dL)	< 2	19	12	1.056	0.36–3.10	0.922
	> 2	15	10			
Post-Tx* Total bilirubin (mg/dL)	< 2	33	12	0.036	0.01–0.32	< 0.001
	> 2	1	10			

* 3 months after treatment with immunosuppressive therapy.

histology appears intriguing. One explanation, however, can be the fact that majority of our patients were malnourished and belonged to the poor socioeconomic group, which may result in an inadequate antibody production by the host immunological system. Also, further studies would be required to identify other serological markers of AIH to facilitate early diagnosis in this group of patients. Our study also showed that seronegative AIH was associated with more severe portal tract inflammation and the presence of esophageal varices. This may indicate that these patients tend to have a rapid progression of disease and by the time the liver biopsy is performed to confirm the diagnosis, they already have advanced hepatic fibrosis. This implies that, in our set up, whilst evaluating young females with features of cirrhosis, liver biopsy should not be delayed if the autoimmune serology turns out to be negative.

Our study showed that while about two thirds of the patients with AIH exhibited good response to treatment, one third were either poor responders or had inadequate

response. Our findings are similar to those noted in other parts of the world. In a Chinese study performed by Zhang Hongwen, good response to treatment was noted in 80.3% of the total 61 AIH patients.^[16] Also, in the Swedish study by Marten Werner, good response within the first year of treatment was noted in 60% patients.^[10] Generally, a good response to immunosuppressive treatment has been noted in both Asian and non-Asian countries.^[2] One limitation of our study was that we only determined biochemical response to treatment and did not demonstrate histological and immunological response by performing a repeat liver biopsy or serum immunoglobulin G level in all patients after three months of immunosuppression.

Our data demonstrated that good response to treatment was associated with high pre-treatment IgG levels, presence of pseudorosettes on liver biopsy and three months post treatment total bilirubin of less than 2 mg/dL. Various studies have been performed in different parts of the world showing varying results. A German study

by Richard Taubert, showed that hyperferritinemia and lower immunoglobulin levels at baseline predict good response to treatment with standard therapy.^[9] This finding is in contrast to ours, which showed better response to treatment with high pre-treatment IgG levels. Whether genetic susceptibility determines the responsiveness to immunosuppression in patients with high pre-treatment IgG needs to be clarified with the help of further research work. A multicenter study from southern Israel showed that lesser degree of liver fibrosis and higher serum albumin levels are associated with good response.^[17] Zhang Hongwen showed that high alkaline phosphatase combined with autoimmune antibody positivity and cirrhosis predict poor response.^[16] The effect of advanced fibrosis and cirrhosis on adverse treatment outcome has been shown by other studies too.^[10,18] Yet, another study by Jing Hieng Ngu from New Zealand showed extremes of ages to be associated with poor response but demonstrated that cirrhosis was not associated with poor prognosis.^[19] The predictors of good response to treatment shown by our multivariate analysis, namely high pre-treatment IgG and low post-treatment total bilirubin, although new, may add food for thought to the already existing pool of data in this field.

CONCLUSION

Autoimmune hepatitis is an important cause of chronic liver disease in young females living in Pakistan. Majority of these patients already have cirrhosis at the time of diagnosis. A negative autoimmune serology does not rule out autoimmune hepatitis and a liver biopsy should strongly be considered when the index of suspicion is high. Seronegative AIH is associated with more severe portal tract inflammation and rapid progression to advanced fibrosis and cirrhosis. Pre-treatment high serum IgG and post-treatment low serum total bilirubin may indicate good response to treatment with immunosuppressants.

Conflict of Interest

There are no conflicts of interest.

REFERENCES

1. Dalekos GN, Koskinas J, Papatheodoridis GV. Hellenic Association for the Study of the Liver Clinical Practice Guidelines: Autoimmune hepatitis. *Ann Gastroenterol* 2019; 32: 1–23.
2. Enomoto H, Nishiguchi S. Similarities and Differences in Autoimmune Hepatitis Epidemiology between East and West: Autoimmune Hepatitis in East Asia, Southeast Asia, and South Asia. *Inflamm Intest Dis* 2017; 1: 150–8.

