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ORIGINAL RESEARCH

Analysis of Clinical Characteristics and Long-Term Prognosis in Young Patients with Hepatitis B Cirrhosis: A Propensity Score Matched Study

Pengyue Zhang[1,2,*], Wenjuan Zhang[1,3,*], Xinlei Chen[1,2], Haoyang Guo[1,2], Xilei Cai[1], Chunhui Tao[1,2], Xiaodan Hong[1], Zhenhua Zhang[1]

[1]Department of Infectious Diseases, The Second Hospital of Anhui Medical University, Hefei, People's Republic of China; [2]Department of Clinical Medicine, The Second School of Clinical Medicine, Anhui Medical University, Hefei, People's Republic of China; [3]Department of Infectious Diseases, Shanghai Fourth People's Hospital, Shanghai, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zhenhua Zhang, Email zhangzhenhua@ahmu.edu.cn

Background: Cirrhosis is rare in young individuals, and clinical differences between young and adult patients remain unclear. This study aimed to evaluate the clinical characteristics and prognosis of HBV-related cirrhosis in young patients.

Methods: A hospital-based retrospective cohort of young cirrhosis patients was analyzed. Multivariable analysis identified risk factors for severe complications during follow-up, while the Cox proportional-hazards model assessed the prognosis of young and adult patients with HBV-related cirrhosis. Prognosis was assessed after baseline covariates were balanced using propensity score matching (PSM).

Results: The study included 545 patients with cirrhosis, including 119 in the younger group. Young patients with HBV-related cirrhosis exhibited significant differences from adult patients in gender, Alb, ALT, AST, and HBV titer. Kaplan-Meier analysis indicated a higher survival rate in the young group (P = 0.04); however, no significant difference remained after PSM. Youth was identified as an independent risk factor for gastrointestinal bleeding during follow-up (OR = 3.61, 95% CI: 1.62–8.00, P = 0.002). Additionally, age and elevated ALP levels were independent risk factors for survival. The Cox-based prediction model showed moderate prognostic performance, with a C-index of 0.69.

Conclusion: After baseline differences were balanced, young patients with HBV-related cirrhosis showed no survival advantage. Vigilant monitoring for serious complications, particularly gastrointestinal bleeding, is warranted. These findings may inform targeted interventions to reduce the burden of early onset cirrhosis.

Plain Language Summary:

- Despite preserved liver function, younger patients showed comparable long-term outcomes to elderly after confounder adjustment.
- Close monitoring for gastrointestinal bleeding remains crucial in younger cases.
- The developed prognostic model aids hepatitis B cirrhosis management.

Keywords: cirrhosis, hepatitis B virus, surveillance, prognosis

Introduction

Cirrhosis is an advanced, irreversible liver disease characterized by diffuse hepatic damage. It is highly prevalent in low- and middle-income countries and ranks as the 14th leading cause of death globally. Cirrhosis results in numerous systemic complications, including ascites and portal hypertension, which significantly affect quality of life and prognosis.[1] Despite advancements in diagnosis and treatment, managing cirrhosis remains challenging due to its variable progression, high risk of decompensation, and limited reversibility. The clinical manifestations and mortality rates

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associated with cirrhosis vary considerably among individuals, largely influenced by the underlying etiology, geographic region, and socioeconomic factors.[2] Although typically diagnosed in the elderly, studies have shown that less than 5% of cases occur in individuals under 35 years of age.[3] Due to its rarity, cirrhosis in young populations has received limited attention, and it remains unclear whether age at diagnosis significantly impacts prognosis or treatment strategies.

The risk of liver disorders increases with age, and the incidence and prognosis of end-stage liver diseases, including hepatocellular carcinoma (HCC), differ significantly among age groups.[4] However, conflicting data exist regarding the clinical presentation and prognosis of cirrhosis in young patients. Sarin et al[3] reported that the etiology, clinical presentation, natural history, and survival of young patients were not significantly different from elderly cirrhosis. In contrast, another study retrospectively analyzed the clinical course and survival of 83 young cirrhosis aged 15 to 30 years, revealing a 5 year survival rate of 70%, which was significantly better than adult.[5] As a result, whether the prognosis of cirrhosis differs between young and adult patients remains unclear. The lack of age-stratified analyses has limited understanding of disease progression. Identifying factors is essential for optimizing surveillance, guiding treatment, and improving outcomes.

Recent epidemiological studies indicate that hepatitis B virus (HBV) cirrhosis accounts for more than 45% of cirrhosis cases and approximately 50% of cirrhosis-related deaths, Despite widespread vaccination and the availability of antiviral therapies such as tenofovir and entecavir, HBV infection remains the leading cause of cirrhosis, particularly in endemic regions like sub-Saharan Africa and East Asia.[6] This study aimed to compare the clinical characteristics, prognostic factors, and survival outcomes between young and older cirrhotic patients, with a particular focus on the prognostic risk factors in young patients with HBV-related cirrhosis. The findings may provide a foundation for targeted interventions to mitigate the growing burden of early onset cirrhosis in HBV-endemic regions.

Materials

Patients Selection

This retrospective cohort study was conducted at a tertiary care center, including consecutive hospitalized patients with an initial diagnosis of cirrhosis between January 2010 and December 2023. Data were extracted from the electronic medical record database of the Second Affiliated Hospital of Anhui Medical University. Patients aged 40 years or younger comprised the observation group, while older cirrhotic patients during the same period served as the control group. Exclusion criteria included a prior diagnosis of primary liver malignancy, severe organ failure, or incomplete clinical data (Figure S1). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Hospital Ethics Committee (SL-YX2024-204). Informed consent was obtained from all patients upon admission.

