J Korean Med Sci. 2026 Apr 6;41(13):e108
https://doi.org/10.3346/jkms.2026.41.e108
eISSN 1598-6357·pISSN 1011-8934

JKMS

Pediatrics
Original Article

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Clinical Outcomes of Children With Autoimmune Hepatitis in Korea: A Nationwide Multicenter Study

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Received: Mar 25, 2025
Accepted: Jul 8, 2025
Published online: Mar 6, 2026

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ABSTRACT

Background: Autoimmune hepatitis (AIH) is a rare chronic liver disease with limited data on long-term outcomes. This study aimed to investigate the clinical characteristics and prognosis of pediatric AIH patients in Korea.
Methods: We retrospectively reviewed the medical records of 44 patients diagnosed with AIH under 19 years of age between January 2007 and August 2023 at nine tertiary university hospitals in Korea. Clinical data, including laboratory findings, treatment, and outcomes such as biochemical remission and survival rates, were analyzed.
Results: The median age at diagnosis was 12 years, and 57% were female. Type 1 AIH was predominant, and 7% of cases were autoimmune sclerosing cholangitis. Twenty-three percent of patients had coexisting autoimmune diseases. Jaundice was the most common symptom, and 7% of patients had cirrhosis at diagnosis. All patients were seropositive for autoantibodies, with 93% testing positive for antinuclear antibodies. Patients who received an initial corticosteroid dose of ≥ 1 mg/kg/day had higher biochemical remission rates from 6 months to 5 years compared to those who received a lower dose. Remission rates did not differ significantly between azathioprine monotherapy and corticosteroid combination therapy. The ten-year overall survival rate was 95%, while the clinical event-free survival was 70%. An initial total bilirubin level ≥ 1.0 mg/dL at diagnosis was associated with poorer clinical event-free survival.
Conclusion: Type 1 AIH is predominant in Korean children, with a relatively low cirrhosis rate at diagnosis. Standard-dose corticosteroids were effective in achieving biochemical remission. Initial bilirubin levels may serve as a prognostic marker for long-term outcomes.

Keywords: Hepatitis; Autoimmune; Cholangitis; Sclerosing; Child

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Funding
This research was supported by Grant No. 0420233050 from the Seoul National University Hospital (SNUH) Research Fund.

Disclosure
The authors have no potential conflicts of interest to disclose.

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Conceptualization: Lee KJ, Ko JS. Data curation: Lee YJ, Lee EJ, Koh H, Choi HJ, Oh SH, Kang KS, Choe BH, Kim SH, ES Kim, Kim MJ, Kim SY. Formal analysis: Ahn JE, Lee KJ. Funding acquisition: Lee KJ, Ko JS. Investigation: Lee YJ, Lee EJ, Koh H, Choi HJ, Oh SH, Kang KS, Choe BH, Kim SH, ES Kim, Kim MJ, Kim SY. Methodology: Lee KJ, Ko JS, Ahn JE. Writing - original draft: Lee KJ, Ahn JE. Writing - review & editing: Lee KJ, Ko JS.

INTRODUCTION

Autoimmune hepatitis (AIH) is a rare, chronic liver disease characterized by immune-mediated inflammation, which can lead to cirrhosis and liver failure. Its pathogenesis involves a multifactorial interaction of genetic predisposition, immune dysregulation, and environmental triggers.[1]

The prevalence of AIH varies across populations and age groups. Globally, AIH, including pediatric cases, affects an estimated 15.65 per 100,000 individuals.[2] However, pediatric AIH remains less documented than adult cases. In South Korea, AIH prevalence is lower than in western countries, with an age-adjusted rate of 4.82 per 100,000 individuals reported between 2009 and 2013. Among children, the estimated prevalence is approximately 0.5 per 100,000 children.[3]

AIH presentation differs across populations, with Hispanics showing a high prevalence of cirrhosis and Asians experiencing a poorer survival rate.[4] Furthermore, pediatric AIH also exhibits distinct clinical profiles. However, due to its low prevalence, research on pediatric AIH is limited worldwide, with studies predominantly confined to retrospective studies and long-term observational cohorts.[5-7] In Korea, the most recent study on pediatric AIH, conducted in 2004, was a single-center retrospective study involving only 14 patients, insufficient for a nationwide perspective.[8] The clinical characteristics, treatment regimens, and long-term prognosis of pediatric AIH remain poorly understood, especially in Asian countries.

This study aims to fill knowledge gaps in pediatric AIH through a comprehensive analysis of clinical features, induction and maintenance therapies, treatment responses, and long-term outcomes in Korea. Furthermore, we sought to identify factors associated with poor prognosis.

METHODS

Study design

This retrospective multicenter study was conducted across nine tertiary university hospitals in Korea, all of which are liver transplantation (LT) centers. These hospitals are located in Seoul (5 centers), Yangsan (1), Gwangju (1), Daegu (1), and Jeju (1). Medical records were reviewed to collect data on demographics, anthropometric measurements, medical history, clinical presentation, biochemical parameters, histological and radiological findings, treatment responses, and outcomes. Data were collected at diagnosis and at follow-up intervals of one month, six months, one year, two years, five years, seven years, and ten years.

