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ORIGINAL RESEARCH

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Effect and safety analysis of Yiqi Yangxue Jiedu decoction combined with entecavir in the treatment of male patients with decompensated hepatitis B cirrhosis

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Abstract

Background: This study aimed to evaluate the efficacy and safety of Yiqi Yangxue Jiedu Decoction & Entecavir in male patients with decompensated hepatitis B cirrhosis. **Methods**: A retrospective analysis was conducted using clinical data from 195 male patients with decompensated hepatitis B cirrhosis treated at our hospital between February 2022 and February 2024. Based on treatment regimens, the patients were divided into the observation group (100 cases), treated with Yiqi Yangxue Jiedu Decoction and Entecavir, the control group (95 cases), treated with Entecavir. Both groups received standard Western medicine treatment. The clinical efficacy and safety of the treatments were compared. **Results**: The total effective rate in the observation group was significantly higher ($p < 0.05$). Among the observation group, patients with moderate liver cirrhosis exhibited a significantly higher total effective rate than those with severe liver cirrhosis, patients with low viral load demonstrated a significantly higher total effective rate than high viral load ($p < 0.05$). Post-treatment, the observation group showed significantly reduced alanine aminotransferase (ALT), total bilirubin (TBIL) levels and increased albumin (ALB) levels than the control group ($p < 0.05$). The observation group had significantly lower levels of type III procollagen (PC III), type IV collagen (IV-C), laminin (LN) and hyaluronic acid (HA) ($p < 0.05$), shorter prothrombin time (PT), higher prothrombin activity (PTA) post-treatment than control group ($p < 0.05$), while the incidence of adverse reactions was comparable of two groups ($p < 0.05$). After six months of follow-up, the observation group exhibited a significantly lower incidence of delayed adverse events ($p < 0.05$). **Conclusions**: The combination of Yiqi Yangxue Jiedu Decoction and Entecavir significantly improves treatment efficacy, enhances liver function recovery, reduces liver fibrosis in male patients with decompensated hepatitis B cirrhosis. The regimen also demonstrated good safety, supporting its potential for broader clinical application.

Keywords

Yiqi Yangxue Jiedu decoction; Entecavir; Decompensated hepatitis B cirrhosis

1. Introduction

Hepatitis B virus (HBV) infection is the primary cause of chronic hepatitis B (CHB), a significant global public health burden [1], and is characterized by liver tissue inflammation, necrosis and fibrosis induced by viral replication [2]. Among untreated chronic HBV carriers, approximately 15%–40% progress to cirrhosis or hepatocellular carcinoma (HCC) [3]. The World Health Organization (WHO) estimated that, in 2019, the global prevalence of hepatitis B surface antigen (HBsAg) was 3.8%, with 296 million individuals chronically infected and nearly 820,000 deaths attributed to HBV-related diseases [4].

Persistent inflammatory damage to the liver often advances to cirrhosis. When the liver's compensatory capacity is exceeded, the condition progresses to the decompensated stage, which is associated with severe complications, including ascites, septicemia, pleural effusion, jaundice, hepatic encephalopathy and multi-organ involvement [5, 6]. In advanced cases, these complications can become life-threatening, and the primary clinical treatment goals are to improve liver function, alleviate symptoms and delay disease progression, which may ultimately improve patient survival and quality of life [7]. Entecavir is widely used in clinical practice for treating hepatitis B as it inhibits HBV polymerase activity, blocks viral DNA replication and exerts a potent antiviral effect [8]. However, the progressive nature of liver cirrhosis often limits the effectiveness of monotherapy with Western antiviral drugs, leading to the frequent adoption of combination therapies in clinical

practice. From the perspective of Traditional Chinese Medicine (TCM), decompensated hepatitis B cirrhosis falls under the categories of "distension" and "hypochondriac pain" as they are believed to result from Qi stagnation, blood stasis and phlegm-dampness. In the field of TCM, it is hypothesized that internal stagnation of damp-heat and mixed turbidity obstructs the flow of Qi and blood, and therefore, the treatment focuses on soothing the liver, regulating Qi, activating blood circulation, resolving phlegm and eliminating dampness [9]. Although Western medicine provides effective management for decompensated cirrhosis, it often falls short in achieving complete recovery, while TCM has shown promising potential in improving clinical outcomes for this condition.