Data Collection

The gold standard for diagnosing cirrhosis is histopathological examination; however, in clinical practice, diagnosis is predominantly based on non-invasive methods due to various limitations. In this study, the diagnosis was primarily established through clinical features suggestive of cirrhosis, following established clinical guidelines,[7] and supported by imaging findings (enhanced CT or MRI findings). These imaging criteria included surface irregularities or nodules, altered liver morphology, cirrhotic nodules (such as regenerative or dysplastic nodules), or evidence of portal hypertension. The etiology of cirrhosis was categorized based on serological and pathological findings: chronic HBV infection was identified in patients with positive hepatitis B surface antigen (HBsAg) or a clear history of hepatitis B, while chronic hepatitis C infection was diagnosed in patients with positive anti-hepatitis C virus (HCV) antibodies and further HCV RNA testing. Detailed alcohol consumption histories were obtained for all patients. Chronic alcoholic liver disease was defined as ethanol intake of 60 g per day or more for men and 50 g per day or more for women, sustained for over five years. For cirrhotic patients who tested negative for hepatitis B and C antibodies and reported no significant alcohol consumption, additional diagnostic tests such as ceruloplasmin, anti-liver antibodies, and anti-mitochondrial antibodies were conducted to determine the underlying cause of cirrhosis. All autoimmune liver diseases are definitively diagnosed through liver tissue biopsy.

The researchers reviewed the medical records to obtain detailed clinical and laboratory data, including: 1) patient demographics; 2) subjective symptoms such as malaise, abdominal pain, and other clinical manifestations at admission; 3)

serum biochemical markers, including hemoglobin (Hb), platelet count (PLT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin (Alb), total bilirubin (TBIL), gamma-glutamyltransferase (GGT), prothrombin activity (PTA), and markers of viral hepatitis. Imaging studies, such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), were used to assess for splenomegaly, ascites, and other features of portal hypertension. The presence of cholecystitis and gallbladder stones was diagnosed based on abdominal ultrasound or CT findings. The AST-to-platelet ratio index (APRI) and the fibrosis-4 (FIB-4) score are non-invasive scoring systems based on serum biochemical data.[7,8] According to the 2018 guidelines of the American Association for the Study of Liver Diseases (AASLD), elevated ALT levels were defined as >35 U/L in men and >25 U/L in women.[9]

Follow-Up

Patients with hepatitis B cirrhosis were systematically monitored throughout the study period following baseline data collection. Follow-up data were obtained through scheduled telephone interviews and electronic medical records in the physician workstation system. Regular assessments included liver function tests, serum HBV DNA levels, and imaging studies, typically conducted every 3 to 6 months. Disease progression was evaluated based on changes in HBV viral load, hepatic decompensation events, and complications. HCC is diagnosed through imaging studies, elevated alpha-fetoprotein (AFP) levels, and positive liver biopsy results. Adverse clinical events such as upper gastrointestinal bleeding(GIB), hepatic encephalopathy(HE), and spontaneous peritonitis(SBP) were systematically recorded and classified according to established clinical guidelines. Follow-up was conducted until December 2024, and patient outcomes were categorized as survival, death, or loss.

Statistical Analysis

Quantitative data were expressed as means ± standard deviation (x ± s) when they followed a normal distribution, with independent samples *t*-tests used for intergroup comparisons. For data that did not conform to a normal distribution, medians and interquartile ranges were employed. Comparisons of categorical data were conducted using the χ^2-test or Fisher's test. Univariate and multivariate analyses were performed using binary logistic regression. Group differences in complication frequencies were also assessed using χ^2-test or Fisher's test. To evaluate the prognostic impact of age, all patients diagnosed with HBV-related cirrhosis were included in the Cox proportional hazards analysis. Univariate and multivariate regression models were applied to identify variables independently associated with overall survival. Survival from the first diagnosis of cirrhosis was analyzed using the Kaplan-Meier method, with comparisons made using the Log rank test. The prognostic model was developed using the survival and rms packages, with model discrimination assessed by the concordance index (C-index), which reflects the ability of the model to correctly rank patient risk over time. Restricted cubic splines(RCS) were used to evaluate the nonlinear relationships.[10]

Propensity score matching (PSM) analysis was implemented to balance baseline characteristics between young and elderly patients with hepatitis B cirrhosis.[11] The PSM process was conducted using the SPSS (version 27.0 IBM Corp., NY, USA) extension program, with age grouping as the dependent variable and each covariate as an independent variable. Propensity scores were estimated through logistic regression, and 1:1 nearest neighbor matching was performed with a match tolerance of 0.1. Analyses were repeated in the PSM-adjusted population to examine independent risk factors. All graphs drawn with R (version 4.2.2) and GraphPad Prism (version 10.1.2). $P < 0.05$ was considered statistically significant unless otherwise stated.

Results

Patient Characteristics

A total of 545 patients with cirrhosis were included in the study, with ages ranging from 16 to 85 years (mean age: 52.93 ± 13.31 years). The cohort comprised 384 males and 161 females, including 119 young patients (≤40 years) and 426 adult patients (>40 years). The younger group had a higher proportion of males and significantly elevated PLT, serum ALT, and TBIL levels ($P < 0.05$). However, no significant differences were observed in Alb, AST, AFP, or coagulation parameters between the two groups. The prevalence of gallstones was significantly higher in older patients (41.10% vs 19.66%, $P = 0.02$). Detailed baseline characteristics of both groups are presented in Table S1.