Study participants

This study included children diagnosed with AIH under the age of 19 between January 2007 and August 2023. Patients were identified using the International Classification of Disease, Tenth Revision code for AIH (K75.4) and the Rare Intractable Disease (RID) code V175. The RID system in Korea is highly reliable, as registration requires physician's confirmation based on clinical, laboratory, and histological findings. AIH was diagnosed based on elevated aminotransferases and IgG levels, characteristic autoantibodies, compatible histology, and exclusion of other liver diseases.[9,10] To ensure diagnostic accuracy, only patients who received treatment or were followed for at least six months were included. Autoimmune sclerosing cholangitis (ASC) was diagnosed in patients with cholangiographic evidence of

multifocal bile duct strictures and dilatation or histological features of sclerosing cholangitis despite normal cholangiography.[11]

Definitions for outcomes

Acute severe AIH was defined by the presence of jaundice and a prolonged prothrombin time-international normalized ratio (PT-INR) of 1.5–2.0, without encephalopathy or prior chronic liver disease. Pediatric acute liver failure (PALF) was characterized by the acute onset of liver disease without preexisting chronic liver disease, with coagulopathy unresponsive to vitamin K: prothrombin time (PT) ≥ 15 seconds or PT-INR ≥ 1.5 with hepatic encephalopathy, or PT ≥ 20 seconds or PT-INR ≥ 2 even without encephalopathy.[12] Cirrhosis was confirmed histologically by stage 4 fibrosis on the METAVIR scoring system.[13] Secondary findings associated with portal hypertension, including splenomegaly, esophageal varices, and ascites, were also collected.

Biochemical remission was defined as the normalization of serum aspartate transaminase (AST), alanine transaminase (ALT), and IgG levels within age-specific reference ranges. Complete biochemical response was achieved when biochemical remission occurred within six months of treatment initiation. A subgroup analysis evaluated biochemical remission rates based on initial corticosteroid dosage. Patients in the low-dose group received < 1 mg/kg/day of corticosteroids, while those in the standard-dose group received ≥ 1 mg/kg/day, with a maximum of 60 mg/day. Patients with indeterminate initial corticosteroid dosage were excluded from the subgroup analysis.

Non-response was defined as < 50% reduction in serum transaminase levels within the first four weeks of treatment, while incomplete response indicated partial improvement insufficient for biochemical remission. Relapse was characterized by the exacerbation of disease activity after remission or medication withdrawal. Treatment failure was defined as worsening laboratory parameters despite ongoing treatment, and treatment intolerance was determined by the occurrence of treatment-related adverse events leading to medication discontinuation.[6,12,14]

Overall survival rate was defined as the proportion of patients alive throughout the follow-up, regardless of LT. Native liver survival (NLS) rate represented the proportion of patients retaining their original liver without LT. Relapse-free survival rate was the proportion of patients surviving without relapse after achieving biochemical remission. Clinical event-free survival (CEFS) was defined as survival without complications of chronic liver disease, including cirrhosis, ascites, splenomegaly, varices, hepatic encephalopathy, hepatocellular carcinoma, LT, or death.

Statistical analysis

All statistical analyses were conducted using SPSS software (version 29.0, IBM Corp., Armonk, NY, USA). *P* values below 0.05 were considered statistically significant. Continuous variables were presented as medians with interquartile ranges (IQRs), and categorical variables as frequencies (number) and percentages (%). Kaplan-Meier survival analysis was performed to assess overall survival, NLS, CEFS, and relapse-free survival rates. The log-rank test was used to compare survival outcomes between groups.

Ethics statement

This study was approved by the Institutional Review Board of all participating hospitals, including Seoul National University Hospital (No. 2308-174-1461), and the requirement for

written informed consent was waived due to its retrospective nature. The study complied with the principles of the Declaration of Helsinki.

RESULTS

Baseline characteristics

This study comprised 44 patients with a median diagnosis age of 12.4 (IQR, 9.5–16.0) years and a slight female predominance (57%). Liver biopsy was performed in all patients, and magnetic resonance cholangiopancreatography was conducted in 14 patients at diagnosis. Forty (91%) were classified as type 1 autoimmune hepatitis (AIH-1), one (2%) as type 2 autoimmune hepatitis (AIH-2), and three (7%) as ASC (**Table 1**). Among ASC cases, two were confirmed by cholangiography and histology, while one was diagnosed based on histopathology alone. Thirteen patients (30%) were asymptomatic and identified incidentally due to elevated liver enzymes. Among symptomatic patients, jaundice was the most common (n = 16), followed by fever (n = 8), abdominal pain (n = 7), fatigue (n = 7), weight loss (n = 3), nausea/vomiting (n = 3), rash (n = 2), and myalgia (n = 1). Cirrhosis was confirmed histologically in three patients (7%) diagnosed at 5.7, 9.0, and 11.7 years of age. Six patients exhibited secondary features of portal hypertension, including splenomegaly (n = 4), varices (n = 2) and ascites (n = 1). Including these patients along with those with histological evidence of cirrhosis, seven patients (16%) were considered to have cirrhosis at diagnosis. Four patients had acute severe AIH, but no cases of PALF or hepatic