The prevalence of hepatitis B and cirrhosis is generally higher in males compared to females, which facilitates the availability of a larger sample size of male patients for analysis. Furthermore, physiological, hormonal and immune differences between sexes can influence disease progression and treatment outcomes [10]. By focusing on male patients, this study minimizes potential confounding factors related to gender for more consistent and comparable results, as hormonal variations associated with female physiological cycles, pregnancy and menopause can affect liver function and drug metabolism; therefore, excluding these variables enhances the study's validity [11]. Based on this rationale, we selected 195 male patients with decompensated hepatitis B cirrhosis to evaluate the clinical efficacy and safety of Yiqi Yangxue Jiedu Decoction combined with Entecavir to provide additional evidence for clinical practice.

2. Materials and methods

2.1 General data

This retrospective study analyzed the clinical data of 195 male patients with decompensated hepatitis B cirrhosis who were treated at our hospital between February 2022 and February 2024. The patients were divided into two groups based on recorded treatment regimens: the observation group (100 cases) and the control group (95 cases). The general characteristics of the two groups are presented in Table 1, and the statistical analysis revealed no significant differences between the groups ($p > 0.05$), indicating that the groups were comparable. This study was approved by the hospital's ethics committee (Approval no. 2024-008).

The study inclusion criteria comprised of patients (1) diagnosed with decompensated cirrhosis secondary to CHB, meeting the diagnostic criteria [12] and confirmed by B-ultrasound and CT examination, (2) aged 18 to 75 years, and (3) had HBV DNA >20 IU/mL.

The exclusion criteria included: (1) allergy to the drugs used in this study, (2) presence of heart or kidney failure, (3) diagnosis of other types of hepatitis, such as hepatitis C, (4) presence of other infectious diseases, (5) malignant tumors, and (6) severe mental illness or consciousness disorders.

2.2 Treatment methods

As this was a retrospective study, the treatment methods were documented in existing case files. Both groups received conventional Western medical treatment, which included symptomatic care as follows: (1) Liver protection and enzyme reduction: Patients were administered Vitamin E, reduced glutathione, compound glycyrrhizin S, and magnesium isoglycyrrhizinate, depending on the severity of liver dysfunction; (2) Intrahepatic cholestasis: Ademetionine disulfate was prescribed to promote bile flow and alleviate jaundice; (3) Ascites: Furosemide and spironolactone were administered orally. When necessary, abdominal puncture for ascites drainage was performed, with a maximum drainage of 5000 mL of fluid; and (4) Hypoalbuminemia: Intravenous albumin infusion was provided.

In addition, the control group received antiviral therapy with Entecavir. Entecavir dispersible tablets (Shandong Lukang Pharmaceutical Co. Ltd., Jining, China, H20130062) were administered orally at a dose of 0.5 mg once daily, either on an empty stomach or 2 hours before or after meals, for a duration of one year.

The observation group received the same treatment as the control group, with the addition of a self-formulated Yiqi Yangxue Jiedu Decoction. The decoction was composed of a base prescription and symptom-specific modifications. The base prescription included the following herbs: 30 g of Raw Astragalus (Sheng Huangqi); 20 g each of Hedyotis diffusa (Baihua Sheshecao), Scutellaria barbata (Ban Zhilian) and Alisma orientalis (Ze Xie); 15 g each of Angelica sinensis (Dang Gui), Paeoniae Radix Rubra (Chi Shao), Chicken Gizzard Membrane (Ji Neijin), Vinegar Turtle Shell (Cu Bie Jia) and Salvia miltiorrhiza (Dan Shen); 10 g each of Radix Curcumae (Yu Jin), Atractylodes macrocephala (Bai Zhu), Eupatorium (Ze Lan), Curcuma longa (Jiang Huang), Scutellaria baicalensis (Huang Qin), Bupleurum chinense (Chai Hu) and Smilax glabra (Tu Fuling); and 5 g of Licorice (Gan Cao).

Symptom-specific modifications were added as needed, based on the presentation of specific symptoms: (1) For abdominal distention and urgency, 12 g each of Magnolia officinalis and Dried Tangerine Peel were included. (2) For hypochondriac pain, 15 g each of Radix Curcumae and Cyperus rotundus were added. (3) For severe damp-heat conditions, 15 g each of Artemisia capillaris and Gardenia were incorporated. (4) For ascites, 12 g each of Plantago and Lysimachia were added. (5) For irritability and a bitter taste in the mouth, 10 g each of Pinellia and Dried Tangerine Peel were included. (6) For yellowing of the face and skin, 20 g of Artemisia capillaris was added. (7) For elevated transaminase levels, 20 g each of Polygonum cuspidatum and Herba Patriniae were included (8). For splenomegaly, 10 g of Pangolin scales were added. This formulation was tailored to address the individual symptoms and underlying conditions of the patients in the observation group. The decoction was prepared by boiling the herbs in water, concentrating the liquid to 200 mL, and dividing it into two doses for oral administration in the morning and evening, and the treatment was continued for one year.