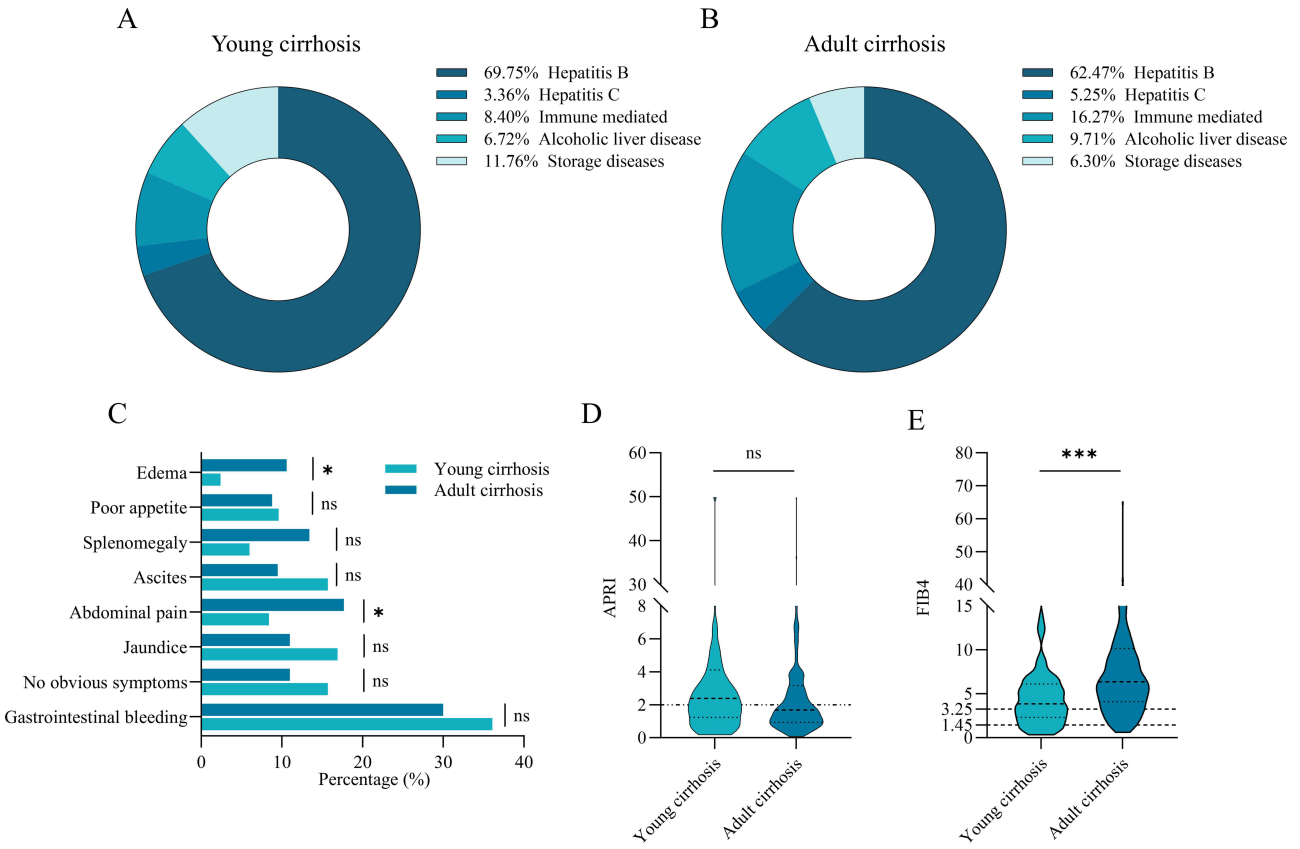

Figure 1 Clinical characteristics of cirrhosis in different ages. Etiology of cirrhosis in young (**A**) and adult patients (**B**); Clinical manifestations at the first diagnosis of cirrhosis (**C**); Liver noninvasive fibrosis scores of APRI(D); Liver noninvasive fibrosis scores of FIB4 (**E**).
Notes: ns indicates P > 0.05, * indicates P < 0.05, *** indicates P < 0.001.

Regarding etiological factors, HBV infection remained the primary cause of cirrhosis, accounting for 69.75% in the young group and 62.47% in the adult group (Figure 1A and B). Among the major etiologies, the prevalence of autoimmune cirrhosis was significantly lower in the younger group compared to the adult group (16.27% vs 8.4%), whereas storage diseases accounted for a higher proportion of cirrhosis cases in younger patients (11.76% vs 6.30%).

Young Hepatitis B-Related Cirrhosis

Given that HBV infection remains the primary etiology of cirrhosis, this study specifically analyzed HBV-related cases (Table 1), including 83 patients in the younger group (74 males, 9 females) and 283 in the adult group (217 males, 66 females). A documented family history of hepatitis B was present in 35 younger patients and 37 adult patients, with a statistically significant difference between the groups ($\chi^2 = 34.38$, $P < 0.001$). Additionally, the proportion of patients with an HBV disease duration exceeding 10 years was significantly higher in the younger group (56.61% vs 42.05%, $P < 0.001$). In terms of initial clinical manifestations, adult patients frequently presented with bilateral lower limb edema and abdominal pain (Figure 1C). Regarding non-invasive fibrosis scores, no significant difference was found in the APRI scores between the young and adult groups ($P = 0.854$), whereas FIB-4 scores were significantly higher in the adult group than in the young group ($P < 0.001$) (Figure 1D and E).

Beyond differences in sex distribution, significant disparities in laboratory parameters were observed between younger and older patients with HBV-related cirrhosis. Serum Alb, ALT, AST, and TBIL levels were significantly higher in the younger group, whereas fasting glucose and PTA were lower. Quantitative analysis of HBV markers revealed that HBsAg and HBeAg levels were markedly elevated in younger patients ($P^{\text{HBsAg}} < 0.001$, $P^{\text{HBeAg}} < 0.001$). To facilitate comparisons of viral load and subsequent prognostic assessments, PSM was performed for Alb, ALT, AST, and TBIL, as these parameters reflect liver functional reserve. Notably, even after adjusting for these confounders, HBsAg and HBeAg levels remained significantly higher in the younger group, and HBV DNA exhibited a similar trend.

Table 1 Clinical Characteristics of HBV-Related Cirrhosis Across Different Age Groups