Table 1. Baseline clinical characteristics

Variables	Values (N = 44)
Demographics	
Age at diagnosis, yr	12.4 (9.5–16.0)
Female	25 (56.8)
Height at diagnosis (z-score; n = 38)	0.28 (−0.61 to 0.99)
Weight at diagnosis (z-score; n = 38)	0.27 (−1.24 to 1.02)
Body mass index, kg/m^2 (z-score; n = 39)	−0.28 (−1.10 to 0.94)
Type	
Type 1 autoimmune hepatitis	40 (90.9)
Type 2 autoimmune hepatitis	1 (2.3)
Autoimmune sclerosing cholangitis	3 (6.8)
Concomitant liver diseases	
Nonalcoholic fatty liver disease	7 (15.9)
History of hepatotoxic drugs	4 (9.1)
Other autoimmune diseases	
Autoimmune thyroiditis	5 (11.4)
Systemic lupus erythematosus	2 (4.5)
Ulcerative colitis	2 (4.5)
Hemolytic anemia	2 (4.5)
Subtotal	10 (22.7)
Family history of autoimmune diseases	
Rheumatoid arthritis	4 (9.1)
Hashimoto's thyroiditis	1 (2.3)
Autoimmune hepatitis	1 (2.3)
Antiphospholipid syndrome	1 (2.3)
Others	1 (2.3)
Subtotal	8 (18.2)
Liver-related complications at diagnosis	
Liver cirrhosis	3 (6.8)
Acute severe autoimmune hepatitis	4 (9.1)

Values are presented as number (%), mean ± standard deviation, or median (interquartile range).

https://doi.org/10.3346/jkms.2026.41.e108

encephalopathy were observed. All patients with initial cirrhosis or acute severe AIH were diagnosed with AIH-1.

Concomitant autoimmune diseases occurred in 10 patients (23%), most frequently autoimmune thyroiditis, followed by systemic lupus erythematosus (SLE), ulcerative colitis, and hemolytic anemia. Eight (18%) had a family history of autoimmune diseases.

Median laboratory values at diagnosis were as follows: IgG 1,952.0 (IQR, 1,450.0–2,976.5) mg/dL; AST 372.0 (IQR, 150.0–617.0) IU/L; ALT 371.0 (IQR, 147.0–593.0) IU/L; alkaline phosphatase 312.0 (IQR, 179.8–448.0) IU/L; γ-glutamyl transferase 110.0 (IQR, 63.0–211.5) IU/L; total bilirubin (TB) 1.70 (IQR, 0.90–4.80) mg/dL; direct bilirubin 1.40 (IQR, 0.40–4.24) mg/dL; PT-INR 1.22 (IQR, 1.08–1.38); platelet count 224.0 (IQR, 162.3–304.8) × 10^3/μL. All 44 patients tested positive for at least one autoantibody, with antinuclear antibodies (ANAs) being the most prevalent (93%, median titer 1:160). Smooth muscle antibodies were detected in 34% (14/41), anti-liver kidney microsomal type 1 antibodies in 3% (1/38), and anti-neutrophil cytoplasmic antibodies (ANCAs) in 36% (9/25). Among the three ASC patients, ANCA was tested in two, and both were positive. No patients tested positive for anti-mitochondrial or anti-soluble liver antigen antibodies.

Therapeutic management

Corticosteroids were the most commonly administered initial treatment (39/44, 89%), while azathioprine (AZA) became the primary agent after six months (**Fig. 1A**). In the subgroup analysis, 21 patients (57%) received low-dose and 16 (43%) received standard-dose corticosteroids. From six months to seven years, immunosuppressant monotherapy predominated, comprising more than 50% of treatment protocols, followed by combination therapy with corticosteroids (**Fig. 1B**). Of the five patients who were followed up at 10 years, three had achieved remission and were being monitored without any medication. The remaining two patients continued to receive combination therapy with corticosteroids due to disease relapse. Biochemical remission rates did not differ significantly between AZA monotherapy and combination therapy ($P > 0.05$), nor across AZA doses (range 0.7–1.6 mg/kg/day) or height z-scores (**Table 2**).

Seven patients, all with AIH-1, received second-line immunosuppressants, including tacrolimus (n = 3), cyclosporine (n = 3), and mycophenolate mofetil (MMF; n = 1). Tacrolimus was initiated in two patients with a history of allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia and one with insufficient biochemical response. Cyclosporine replaced AZA in three patients due to elevated liver enzymes (n = 2) or severe fatigue (n = 1). MMF was introduced following relapse on AZA in the tenth year.

Treatment outcomes

The complete biochemical response rate was 33% (14/43), and biochemical remission rates ranged from 52–55% between 1 and 5 years, peaking at 70% at 7 years and 60% at 10 years. The complete biochemical response rate was significantly higher in the standard-dose group (63%) than in the low-dose group (14%; $P = 0.005$). Biochemical remission rates at 1, 2, and 5 years were also significantly higher in the standard-dose group (**Table 3**).

The incomplete remission rate was 65% at 6 months, declining to 31% at 1 year, 33% at 2 years, 19% at 5 years, and 20% at 7 years. Six patients relapsed: three at 5 years, one at 7 years, and two at 10 years. The non-response rate at four weeks was 14%, all with AIH-1.