A personalized medication plan was developed based on the patient's specific condition, as detailed below:

1. Adjustment of Dosage Based on Patient-Specific Conditions:

- Severity of Disease: The dosage was tailored to the

TABLE 1. Comparison of general information between two groups.

Group	n	Age (yr)	Disease duration (yr)	Child-Pugh classification (B/C)
Observation group	100	48.37 ± 3.56	5.37 ± 1.10	70/30
Control group	95	48.25 ± 3.67	5.45 ± 1.21	68/27
t	-	0.231	0.490	0.059
p	-	0.817	0.625	0.809
Group	n	Body mass index (BMI) (kg/m^2)	HBeAg status (positive/negative)	HBsAg status (positive/negative)
Observation group	100	22.59 ± 1.42	(63/37)	(72/28)
Control group	95	22.39 ± 1.37	(60/35)	(65/30)
t	-	1.044	0.001	0.299
p	-	0.298	0.982	0.585

HBsAg: hepatitis B surface antigen; HBeAg: Hepatitis B e antigen; B/C: Class B/Class C.

degree of liver dysfunction, cirrhosis stage (*e.g.*, Child-Pugh classification) and the presence of complications. For patients in the decompensated stage, higher doses of Qi- and blood-tonifying herbs were prescribed.

• Symptom Presentation: Adjustments were made according to specific symptoms, such as fatigue, poor appetite, jaundice or ascites. For patients with significant Qi and blood deficiency, the quantities of Raw Astragalus and Angelica Sinensis were increased.

2. Consideration of Patient Constitution:

• Constitution Classification: TCM identifies various constitutions (*e.g.*, Qi deficiency, blood deficiency, Yin deficiency and Yang deficiency). Dosages of specific herbs were modified accordingly, such as increasing Raw Astragalus for Qi deficiency or adding Angelica Sinensis and Paeoniae Radix Rubra for blood deficiency.

• Age and Gender: These were considered in dose adjustments, with elderly male patients often requiring more cautious modifications to minimize potential adverse effects.

3. Monitoring Therapeutic Effects and Adverse Reactions:

• Therapeutic Assessment: Liver function indicators (*e.g.*, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin) and clinical symptoms were regularly monitored, allowing for dynamic adjustments to the medication dosage as necessary.

• Adverse Reaction Monitoring: Patients were closely observed for any adverse reactions, such as allergic responses or indigestion. If such reactions occurred, the dosage was adjusted or the formula was modified accordingly.

4. Combination with Western Medical Treatments:

• Drug Interactions: Since both groups received Entecavir, potential interactions between Chinese and Western medicines were carefully evaluated. The decoction dosage was adjusted to prevent adverse interactions.

• Treatment Coordination: Coordination between Chinese and Western treatments was prioritized to enhance the overall therapeutic efficacy and minimize side effects.

5. Patient Feedback and Involvement:

• Patient Education: The patients were informed about the treatment plan, including its purpose and expected outcomes. Active feedback on their experiences and symptom changes was encouraged to facilitate timely adjustments.

• Personalized Guidance: Detailed instructions on medication usage, including timing, administration methods and dietary considerations, were provided to improve adherence to the treatment regimen.

6. Clinical Research and Data:

• Database: Patient data related to the decoction's efficacy and safety, considering variations in doses and constitutions, were systematically collected to support the creation of future personalized treatment protocols.

• Continuous Improvement: Based on clinical observations and research findings, the treatment plan was continuously refined, with further exploration of rational dose-response relationships to optimize patient outcomes.

Standardizing the herbal decoction preparation and quality control process to ensure efficacy and safety:

1. Selection and Source of Raw Materials

• Herb Selection: All herbs were purchased from certified and legally compliant Chinese medicine suppliers, with valid quality inspection reports and production licenses.

• Confirmation of Herb Varieties: The species, origin and medicinal parts of the herbs, such as Hedyotis diffusa, Scutellaria barbata, Alisma orientalis, Angelica sinensis, Paeoniae Radix Rubra, chicken gizzard membrane, vinegar turtle shell and Salvia miltiorrhiza, were verified to comply with pharmacopoeial standards.