Variables	Before Propensity Score Matching			After Propensity Score Matching (1:1)		
	Young (≤40 Years)	Adult (>40 Years)	*P* value	Young (≤40 Years)	Adult (>40 Years)	*P* value
Age, years	33.55±4.98	56.88±8.90	<0.001	33.61±4.91	55.06±9.23	<0.001
Sex, male, n(%)	74 (89.15)	217 (76.67)	0.016	63 (63/72)	63 (63/72)	1.000
PLT (*10^9/L)	92.33±76.20	87.04±67.47	0.451	94.70±76.16	84.75±62.32	0.341
ALB (g/L)	33.97±7.95	32.12±6.45	0.031	33.88±7.38	33.42±6.69	0.810
ALT, IQR (U/L)	45.50 (29.25, 127.50)	35.00 (21.00, 59.00)	<0.001	44.00 (29.00, 95.00)	38.00 (22.00, 67.00)	0.122
AST, IQR (U/L)	52.50 (30.50, 120.00)	42.00 (28.00, 77.00)	0.023	48.00 (30.00, 110.00)	41.50 (29.00, 87.25)	0.281
TBIL, IQR (μmol/L)	31.00 (19.47, 55.20)	20.60 (14.80, 32.50)	0.071	27.90 (19.40, 53.10)	21.95 (16.77, 42.80)	0.480
ALP (U/L)	112.12±64.84	118.85±74.07	0.164	104.31±59.58	113.05±63.67	0.400
GGT, IQR (U/L)	52.0 (28.00, 96.75)	46.00 (25.00, 102.00)	0.960	47.00 (26.00, 74.00)	62.00 (30.25, 111.0)	0.371
Glu (mmol/L)	5.37±1.77	6.16±4.88	0.023	5.33±1.72	5.73±2.06	0.217
PTA (%)	63.19±14.93	67.94±18.57	0.012	62.79±14.26	65.78±19.84	0.314
AFP, IQR (ng/mL)	6.80 (2.04, 99.47)	3.84 (1.84, 24.42)	0.261	5.90 (2.02, 65.00)	3.85 (1.58, 73.67)	0.723
HBV-DNA (×10^4)	13.00 (0.55, 186.50)	0.19 (0.05, 44.95)	<0.001	6.73 (0.05, 210.00)	0.10 (0.05, 94.95)	0.001
HBsAg (IU/mL)	1590.43 (681.0, 3036.71)	812.76 (64.5, 2015.98)	<0.001	1511.6 (697.13, 3153.61)	513.14 (10.72, 1648.13)	0.004
HBeAg (S/CO)	1.61 (0.37, 146.71)	0.40 (0.31, 0.65)	<0.001	1.61 (0.34, 142.34)	0.44 (0.37, 0.55)	0.060
HBeAb (S/CO)	1.29 (0.05, 5.81)	0.09 (0.01, 1.32)	<0.001	1.31 (0.05, 4.98)	0.07 (0.02, 0.91)	0.004
HBcAb (S/CO)	9.33 (8.35, 10.41)	8.77 (7.25, 9.96)	0.005	9.26 (8.32, 10.34)	8.07 (6.89, 9.14)	0.003

Abbreviations: PLT, Platelet; ALB, Albumin; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, Total Bilirubin; ALP, Alkaline Phosphatase; GGT, γ-Glutamyltranspeptidase; Glu, Glucose; PTA, Prothrombin Activity Percentage; AFP, Alpha-Fetal Protein; IQR, Interquartile range.

Severe Complications of HBV-Related Cirrhosis

Patients with cirrhosis are prone to various complications, including GIB, HE, SBP, and HCC, all of which significantly impact quality of life and survival. In a follow-up study of patients with HBV-related cirrhosis, risk factors for severe complications were analyzed. Regression analyses were conducted with various complications as outcome variables. Variables with $P < 0.1$ in the univariate analysis were included in the multivariate logistic regression (Tables S2–S5). The results indicated that younger age was an independent risk factor for GIB during follow-up (OR = 3.61, 95% CI: 1.62–8.00, $P = 0.002$), whereas age over 40 years was independently associated with an increased risk of HCC (OR = 5.96, 95% CI: 1.93–18.36, $P = 0.002$). Although younger age was identified as a potential risk factor for SBP in univariate analysis ($P = 0.03$), it did not reach statistical significance in the multivariate model ($P = 0.051$). Additionally, while PTA was considered a protective factor against HE, its association remained weak (OR = 0.942, 95% CI: 0.907–0.979, $P = 0.002$) (Figure 2).

Overall, GIB was the most common complication, occurring in 41.71% of patients, while HCC developed in 27.59% of cases during the follow-up period. The younger group exhibited a higher risk of GIB and SBP but a lower risk of HCC compared to the adult group. However, after PSM, only the difference in HCC incidence remained statistically significant (Figure 3A and B).

Survival and Prediction Nomogram

Patients with hepatitis B cirrhosis were followed for an average of 33.43 ± 26.99 months, with a median survival time of 128 months (Figure S2). Kaplan-Meier analysis indicated that the survival rate of the young group was higher than adult group (Log rank test, $P = 0.04$). Notably, survival analysis following PSM did not reveal a statistically significant difference between the two groups ($P = 0.58$) (Figure 3C and D).

To minimize bias introduced by arbitrary age groupings and to assess the potential non-linear relationship between age and all-cause mortality in hepatitis B cirrhosis, RCS were employed for flexible modeling and visualization (Figure 4A and B). The analysis demonstrated a positive correlation between age and mortality, with no significant non-linear association observed ($P^{\text{over all}} < 0.001$, $P^{\text{nonlinear}} = 0.322$). Furthermore, after adjusting for covariates such as ALB and ALT in multivariate analyses, the correlation remained statistically insignificant ($P^{\text{over all}} = 0.555$, $P^{\text{nonlinear}} = 0.800$).