https://doi.org/10.3346/jkms.2026.41.e108

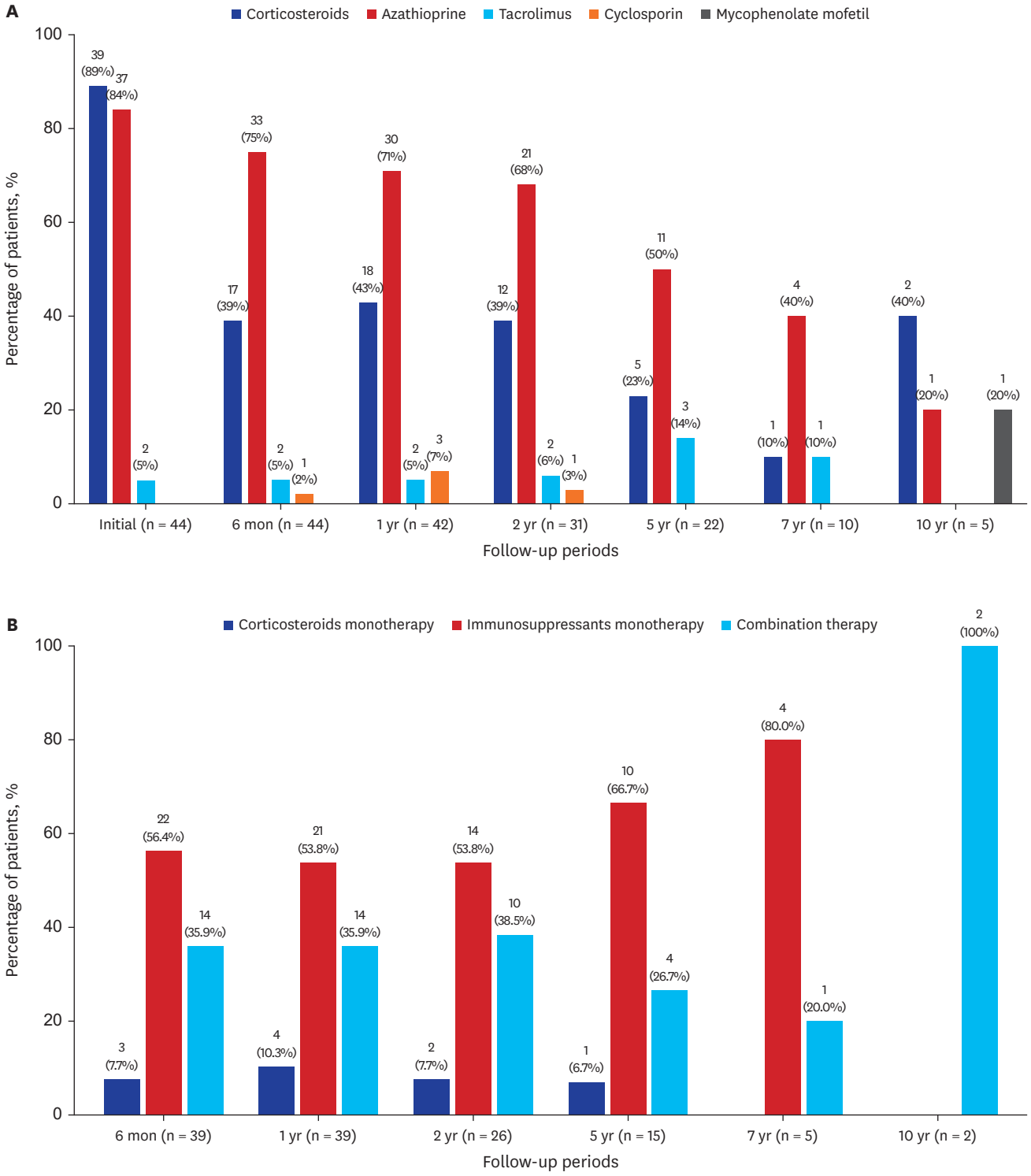

Fig. 1. Treatment patterns and longitudinal changes in Korean children with autoimmune hepatitis. (**A**) Distribution of treatment regimens throughout the follow-up period. (**B**) Proportions of corticosteroid monotherapy, azathioprine monotherapy, and azathioprine-corticosteroid combination therapy.

https://doi.org/10.3346/jkms.2026.41.e108

Table 2. Comparison between azathioprine monotherapy and azathioprine-corticosteroid combination therapy group

Variables	Follow-up duration	Azathioprine monotherapy	Combination therapy	*P* value
Biochemical remission rates	6 mon	8/20 (40.0)	2/13 (15.4)	0.245
	1 yr	12/19 (63.2)	4/11 (36.4)	0.156
	2 yr	6/12 (50.0)	2/8 (25.0)	0.373
	5 yr	3/7 (42.9)	1/3 (33.3)	1.000
	7 yr	0/3 (0.0)	1/1 (100.0)	0.250
Azathioprine dosage	6 mon	(n = 15)	(n = 11)	0.134
		1.45 (1.18–2.12)	0.96 (0.70–1.68)	
	1 yr	(n = 13)	(n = 10)	0.605
		1.38 (0.94–2.21)	1.51 (0.63–1.75)	
	2 yr	(n = 9)	(n = 6)	0.689
		1.26 (0.62–1.75)	1.34 (0.56–1.99)	
	5 yr	(n = 6)	(n = 1)	0.857
		1.00 (0.47–1.61)	1.43	
	7 yr	(n = 3)	(n = 1)	0.500
		1.64 (range 1.04[a])	0.68	
Height z-scores	6 mon	(n = 15)	(n = 11)	0.330
		−0.10 (−0.96 to 0.69)	0.39 (−0.61 to 1.06)	
	1 yr	(n = 13)	(n = 10)	0.563
		0.05 (−0.74 to 0.69)	0.41 (−0.63 to 0.89)	
	2 yr	(n = 9)	(n = 6)	0.388
		0.21 (−0.58 to 0.61)	−0.51 (−2.72 to 0.58)	
	5 yr	(n = 6)	(n = 1)	0.571
		0.15 (−0.44 to 1.11)	2.37	
	7 yr	(n = 3)	-	-
		−0.55		

Values are presented as number (%) or median (interquartile range).
[a]Interquartile range could not be calculated due to insufficient data.