2. Herb Identification

• Appearance and Physical Property Identification: Initial assessments were performed by observing the color, odor, texture and other physical properties of the herbs to ensure they meet established quality standards.

• Microscopic Identification and Chemical Composition Testing: Microscopic analysis was conducted to examine the sliced structure of the herbs, and high-performance liquid chromatography (HPLC) was used to evaluate the content of active ingredients, ensuring compliance with pharmacopoeial requirements.

3. Standardized Decoction Preparation Process

• Herb Proportions: The formula comprised 30 g of raw

Astragalus (Sheng Huangqi), 20 g each of Hedyotis diffusa (Baihua Sheshecao), Scutellaria barbata (Ban Zhilian), and Alisma orientalis (Ze Xie), along with other prescribed herbs.

• Decoction Method: The herbs were placed in a decoction vessel with a measured amount of water, heated to boiling, and then simmered at a controlled temperature until the liquid volume was reduced to 200 mL.

• Boiling Time: Each batch of herbs was decocted once, and the resulting liquid was administered twice daily (morning and evening) for continuous treatment over one year.

4. Finished Product Quality Control

• Appearance and Odor Check: After preparation, the color, clarity and odor of the decoction were inspected to ensure compliance with quality standards.

• Active Ingredient Analysis: The content of active ingredients, such as Astragalus polysaccharides and Salvia miltiorrhiza components, was analyzed to verify that they fall within the therapeutic range.

• Microbial Testing: Microbiological evaluations confirmed the absence of harmful bacteria and fungi, ensuring compliance with pharmaceutical hygiene standards.

5. Storage and Transportation

• Storage Conditions: The decoction was stored in a cool, dry, and dark environment to prevent degradation of its active ingredients.

• Transportation Standards: Transportation was conducted under conditions minimizing exposure to heat and humidity to preserve the decoction's quality.

6. Documentation and Record Keeping

• Standard Operating Procedures (SOP): Comprehensive SOPs were developed, and personnel involved in the preparation process were trained to strictly adhere to standardized protocols.

• Record Management: The detailed records for each batch, including production, inspection, storage and transportation, were maintained for traceability and future review.

7. Clinical Validation

• Follow-up for Efficacy: In clinical settings, patient outcomes and adverse effects were regularly monitored to evaluate the efficacy and safety of the decoction.

• Feedback Mechanism: A robust feedback system was implemented to gather information on potential issues or adverse reactions reported by patients, facilitating necessary adjustments to the treatment process.

The monitoring of resistance and management protocol for antiviral therapy:

1. Monitoring Timepoints

• Baseline Testing: Before treatment initiation, HBV DNA levels and resistance-related gene mutations were measured in all patients.

• Regular Monitoring: HBV DNA testing was conducted every three months during treatment, focusing on detecting resistance mutations at six-month and twelve-month intervals.

• Symptom-Triggered Testing: If a patient had liver function deterioration or virological rebound, such as an increase in HBV DNA levels, resistance testing was promptly performed.

2. Detection Methods

• HBV DNA Quantification: Quantitative Polymerase Chain Reaction (qPCR) was performed to monitor HBV DNA levels periodically for an accurate assessment of viral load.

• Gene Mutation Analysis: Sequencing technologies, such as Sanger sequencing or next-generation sequencing, were utilized to detect resistance-related gene mutations, particularly in the polymerase (pol) gene, including L180M and M204V/I mutations.

3. Evaluation of Monitoring Results

• Virological Response: Changes in HBV DNA levels were assessed to evaluate the patient's virological response. An optimal response is indicated by a rapid decrease in HBV DNA, ideally reaching the lower detection limit after treatment initiation.

• Resistance Mutation Detection: If resistance mutations were identified, the need for adjustments to the antiviral regimen was evaluated by considering clinical symptoms and liver function.

4. Resistance Management

• Treatment Adjustment: When resistance mutations were detected, the treatment was switched to alternative antiviral medications, such as Lamivudine or Tenofovir or combination antiviral therapy to improve efficacy.

• Patient Education: The patients were informed about the risks and implications of antiviral resistance, emphasizing strict adherence to the prescribed treatment regimen to minimize resistance development.

5. Data Recording and Analysis

• Detailed Data Recording: Comprehensive records for HBV DNA levels, resistance testing results and changes in clinical symptoms were maintained for each patient to facilitate future analysis.

• Statistical Analysis: Upon study completion, statistical analyses were conducted to compare the incidence of resistance, virological responses and clinical efficacy between the observation and control groups.