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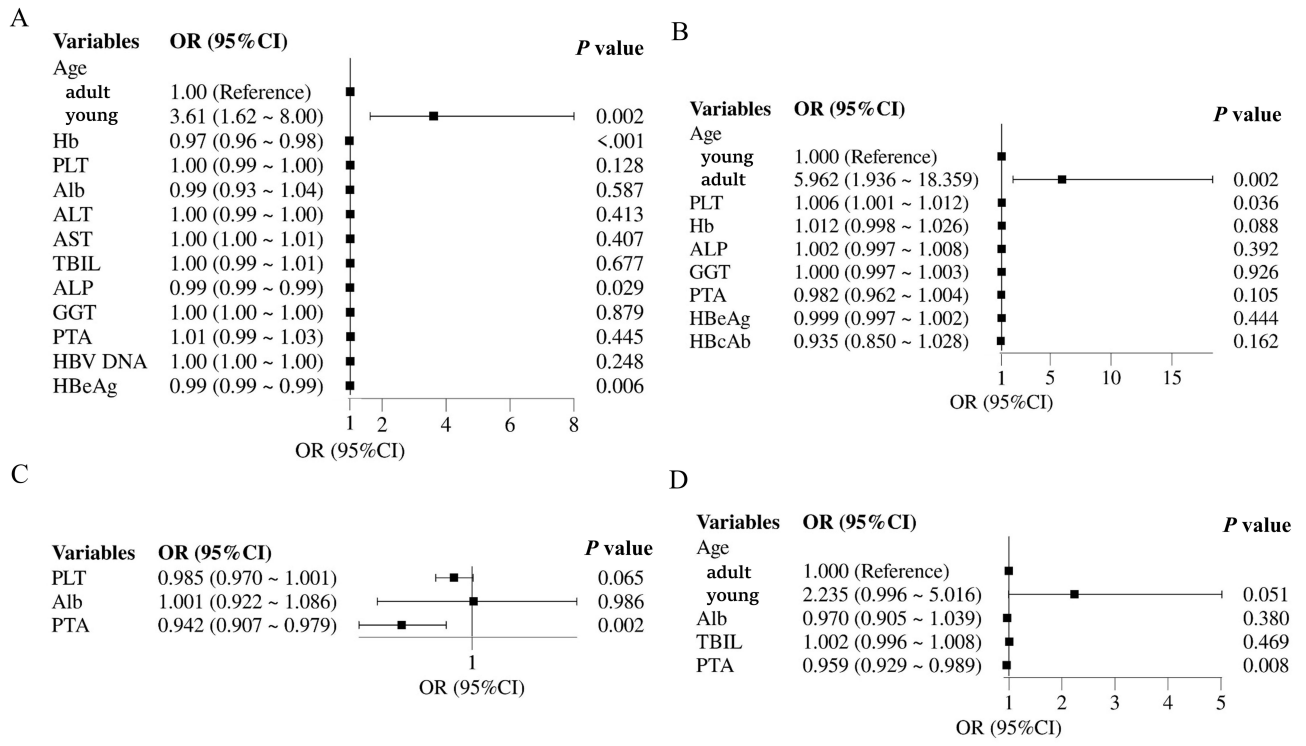

Figure 2 Multivariate logistic regression of risk factors for severe complications of hepatitis B cirrhosis during follow up. (**A**) Gastrointestinal bleeding; (**B**) Hepatocellular carcinoma; (**C**) Hepatic encephalopathy; (**D**) Spontaneous peritonitis.

Abbreviations: Hb, Hemoglobin; PLT, Platelet; ALB, Albumin; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, Total Bilirubin; ALP, Alkaline Phosphatase; GGT, γ-Glutamyltranspeptidase; PTA, Prothrombin Activity Percentage; HBV-DNA, Hepatitis B virus Deoxyribonucleic acid; HbeAg, Hepatitis B e antigen; HBcAb, Hepatitis B core antibody.

We compared demographic characteristics, baseline laboratory parameters, and the occurrence of cirrhosis-related complications between the survival and mortality groups. Compared with the survival group, the death group had a significantly higher mean age (56.46 vs 50.52, $P < 0.001$) and ALP levels (140.43 vs 111.87U/L, $P < 0.01$), while serum ALB and ALT levels were significantly lower ($P < 0.05$). Notably, HBeAg and HBcAb levels were also lower in the death group. After PSM, no significant differences remained between the groups for most variables, except for HBeAg levels and the presence of SBP complications (Table 2).

Univariate and multivariate Cox regression analyses were conducted for variables with $P < 0.1$ in the prognostic variability analysis (Table 3). Multivariate Cox regression identified age (aHR = 1.04, 95% CI: 1.02–1.06, $P = 0.001$) and ALP levels (aHR = 1.01, 95% CI: 1.01–1.01, $P = 0.011$) as independent risk factors for survival. Although ALB appeared to be a potential protective factor, the association was not statistically significant (aHR = 0.97, 95% CI: 0.93–1.01, $P = 0.133$). Recognizing the limitations of using individual metrics to predict prognosis in HBV-related cirrhosis, we evaluated the prognostic significance of these variables in the 366-patient cohort using the rms package. This approach integrates survival time, survival status, and multivariate analysis to construct a nomogram based on Cox regression results (Figures 4C and D). The overall C-index of the model was 0.69 (95% CI: 0.62–0.77, $P = 1.61e-07$), indicating moderate predictive accuracy.

Discussion

Despite a decline in mortality from HBV-related chronic liver disease over the past three decades, the absolute number of deaths continues to rise, with cirrhosis being the primary contributor.[12] However, limited studies have specifically examined the clinical characteristics and prognosis of young cirrhotic patients. In this study, "young cirrhosis" was defined as cirrhosis diagnosed in individuals aged 40 years or younger, aligning with existing research[13,14] and US guidelines that recommend HCC surveillance beginning at age 40.[15,16] Our retrospective cohort analysis revealed that