Table 3. Biochemical remission rates in standard-dose and low-dose groups based on initial corticosteroid dose

Follow-up period	Initial corticosteroid dosage		*P* value
	Low-dose group	Standard-dose group	
6 mo (n = 37)	3/21 (14.3)	10/16 (62.5)	0.005
1 yr (n = 36)	7/20 (35.0)	12/16 (75.0)	0.023
2 yr (n = 26)	5/17 (29.4)	8/9 (88.9)	0.011
5 yr (n = 18)	2/10 (20.0)	7/8 (87.5)	0.015
7 yr (n = 9)	2/4 (50.0)	4/5 (80.0)	0.524
10 yr (n = 4)	1/1 (100.0)	1/3 (33.3)	1.000

Values are presented as number (%).

Among these five patients, four never achieved remission (two required LT), while one achieved remission at 5 years. Treatment failure occurred in a small subset, at 6 months (n = 4), 1 year (n = 5), 2 years (n = 3), and 5 years (n = 3).

The IgG levels gradually improved between six months and two years, with a slight increase after five years, correlating with rising relapse rates. Median ALT, TB, and PT-INR levels normalized by six months and remained stable (**Fig. 2**).

Treatment withdrawal

Among 41 patients, eight (20%) discontinued medication after achieving biochemical remission. The median time from treatment initiation to withdrawal was 28.5 (IQR, 27.4–34.8) months, with a median of 21.5 (IQR, 12.9–28.3) months from remission to withdrawal. Only one patient underwent liver biopsy before withdrawal, showing no definite hepatic inflammation. ANA titers, measured in four patients at withdrawal, were all negative. Relapse occurred in one patient 30 months after discontinuing medication, despite normal IgG (1,260 mg/dL), ALT (9 IU/L), and negative ANA at discontinuation.

https://doi.org/10.3346/jkms.2026.41.e108

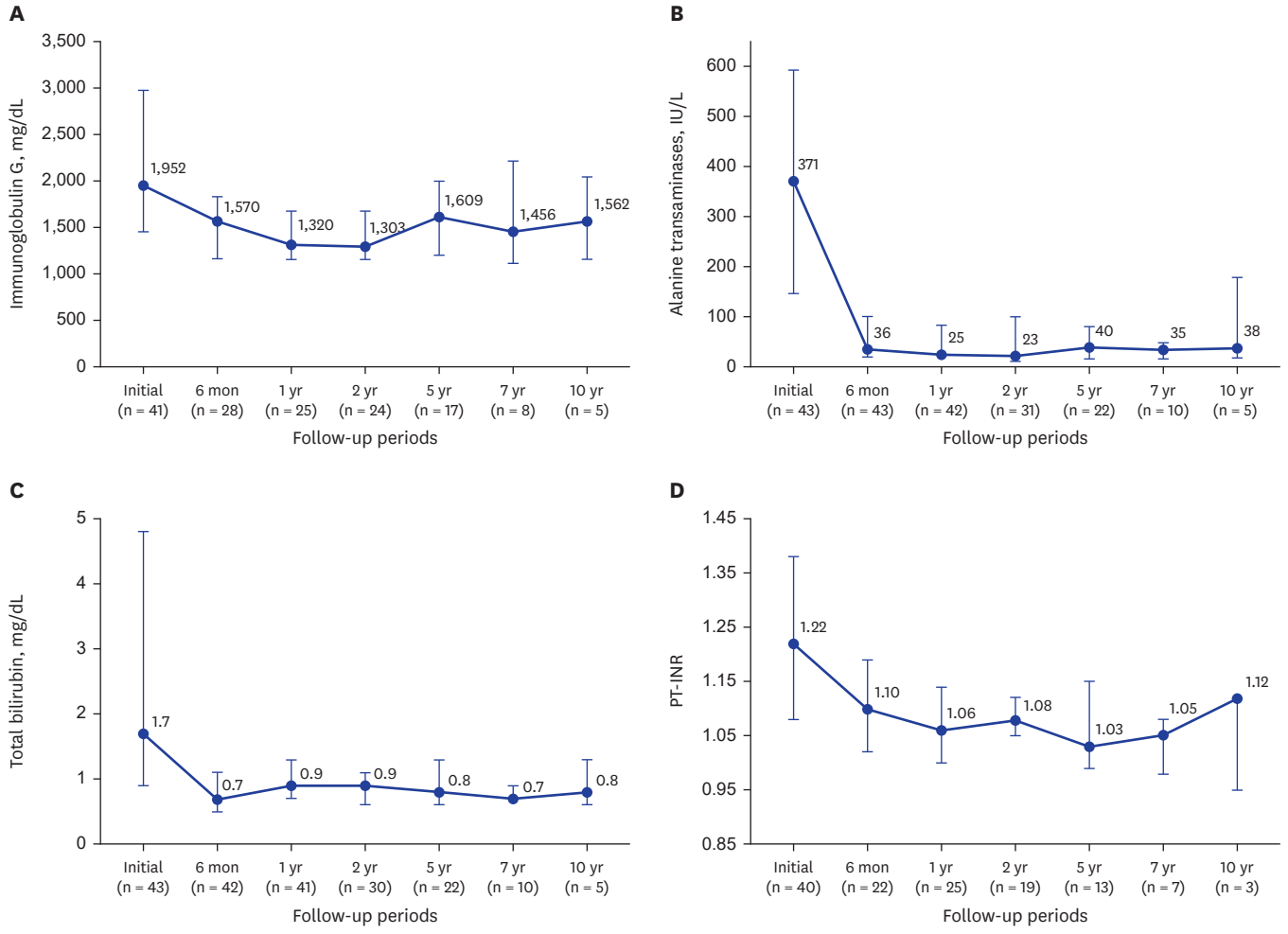

Fig. 2. Longitudinal trends in laboratory parameters: (**A**) IgG, (**B**) alanine transaminase, (**C**) total bilirubin, and (**D**) PT-INR.
PT-INR = prothrombin time-international normalized ratio.