Interventions for adverse events during six-month follow-up after treatment:

1. Regular Monitoring of Liver Function Abnormalities

• Liver Function Tests: Regular assessments of liver function, including ALT, AST and TBIL, were conducted to detect potential abnormalities.

• Treatment Plan Adjustments: If liver function was found to deteriorate, we evaluated the current antiviral drug regimen and considered the need for hepatoprotective medications.

• Lifestyle Interventions: Guidance was provided on lifestyle modifications, such as adopting a healthy diet, abstaining from alcohol and engaging in moderate exercise, to support liver recovery.

2. Imaging Tests for Liver Fibrosis Progression

• Regular Imaging Checks: Periodic liver ultrasounds and elastography were performed to monitor the extent of liver fibrosis.

• Symptom Screening: Patients were educated to recognize liver-related symptoms, such as abdominal pain and fatigue, and to seek medical attention if these occurred.

• Pharmacological Intervention: Based on imaging findings, anti-fibrosis medications, such as antioxidants or anti-inflammatory drugs, were considered when necessary.

3. Monitoring of Drug Side Effects

• Side Effect Monitoring: Liver and kidney function were regularly assessed to detect potential side effects of antiviral drugs.

• Patient Education: They were informed about possible side effects and encouraged to report any discomfort promptly.

• Medication Adjustments: If serious side effects were identified, the treatment plan was reevaluated and medications were modified or switched as needed.

4. Onset of Comorbidities

• Early Screening: Regular screening for complications such as ascites and esophageal varices was performed using diagnostic tools like endoscopy.

• Preventive Measures: High-risk patients were provided with preventive treatments, such as diuretics for ascites or beta-adrenergic antagonists for esophageal varices.

• Education and Support: The patients and their families were educated about potential comorbidities and encouraged to adopt self-management strategies.

5. Virus Mutation and Drug Resistance

• Virus Monitoring: HBV DNA levels were regularly monitored to assess the effectiveness of antiviral therapy.

• Resistance Assessment: If viral load increases were detected, genetic sequencing was performed to identify potential resistance mutations.

• Treatment Adjustments: When resistance mutations were identified, alternative antiviral medications with demonstrated efficacy were considered.

6. Increased Infection Risk

• Infection Monitoring: Complete blood count, liver function and kidney function were regularly assessed to detect signs of infection.

• Vaccination: The patients were vaccinated against common infections, including influenza and pneumonia, to reduce the risk of secondary infections.

• Health Education: The patients were advised to maintain proper hygiene, avoid infection risks and ensure a healthy living environment.

7. Mental Health Issues

• Psychological Assessment: The psychological state of patients was regularly evaluated to identify symptoms of anxiety or depression.

• Psychological Support: Counseling services were provided, and referrals to professional psychologists were made when necessary.

• Support Groups: The patients were encouraged to participate in support groups to share experiences, alleviate psychological burdens and improve emotional well-being.

2.3 Observational indicators

As a retrospective study, all outcome indicators were derived from existing case files.

(1) Clinical Effectiveness: The treatment effect was evaluated based on clinical symptoms, Child-Pugh score, imaging results, laboratory test results, and the "General expert consensus on application of network pharmacology in research and development of new traditional Chinese medicine drugs" [13]. A treatment outcome was considered significantly effective if, after one year of treatment, the major symptoms and ascites disappeared, liver and spleen enlargement stabilized, liver function returned to normal, the Child-Pugh score decreased to 5–6 points and the TCM symptom score decreased by more than 90%. Comparatively, a treatment outcome was classified as effective if the major symptoms improved, ascites decreased by more than 50% but did not completely resolve, liver function improved but did not fully normalize, the Child-Pugh score decreased but did not reach 5–6 points, and the TCM symptom score decreased by 40%–90%. A treatment outcome was deemed ineffective if the above criteria were not met, and the TCM symptom score decreased by less than 40%. The total effective rate was calculated using the following formula:

Total effective rate = [(Number of Significantly effective + effective cases)/Total number of cases] × 100%.

(2) Liver Function Indicators: Peripheral blood samples (5 mL) were collected from patients in both groups before and after treatment. The supernatant was analyzed using a Toshiba TBA-40FR automatic biochemical analyzer to measure levels of alanine aminotransferase (ALT), total bilirubin (TBIL) and albumin (ALB).