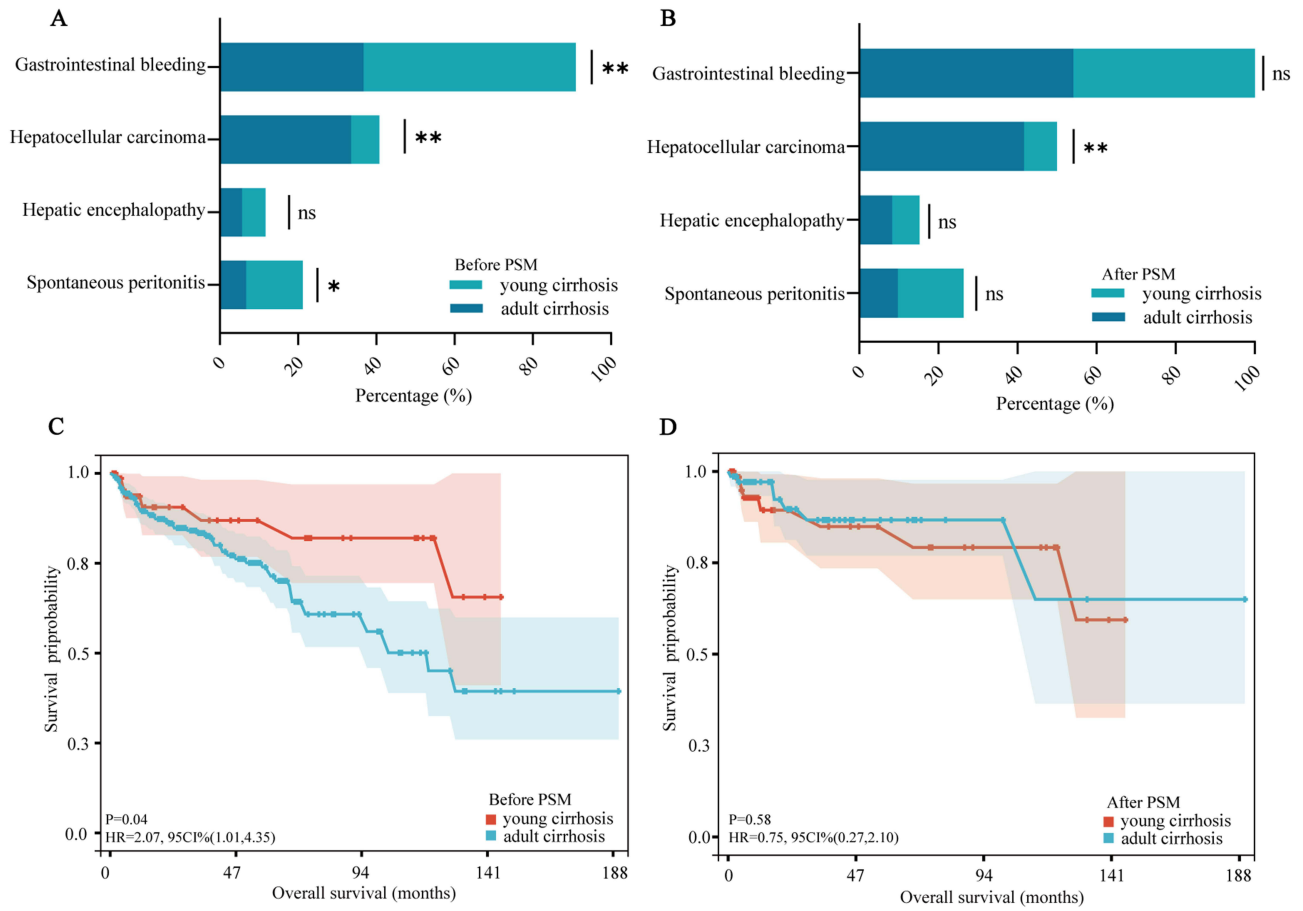

Figure 3 Prognosis analysis of HBV-related cirrhosis. Comparison of complication rates in young and adult HBV-related cirrhosis before (**A**) and after PSM (**B**); Overall survival in young and adult HBV-related cirrhosis before (**C**) and after PSM (**D**).
Notes: ns indicates P > 0.05, * indicates P<0.05, ** indicates P<0.01.
Abbreviation: PSM, Propensity score matching.

69.75% of young cirrhosis cases were attributable to HBV. Compared to older patients, young individuals with HBV cirrhosis exhibited higher ALB, ALT, and AST levels, along with increased HBsAg and HBeAg titers. Notably, younger age was identified as an independent risk factor for GIB during follow-up, although overall survival was better in younger patients. However, after PSM, survival differences between the two groups were no longer statistically significant. Furthermore, a prognostic model incorporating age, ALB, and ALP levels demonstrated clinical value.

The etiology of cirrhosis has undergone significant changes in recent years, with a notable decline in hepatitis B incidence due to widespread neonatal vaccination efforts.[17] Conversely, non-alcoholic fatty liver disease, obesity, and metabolic syndrome are becoming increasingly important global contributors to cirrhosis. Our findings align with previous studies,[18] confirming that chronic hepatitis B remains the predominant cause of cirrhosis in both young and older age groups. Additionally, the prevalence of metabolic diseases was found to be higher among the younger cohort. This increase may be genetically related, while autoimmune liver disease was significantly more prevalent in the elderly group, correlating with the typical onset age of autoimmune hepatitis in middle-aged women aged 40–60 years.[19]

Our study confirms significant differences in the clinical characteristics of young and elderly cirrhosis. The higher prevalence of gallstones in elderly patients also reflects impaired bile circulation, corroborating findings from previous studies.[20] In a healthy state, albumin is synthesized exclusively in the liver, and hypoalbuminemia is common in severe disease states. The serum albumin concentration is a well-established indicator of poor prognosis.[21] Our findings indicate that, at the time of diagnosis, albumin levels are higher in the young population, suggesting that their hepatic reserve