Clinical outcomes and survival rates

Eleven patients (25%) experienced clinical events related to chronic liver disease, including cirrhosis (n = 7), ascites (n = 1), splenomegaly (n = 4), varices (n = 4), LT (n = 2), and death (n = 2). No cases of hepatic encephalopathy or hepatocellular carcinoma were reported. The incidence of clinical events did not differ by sex, AIH subtype, comorbidities, complete biochemical response, or baseline IgG, AST, ALT, PT-INR, or ANA titers. However, baseline TB levels were significantly higher in patients with clinical events (**Supplementary Table 1**).

Two patients died and two underwent LT; all had AIH-1, and none presented with acute severe AIH at diagnosis. Both deaths occurred within one year of diagnosis: one due to SLE-related central nervous system involvement while on cyclosporine, and the other following treatment discontinuation due to delayed diagnosis of AIH. Both transplant recipients had cirrhosis and varices, undergoing LT at 2 and 7 years after diagnosis.

The overall survival rates at 1, 5, and 10 years were 98%, 95%, and 95%, respectively, while NLS rates were 98%, 92% and 79% (**Fig. 3A**). The relapse-free survival rates at these intervals were 95%, 73%, and 55%, and CEFS rates were 86%, 75%, and 70% (**Fig. 3B and C**). The

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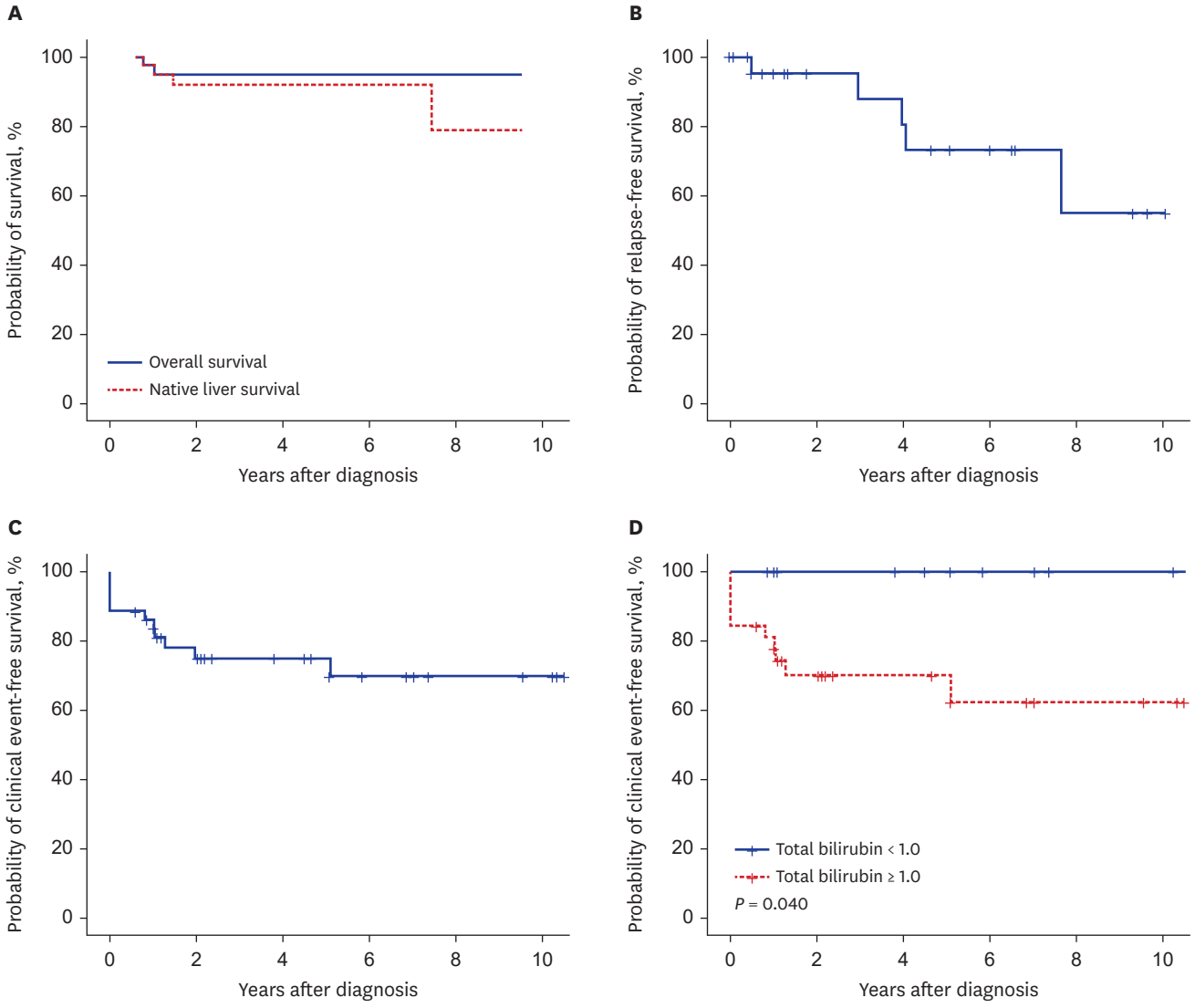