(3) Liver Fibrosis Indicators: Peripheral blood (5 mL) was collected from both groups of patients before and after treatment, and the levels of type III procollagen (PC III), type IV collagen (IV-C), laminin (LN) and hyaluronic acid (HA) were measured using radioimmunoassay.

(4) Coagulation Function Indicators: The PT (Prothrombin Time) and PTA (Prothrombin Activity) between the two groups were compared.

• Prothrombin Time (PT): Venous blood was collected in purple or blue vacuum tubes (without anticoagulant) and gently inverted for mixing. After centrifugation (3000 RPM for 5–10 minutes), the plasma was carefully separated. The plasma was mixed with reagents containing coagulation factors (*e.g.*, prothrombin, factors V, VII and X), and calcium ions were added to reactivate coagulation. The time taken from calcium addition to clot formation was recorded in seconds, with a normal range of 11–15 seconds.

• PTA: This was calculated based on the PT result and is typically expressed as a percentage:

PTA (%) = (Normal PT/Patient PT) × 100%

(5) Adverse Reactions: The occurrence of adverse reactions, including dizziness, fatigue, nausea and insomnia during treatment, was monitored and recorded for both groups.

(6) Delayed Adverse Events During Follow-Up: Statistical analysis was performed to evaluate potential delayed adverse events during the six-month follow-up period. These included liver function abnormalities, such as the progression of liver fibrosis or deterioration of liver function. Drug side effects were also assessed, including incidences of liver and kidney dysfunction, allergic reactions or digestive system discomfort. Complications, such as the development of ascites, esophageal variceal bleeding or hepatic encephalopathy, were monitored. The occurrence of bacterial or other types of infections was recorded. Additionally, psychological health concerns, including anxiety and depression, were evaluated.

2.4 Statistical methods

Statistical analysis was conducted using SPSS 22.0 software (IBM, Armonk, NY, USA). Normally distributed continuous data were presented as mean ± standard deviation ($\bar{x} \pm s$). Comparisons between groups for these data were performed using independent sample *t*-tests. Count data were expressed as percentages (%), and between-group comparisons were conducted using the chi-square test. A value of $p < 0.05$ was considered to indicate statistical significance.

3. Results

3.1 Treatment effects

After treatment, the total effective rate in the observation group was significantly higher than the control group ($p < 0.05$, Table 2). In the observation group, patients with moderate liver cirrhosis had a significantly higher total effective rate compared to those with severe liver cirrhosis ($p < 0.05$, Table 3). Additionally, the total effective rate was significantly higher in the low viral load subgroup compared to the high viral load subgroup ($p < 0.05$, Table 4).

3.2 Liver function indicators

After treatment, both groups exhibited significantly reduced levels of ALT and TBIL, along with significantly increased levels of ALB, compared to their baseline values. Additionally, post-treatment levels of ALT and TBIL in the observation group were significantly lower than those in the control group, while the ALB level in the observation group was significantly higher than in the control group ($p < 0.05$, Table 5).

3.3 Liver fibrosis indicators

After treatment, both groups exhibited significantly reduced levels of PC III, IV-C, LN and HA compared to their baseline values, but the levels of PC III, IV-C, LN and HA in the observation group were significantly lower than those in the control group after treatment ($p < 0.05$, Table 6).

3.4 Coagulation function indicators

After treatment, the observation group had shorter PT and higher PTA than the control group ($p < 0.05$, Table 7).

3.5 Adverse reactions

We observed no significant difference in the incidence of adverse reactions between the two groups ($p > 0.05$, Table 8).

3.6 Follow-up

After six months of follow-up, the incidence of potential delayed adverse events in the observation group was significantly lower than that in the control group (Table 9, $p < 0.05$).

4. Discussion

In recent years, the incidence of hepatitis B has been increasing annually, with approximately 8%–20% of hepatitis B patients progressing to cirrhosis [14]. Hepatitis B cirrhosis arises from diffuse parenchymal lesions caused by chronic HBV infection, leading to excessive deposition of liver fibrosis. In its advanced stages, the condition is often associated with severe complications, posing significant risks to patients' lives and overall health [15, 16]. Epidemiologi-

TABLE 2. Comparison of therapeutic effects of two groups (n (%)).

Group	n	Significantly effective	Effective	Ineffective	Total effective rate
Observation group	100	50 (50.00)	46 (46.00)	4 (4.00)	96 (96.00)
Control group	95	35 (36.84)	40 (42.11)	20 (21.05)	75 (78.95)
χ^2					13.613
p					0.001

TABLE 3. Comparison of therapeutic effects of different severity levels of liver cirrhosis in the observation group (n (%)).