3. Gurung A, Assis DN, McCarty TR, Mitchell KA, Boyer JL, Jain D. Histologic features of autoimmune hepatitis: a critical appraisal. *Hum Pathol* 2018; 82: 51–60.
4. Lohse AW, Chazouilleres O, Dalekos G, Drenth J, Heneghan M, Hofer H, *et al.* EASL clinical practice guidelines: autoimmune hepatitis. *J Hepatol* 2015; 63: 971–1004.
5. Lammert C, Loy VM, Oshima K, Gawrieh S. Management of Difficult Cases of Autoimmune Hepatitis. *Curr Gastroenterol Rep* 2016; 18: 9.
6. Linzay CD, Sharma B, Pandit S. Autoimmune Hepatitis. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
7. Baven-Pronk MAMC, Biewenga M, van Silfhout JJ, van den Berg AP, van Buuren HR, Verwer BJ, *et al.* Role of age in presentation, response to therapy and outcome of autoimmune hepatitis. *Clin Transl Gastroenterol* 2018; 9: 165.
8. Abdel-Razik A, Mousa N, Zakaria S, Elhelaly R, Elzebery R, Zalata K, *et al.* New predictive factors of poor response to therapy in autoimmune hepatitis: role of mean platelet volume. *Eur J Gastroenterol Hepatol* 2017; 29: 1373–9.
9. Taubert R, Hardtke-Wolenski M, Noyan F, Lalanne C, Jonigk D, Schlue J, *et al.* Hyperferritinemia and hypergammaglobulinemia predict the treatment response to standard therapy in autoimmune hepatitis. *PLoS One* 2017; 12: e0179074.
10. Werner M, Wallerstedt S, Lindgren S, Almer S, Bjornsson E, Bergquist A, *et al.* Characteristics and long-term outcome of patients with autoimmune hepatitis related to the initial treatment response. *Scand J Gastroenterol* 2010; 45: 457–67.
11. Mack CL, Adams D, Assis DN, Kerkar N, Manns MP, Mayo MJ, *et al.* Diagnosis and Management of Autoimmune Hepatitis in Adults and Children: 2019 Practice Guidance and Guidelines From the American Association for the Study of Liver Diseases. *Hepatology* 2019; Dec 21, 2019. Online ahead of print.
12. Ishak K, Baptista A, Bianchi L, Callea F, DeGroot J, Gudat F, *et al.* Histological grading and staging of chronic hepatitis. *J Hepatol* 1995; 22: 696–9.
13. Choudhuri G, Somani SK, Baba CS, Alexander G. Autoimmune hepatitis in India: profile of an uncommon disease. *BMC Gastroenterol* 2005; 5: 27.
14. Amarapurkar D, Dharod M, Amarapurkar A. Autoimmune hepatitis in India: single tertiary referral centre experience. *Trop Gastroenterol* 2015; 36: 36–45.
15. Yang F, Wang Q, Bian Z, Ren LL, Jia J, Ma X. Autoimmune hepatitis: East meets west. *J Gastroenterol Hepatol* 2015; 30: 1230–6.
16. Zhang HW, Liu HM, Lin R, Zhou L, Zhang J, Liu WT. [Clinical features of autoimmune hepatitis patients with poor response to treatment]. *Zhonghua Gan Zang Bing Za Zhi* 2017; 25: 755–9.
17. Delgado JS, Vodonos A, Malnick S, Kriger O, Wilkof-Segev R, Delgado B, *et al.* Autoimmune hepatitis in southern Israel: a 15-year multicenter study. *J Dig Dis* 2013; 14: 611–8.
18. Selvarajah V, Montano-Loza AJ, Czaja AJ. Systematic review: Managing suboptimal treatment responses in autoimmune hepatitis with conventional and nonstandard drugs. *Aliment Pharmacol Ther* 2012; 36: 691–707.
19. Ngu JH, Geary RB, Frampton CM, Stedman CA. Predictors of poor outcome in patients with autoimmune hepatitis: a population-based study. *Hepatology* 2013; 57: 2399–406.

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