Fig. 3. Probability of overall survival, native liver survival, relapse-free survival, and clinical event-free survival. (**A**) Overall survival and native liver survival. (**B**) Relapse-free survival. (**C**) Clinical event-free survival. (**D**) Clinical event-free survival depending on total bilirubin levels at diagnosis (P = 0.040, log-rank). (**E**) Clinical event-free survival depending on PT-INR at diagnosis (P = 0.080, long-rank). (**F**) Clinical event-free survival depending on complete biochemical response (P = 0.400, long-rank).
PT-INR = prothrombin time-international normalized ratio.

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10-year CEFS rate was significantly higher in patients with an initial TB < 1.0 mg/dL than in those with TB ≥ 1.0 mg/dL (100% vs. 62%, P = 0.040; **Fig. 3D**). The 10-year CEFS probability did not differ significantly based on initial PT-INR or complete biochemical response (**Fig. 3E and F**).

DISCUSSION

AIH differs between adults and children in clinical manifestations, disease progression, and treatment responses, although both share features such as female predominance and specific autoantibodies.[15,16] Ethnicity, sex, age, and genetic and environmental factors influence clinical characteristics and outcomes,[4,17] yet pediatric AIH remains poorly studied

https://doi.org/10.3346/jkms.2026.41.e108

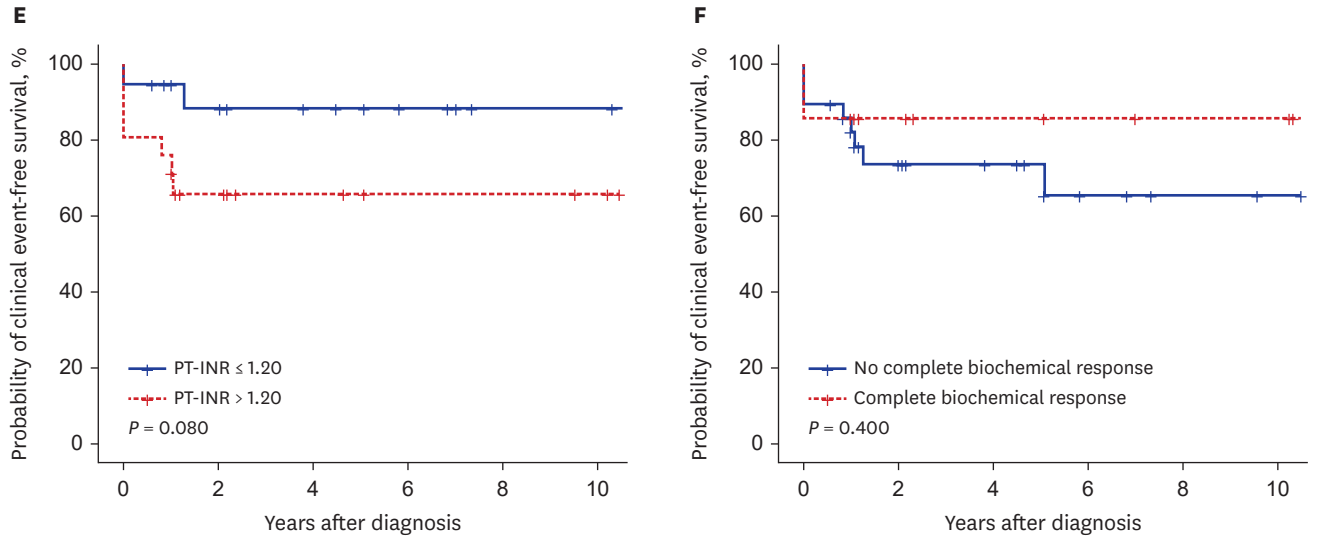

Fig. 3. (Continued) Probability of overall survival, native liver survival, relapse-free survival, and clinical event-free survival. (**A**) Overall survival and native liver survival. (**B**) Relapse-free survival. (**C**) Clinical event-free survival. (**D**) Clinical event-free survival depending on total bilirubin levels at diagnosis (P = 0.040, log-rank). (**E**) Clinical event-free survival depending on PT-INR at diagnosis (P = 0.080, long-rank). (**F**) Clinical event-free survival depending on complete biochemical response (P = 0.400, long-rank).
PT-INR = prothrombin time-international normalized ratio.

in Asia.[8,18,19] This nationwide, multicenter, retrospective study evaluated the clinical characteristics, long-term prognosis, and real-world treatment regimens in Korean children with AIH to support future guidelines.

AIH-2 is common in western pediatric populations, with reported frequencies of 38% in the United Kingdom,[20] 44% in France,[6] 9% in the United States,[21] and 13% in Canada.[7] In contrast, East Asian adult studies showed AIH-1 predominance (up to 97% in Korea, 100% in Taiwan, and 92% in Singapore).[17,22,23] Pediatric data also showed a lower prevalence of AIH-2—16% in Malaysia[18] and none in a Korean single-center study.[8] Consistently, only one patient in this study was diagnosed with AIH-2, demonstrating ethnic differences in AIH presentation.