Severity of liver cirrhosis	Significantly effective	Effective	Ineffective	Total effective rate
Moderate (70)	31 (44.29)	35 (50.00)	4 (5.71)	66 (94.29)
Severe (30)	12 (40.00)	12 (40.00)	6 (20.00)	24 (80.00)
χ^2				4.762
p				0.029

TABLE 4. Comparison of therapeutic effects of different viral loads in observation groups (n (%)).

Viral load	Significantly effective	Effective	Ineffective	Total effective rate
Low viral load (35)	20 (57.14)	15 (42.86)	0	35 (100.00)
High viral load (65)	23 (35.38)	32 (49.23)	10 (15.38)	55 (84.62)
χ^2				5.983
p				0.014

TABLE 5. Comparison of liver function indicators ($\bar{x} \pm s$).

Group	n	ALT (U/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	72.79 ± 10.34	32.34 ± 6.13	32.476	<0.001
Control group	95	73.86 ± 10.54	54.78 ± 7.63*	14.775	<0.001
t	-	0.715			
p	-	0.475			
Group	n	TBIL (μmol/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	50.13 ± 7.52	15.12 ± 3.82	41.294	<0.001
Control group	95	51.05 ± 6.96	24.37 ± 4.73*	29.754	<0.001
t	-	0.877			
p	-	0.381			
Group	n	ALB (g/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	30.13 ± 4.63	38.12 ± 5.62	10.251	<0.001
Control group	95	30.54 ± 4.51	33.45 ± 4.27*	4.561	<0.001
t	-	0.626			
p	-	0.532			

**Post-treatment comparison between the observation group and the control group, $p < 0.05$.*
ALT: alanine aminotransferase; TBIL: bilirubin; ALB: albumin.

TABLE 6. Comparison of liver fibrosis indicators ($\bar{x} \pm s$).

Group	n	PC III (μg/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	134.72 ± 17.83	105.43 ± 10.14	13.225	<0.001
Control group	95	135.03 ± 17.20	123.65 ± 14.23*	5.139	<0.001
t	-	0.123			
p	-	0.902			
Group	n	IV-C (μg/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	92.47 ± 8.26	55.63 ± 6.15	37.95	<0.001
Control group	95	93.35 ± 8.64	72. 35 ± 5.86*	18.939	<0.001
t	-	0.719			
p	-	0.473			
Group	n	LN (μg/mL)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	145.34 ± 6.13	92.85 ± 4.25	73.203	<0.001
Control group	95	146.62 ± 6.30	131.42 ± 5.93*	15.635	<0.001
t	-	1.427			
p	-	0.155			
Group	n	HA (mg/L)		*t*	*p*
		Before treatment	After treatment		
Observation group	100	135.76 ± 18.21	85.63 ± 10.34	26.161	<0.001
Control group	95	135.54 ± 19.05	110.34 ± 10.53*	11.225	<0.001
t	-	0.083			
p	-	0.934			

**Post-treatment comparison between the observation group and the control group, $p < 0.05$.*
PC III: type III procollagen; IV-C: type IV collagen; LN: laminin; HA: hyaluronic acid.

TABLE 7. Comparison of coagulation function indicators between two groups ($\bar{x} \pm s$).

Group	n	PT (s)		PTA (%)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	100	17.65 ± 1.34	13.45 ± 1.03	61.95 ± 15.78	78.93 ± 16.12
Control group	95	17.72 ± 1.63	15.20 ± 1.20	62.39 ± 16.02	73.86 ± 16.21
t	-	0.327	10.959	0.197	2.194
p	-	0.744	<0.001	0.844	0.029

PT: prothrombin time; PTA: prothrombin activity.

TABLE 8. Comparison of Adverse Reactions (n (%)).

Group	n	Dizziness	Fatigue	Nausea	Insomnia	Total
Observation group	100	1 (1.00)	1 (1.00)	0	0	2 (2.00)
Control group	95	1 (1.05)	1 (1.05)	0	2 (2.11)	4 (4.21)
χ^2	-					0.798
p	-					0.372

TABLE 9. Comparison of potential delayed adverse events (n (%)).