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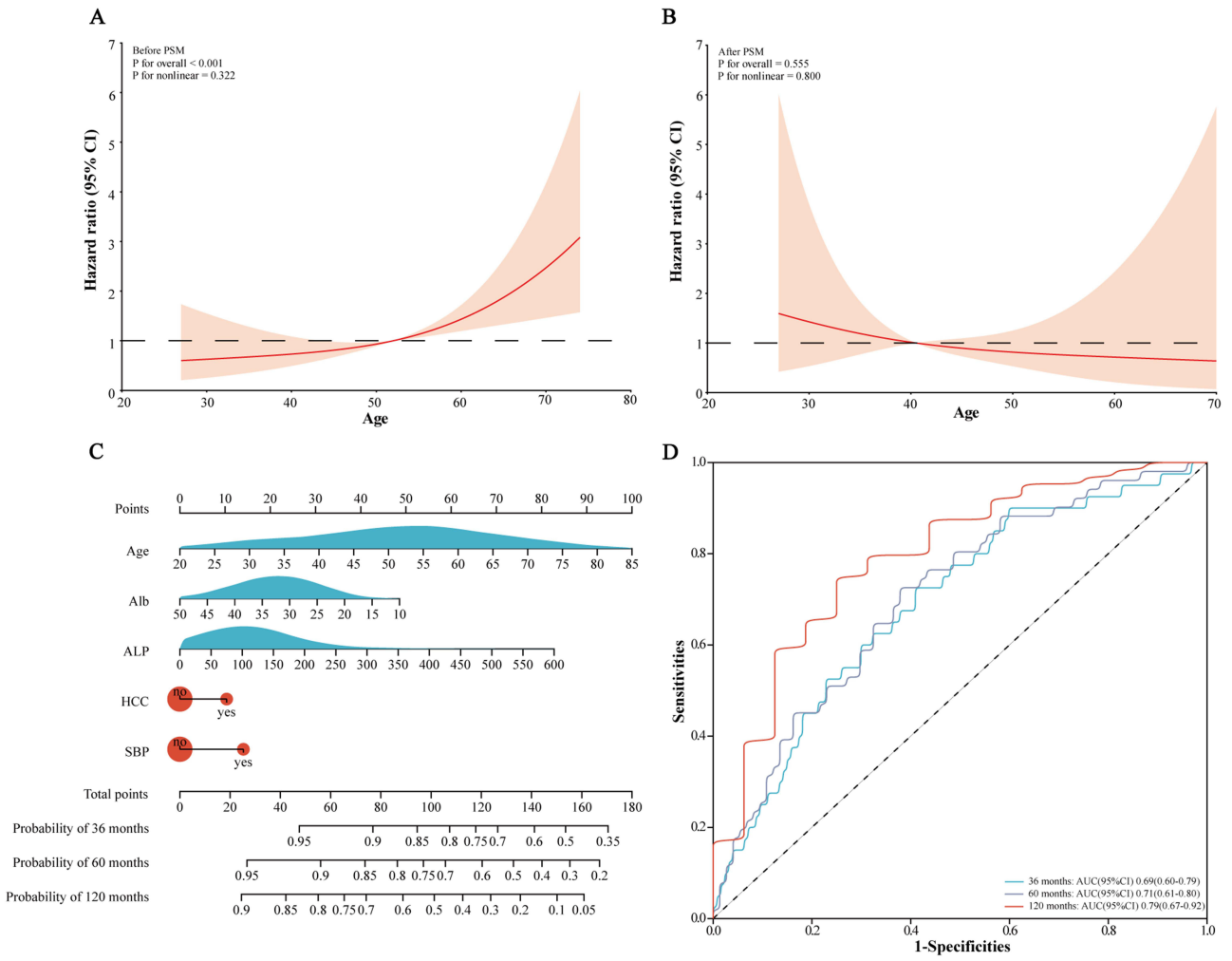

Figure 4 Development of a prognostic scoring model for HBV-related cirrhosis. Restricted cubic spline of the mortality with age in HBV-related cirrhosis before (**A**) and after PSM (**B**); Nomogram chart (**C**) and receiver operating characteristic curve (**D**) for prognostic prediction model based on Cox regression.
Abbreviations: PSM, Propensity score matching; Alb, Albumin; ALP, Alkaline Phosphatase; HCC, Hepatocellular carcinoma; SBP, Spontaneous peritonitis; AUC, Area under the ROC curve.

function is better. This may be attributed to the presence of multiple underlying diseases in the elderly population, which often results in diminished physical function and increased serum albumin depletion.

Chronic hepatitis B is a dynamic infection, with patient age closely linked to the impairment of HBV-specific T cells.[22] The natural history of early chronic HBV infection is divided into four stages based on the virus-host interaction. After 20 to 30 years of persistent infection, patients may enter the immune clearance phase, during which hepatocyte damage occurs, leading to elevated serum transaminase levels.[23,24] In elderly patients, however, HBV replication is less active, indicating that cirrhosis can develop at different stages of chronic hepatitis B.

Cirrhosis complications significantly affect quality of life and prognosis, as reported in previous studies.[3,25] GIB is the most common complication and a major cause of death during follow-up. Young age is an independent risk factor for GIB. Younger individuals tend to experience faster progression of portal hypertension due to better liver regeneration and metabolic capacity, and higher hormone levels may affect vascular function.[26,27] In this study, young patients showed a higher 5-year survival rate than adults before PSM, likely due to better overall condition and liver reserve. This is consistent with our prognostic model, where Alb and ALP were key factors. Young patients also had a higher likelihood of receiving aggressive treatment for gastrointestinal bleeding, while older patients were more prone to HCC, associated with poorer outcomes.

This study showed no significant difference in overall survival between young and elderly cirrhotic patients after PSM. This contrasts with the findings of Keating et al[5] who reported a 5-year overall survival rate of 70% in

Table 2 Comparison of Clinical Characteristics Between the Survival and Mortality Groups in HBV-Related Cirrhosis

Variables	Before Propensity Score Matching			After Propensity Score Matching (1:1)		
	Survival Group	Death Group	*P* value	Survival Group	Death Group	*P* value
Age, years	50.52 ± 12.69	56.46 ± 12.28	<0.001	44.55 ± 13.04	41.57 ± 13.04	0.419
Sex, male, n(%)	238 (79.87)	53 (77.94)	0.722	113 (86.92)	13 (92.86)	0.832
PLT (*10^9/L)	89.82 ± 69.53	85.75 ± 66.34	0.663	92.75 ± 72.37	70.57 ± 37.62	0.261
ALB (g/L)	33.00 ± 6.85	30.58 ± 6.58	<0.01	33.61 ± 6.87	32.98 ± 8.31	0.748
ALT, IQR (U/L)	38.00 (23.00, 73.00)	35.00 (19.00, 53.00)	0.09	42.00 (24.00, 86.50)	34.50 (23.00, 53.50)	0.491
AST, IQR (U/L)	43.00 (29.00, 81.00)	48.50 (29.00, 73.25)	0.915	44.00 (30.25, 105.25)	47.00 (26.25, 70.75)	0.688
TBIL, IQR (μmol/L)	21.20 (14.40, 33.70)	25.25 (16.20, 51.30)	0.100	24.20 (17.15, 45.00)	25.25 (16.75, 62.00)	0.793
ALP (U/L)	111.87 ± 66.54	140.43 ± 74.30	<0.01	105.53 ± 54.33	140.05 ± 109.02	0.281
GGT, IQR (U/L)	50.00 (26.00, 98.25)	58.00 (29.25, 128.75)	0.343	57.00 (28.75, 98.75)	32.00 (22.00, 125.00)	0.700
Glu (mmol/L)	6.05 ± 4.45	5.42 ± 1.72	0.281	5.58 ± 1.94	5.12 ± 1.27	0.385
PTA (%)	67.39 ± 16.98	63.73 ± 21.34	0.213	64.52 ± 16.05	59.90 ± 26.34	0.530
AFP, IQR (ng/mL)	3.96 (1.89, 24.91)	4.60 (2.27, 48.53)	0.214	4.30 (1.68, 65.80)	6.06 (4.11, 65.00)	0.383
HBV-DNA (×10^4)	0.098 (0.05, 40.67)	0.076 (0.05, 1.29)	0.261	0.10 (0.05, 59.25)	0.10 (0.05, 1.68)	0.798
HBsAg (IU/mL)	983.66 (82.60, 2507.91)	533.22 (49.43, 1670.79)	0.121	1320.67 (118.91, 2690.12)	1098.20 (541.43, 2087.54)	0.867
HBeAg (S/CO)	0.40 (0.15, 1.57)	0.11 (0.00, 0.40)	<0.01	0.53 (0.37, 46.47)	0.27 (0.09, 0.42)	0.012
HBeAb (S/CO)	0.11 (0.01, 1.50)	0.12 (0.01, 1.29)	0.632	0.51 (0.02, 2.96)	0.29 (0.04, 1.88)	0.733
HBcAb (S/CO)	9.01 (7.68, 10.27)	8.27 (0.01, 9.59)	0.010	8.94 (7.67, 10.09)	3.29 (0.01, 9.27)	0.060
GIB, n(%)	124 (41.61)	25 (36.76)	0.463	66 (50.77)	9 (64.29)	0.336
HE, n(%)	15 (5.03)	6 (8.82)	0.366	9 (6.92)	2 (14.29)	0.648
HCC, n(%)	76 (25.50)	25 (36.76)	0.061	35 (26.92)	4 (28.57)	0.895
SBP, n(%)	20 (6.71)	11 (16.18)	0.010	14 (10.77)	5 (35.71)	0.027