Cholangiography was performed in 14 patients (32%) with cholestatic features or poor treatment response, diagnosing ASC in three patients (7%). Pediatric studies from Japan[24] and Brazil[25] reported that cholangiography was performed in 32.7–57% of selected AIH patients, with ASC diagnosed in 3–7.3%—similar to our findings. A prospective Indian study[26] recommended cholangiography for patients with cholestatic features, inflammatory bowel disease, or poor immunosuppressive response rather than for all children with AIH, given that ASC was identified in only 10% of cases. However, an English study performed cholangiography in all AIH patients, diagnosing ASC in 49%.[27] Further research is needed to determine whether the low proportion of ASC in our study reflects limited testing or racial differences.

At diagnosis, cirrhosis was confirmed by biopsy in 7% and by secondary evidence in 16%, similar to Japanese findings.[24] A French pediatric study, defining cirrhosis by histology or esophageal varices, reported 68%,[6] and 53% of Malaysian children showed evidence of cirrhosis at diagnosis,[18] substantially higher than in our study. Among biopsy-confirmed cases, cirrhosis prevalence differs by age and ethnicity: 13% in Korean adults, 38% in Caucasian Americans,

https://doi.org/10.3346/jkms.2026.41.e108

and 85% in African Americans.[28,29] A U.S. study reported the highest cirrhosis prevalence in Hispanics (55%), compared with 30% in Caucasians and 29% in Asians.[4]

The complete biochemical response rate was 33%, lower than the 48% reported in a French pediatric study.[6] A Canadian pediatric study reported a 1-year complete response rate of 90%,[7] compared with 55% in our study, while a Korean adult study showed a higher remission rate of 84% after 3.5 months of treatment.[28] Our subgroup analysis revealed that initial corticosteroid dosing significantly influenced early (6-month) and sustained (up to 5-year) responses. Patients receiving < 1 mg/kg/day exhibited lower remission rates than those receiving 1–2 mg/kg/day, supporting guidelines recommending an initial prednisolone dose of 1–2 mg/kg/day (maximum 60 mg/day).[12,30,31] A systematic review[32] further supports our finding, which is the first to underscore the importance of initial corticosteroid dosing in pediatric AIH.

For maintenance treatment, AZA monotherapy or AZA-corticosteroid combination therapy is recommended.[12,30,31] In our study, over 50% of patients transitioned to AZA monotherapy after 6 months of treatment, with no significant difference in remission rates, AZA doses, or height z-scores compared to combination therapy. Despite limited long-term follow-up, these findings align with previous studies indicating AZA monotherapy is as effective as combination therapy in maintaining remission in children.[33-36] Considering the need for prolonged treatment and growth concerns, we advocate for AZA monotherapy when feasible.

Fewer patients discontinued medication compared to the French pediatric study (43%). Among the eight patients who discontinued, only one underwent liver biopsy before withdrawal. However, relapse rate was lower in our study (13%) than in the French study (51%).[6] Although European guidelines previously recommended liver biopsy before withdrawal,[30] recent evidences suggest that relying solely on biochemical parameters does not increase relapse risk.[6,12] In French pediatric patients, relapse rates were comparable regardless of biopsy confirmation,[6] and liver biopsy is no longer deemed essential for treatment cessation in adults.[12] Given its invasive nature, further discussion is needed regarding its necessity in pediatric patients.

The long-term prognosis was favorable, with a 10-year overall survival rate of 95% and NLS rate of 79%, comparable to previous studies,[6,25,37,38] Patients with clinical events had significantly higher initial TB levels, consistent with a Canadian adult study reporting a 5-year CEFS of 88%.[39] Older age, cirrhosis, and elevated TB at diagnosis increased the risk of clinical events. A Brazilian pediatric study found that AIH-2, higher AST, ALT, and albumin levels at presentation, and achieving complete remission were associated with longer NLS, while abnormal cholangiogram correlated with lower NLS.[25]

Although some studies have reported worse outcomes in ASC, a recent pediatric study found no significant differences in prognosis and treatment responses between AIH and ASC.[40] Among AIH patients, those progressing to ASC exhibited similar clinical, laboratory, histological findings and treatment responses, with higher relapse rates being the only difference, which did not impact overall survival or LT requirement. In our study, all cases of cirrhosis, acute severe AIH, second-line treatment, and LT occurred in AIH patients, suggesting ASC does not confer worse outcomes compared to AIH.

This study has limitations, including small sample size and retrospective design, which restricted the standardization of diagnostic and therapeutic protocols. Nonetheless, a key

https://doi.org/10.3346/jkms.2026.41.e108

strength is the inclusion of AIH and ASC patients, rarely studied together in pediatric research, along with insights into second-line treatment and drug withdrawal. This comprehensive analysis of long-term outcomes in pediatric AIH in East Asia provides valuable evidence for future guidelines.

In conclusion, AIH-1 predominates in Korean children, whereas AIH-2 and ASC are rare. Cirrhosis was present in only 7% of patients. AZA monotherapy demonstrated a comparable efficacy to corticosteroid combination therapy. Although biochemical remission rates were lower than in other studies—likely due to the frequent use of low initial corticosteroid doses—overall survival and NLS were favorable. Given the association between high TB levels at diagnosis and poor liver outcomes, careful monitoring of these patients is warranted.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Comparison of clinical characteristics between patients with and without complications

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