Abbreviations: PLT, Platelet; ALB, Albumin; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, Total Bilirubin; ALP, Alkaline Phosphatase; GGT, γ-Glutamyltranspeptidase; Glu, Glucose; PTA, Prothrombin Activity Percentage; AFP, Alpha-Fetal Protein; IQR, Interquartile range; GIB, Gastrointestinal bleeding; HE, Hepatic encephalopathy; HCC, Hepatocellular carcinoma; SBP, Spontaneous peritonitis.

Table 3 Cox Proportional Hazards Analysis Predicting the Mortality

Variables	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	*P* value	aHR (95% CI)	*P* value
Age	1.04 (1.02–1.06)	<0.001	1.04 (1.02–1.06)	0.001
ALB	0.96 (0.93–0.99)	0.029	0.97 (0.93–1.01)	0.133
ALT	1.01 (1.00–1.01)	0.783		
ALP	1.01 (1.01–1.01)	0.002	1.01 (1.01–1.01)	0.011
HBeAg	1.00 (0.99–1.01)	0.891		
HBcAb	0.99 (0.92–1.06)	0.691		
HCC	1.70 (1.03–2.79)	0.037	1.29 (0.77–2.18)	0.332
SBP	1.74 (0.91–3.31)	0.091	1.41 (0.70–2.85)	0.335

Abbreviations: ALB, Albumin; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; HCC, Hepatocellular carcinoma; SBP, Spontaneous peritonitis; HR, Hazard ratio.

young cirrhotic patients, which was significantly higher than in elderly patients. The discrepancy in results may primarily stem from differences in the study populations and control groups. Keating et al used data from a previous study comparing adult cirrhotic patients, while our study focused on elderly cirrhotic patients admitted during the same period. Furthermore, our study specifically targeted HBV-related cirrhosis patients, unlike studies that included all types of cirrhosis, which may limit comparability. Additionally, Lammers et al[28] found higher ALP levels were linked to worse prognosis in autoimmune cirrhosis, emphasizing the importance of ALP

measurements. Elevated ALP can indicate biliary obstruction or liver tumors and is associated with conditions like hepatitis and alcohol abuse.[29] In cirrhosis, ongoing hepatic injury contributes to elevated ALP levels, which reflect cholestasis, fibrosis progression, and impaired liver function, thereby influencing prognosis.[30,31] Further studies are needed to clarify the dynamic changes of ALP during disease progression.

This study focuses on the relatively uncommon population of young patients with HBV-related cirrhosis and delineates their distinct clinical characteristics and unique prognostic features. Additionally, we constructed a prognostic model using nomogram diagrams, providing a valuable reference for clinical diagnosis and treatment strategies. However, there are some limitations. Firstly, being a retrospective design, it is susceptible to unforeseen confounders, such as variations in nutritional status and differences in antiviral medications. To mitigate this limitation, we meticulously reviewed medical records and identified potential confounding variables for correction, employing multivariate and propensity score matching analyses. Secondly, our study was restricted to evaluating patients with decompensated cirrhosis, which may limit the generalizability of our findings to those receiving outpatient treatment for compensated cirrhosis. Additionally, the small sample size may highlight individual patient risk profiles while undermining the representation of the group as a whole. Future studies on cirrhosis in younger populations should rely on prospectively collected multicenter cohorts to generate stronger evidence. Broader HBV-related cirrhosis populations are needed for external validation, and multicenter prospective research is essential for identifying additional risk factors and improving risk stratification in this understudied group.

Conclusion

This study shows that HBV is the main cause of young cirrhosis, young age was an independent risk factor for GIB, and factors like age, ALP, and ALB were predictive of prognosis. Despite better liver function, young cirrhosis did not have a significantly better survival rate than older, emphasizing the need for close monitoring, particularly for portal hypertension and GIB.

Abbreviations

HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; AFP, alpha-fetoprotein; ALP, alkaline phosphate; ALB, albumin; TB, total bilirubin; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; PTA, prothrombin activity; GGT, gamma-glutamyltransferase; IQR, interquartile range; HCV, hepatitis C virus; GIB, Gastrointestinal bleeding, HE, Hepatic encephalopathy, SBP, Spontaneous peritonitis; OR, odds ratio; CI, confidence interval; PSM, propensity score matching; RCS, restricted cubic splines.

Data Sharing Statement

The datasets generated or analyzed during this study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Approval for the research protocol was obtained from the Ethics Committee of Anhui Medical University (No. SL-YX2024-204). Informed consent was obtained in writing from each patient. Registry and the Registration: ChiCTR2500105110.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare.

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