Group	n	Abnormal liver function	Progress of liver fibrosis	Drug side effects	Complications	Bacterial or other types of infections	Psychological health issues	Total
Observation group	100	1 (1.00)	0	1 (1.00)	2 (2.00)	0	1 (1.00)	5 (5.00)
Control group	95	3 (3.16)	3 (3.16)	2 (2.11)	4 (4.21)	2 (2.11)	4 (4.21)	18 (18.95)
χ^2	-							9.109
p	-							0.003

cal surveys in China indicate that 2%–5% of patients with compensated hepatitis B cirrhosis progress to decompensated cirrhosis each year, and decompensated cirrhosis represents a critical stage of liver damage, with a five-year clinical mortality rate ranging from 70%–86% [17]. The clinical manifestations of decompensated hepatitis B cirrhosis include ascites, hepatosplenomegaly, jaundice and upper gastrointestinal bleeding, which are often accompanied by symptoms such as insomnia, fatigue and gastrointestinal discomfort, all of which severely impair the patient's quality of life and pose an immediate threat to survival [18, 19].

Clinically, antiviral therapy is the primary treatment for patients in the decompensated phase, and it is often combined with symptomatic management to suppress HBV DNA replication, stabilize cirrhosis, protect liver function and prevent complications for extending survival and improving quality of life [20, 21]. However, antiviral therapy cannot completely eliminate HBV from the body and long-term, high-dose medication can lead to drug resistance. From the perspective of TCM, decompensated hepatitis B cirrhosis is categorized as "abdominal distention", "spider distention" or "accumulation of masses", and the treatment principles focus on reinforcing the body's Qi, dispelling pathogens, nourishing the blood, invigorating the liver and spleen, and resolving accumulations [22, 23].

The results of this study demonstrate that the total effective rate in the observation group was significantly higher than that in the control group. Within the observation group, patients with moderate liver cirrhosis and low viral loads exhibited a significantly higher total effective rate compared to those with severe liver cirrhosis and high viral loads. These findings indicate that combining Yiqi Yangxue Jiedu Decoction with Entecavir is more effective than Entecavir alone in treating decompensated hepatitis B cirrhosis. The enhanced efficacy may result from the complementary benefits of integrating traditional Chinese and Western medicine, as well as the hepatoprotective effects of herbs such as Scutellaria barbata and Hedyotis diffusa in the decoction. Entecavir, a guanosine nucleoside analogue, is a first-line drug for hepatitis B cirrhosis. It undergoes phosphorylation in the body to form triphosphates, which compete with deoxyguanosine triphosphate to inhibit polymerase activation, mRNA negative-strand reverse transcription and HBV DNA positive-strand synthesis. These mechanisms effectively inhibit HBV DNA replication, conferring antiviral effects [24]. However, since Entecavir may cause adverse effects on other organs, there is a need for combination therapies to mitigate side effects and improve patient outcomes. Yiqi Yangxue Jiedu Decoction has demonstrated significant efficacy in treating decompensated hepatitis B cirrhosis by reducing liver stiffness, shrinking the spleen and decreasing portal vein width, which collectively slows the progression of liver cirrhosis. These therapeutic effects

arise from the synergistic actions of its carefully selected ingredients. For example, Raw Astragalus enhances energy levels, improves physiological balance and promotes blood circulation, fluid metabolism and the reduction of dampness. Atractylodes macrocephala strengthens the spleen, supports energy production, and facilitates water metabolism while reducing dampness. Smilax glabra, Scutellaria baicalensis and Hedyotis diffusa work together to clear heat, reduce dampness, cool the blood, detoxify and protect the liver while promoting bile secretion. Salvia miltiorrhiza enhances blood circulation, disperses stasis and supports the unblocking of meridians. Similarly, Eupatorium and Alisma orientalis facilitate blood flow in the liver and spleen, expel heat, reduce dampness and invigorate circulation without compromising physiological balance. Angelica sinensis supports blood activation and nourishment, regulates Qi flow, and strengthens the body's defense mechanisms. Radix Curcumae alleviates stagnation, promotes circulation, and balances the interaction between Qi and blood. Paeoniae Radix Rubra contributes to clearing heat, cooling the blood, improving circulation and resolving stasis. Scutellaria barbata aids in detoxification and promotes diuresis, while Bupleurum chinense alleviates liver Qi stagnation and promotes harmony within the body. Ingredients such as chicken gizzard membrane and vinegar-treated turtle shell nourish Yin, soften hard masses, resolve stagnation, and improve digestion and blood flow. Finally, licorice harmonizes the actions of the formula's components and alleviates spasms. Taken together, the formula acts comprehensively to clear heat, expel dampness, protect the liver, strengthen the spleen, improve blood and Qi circulation, and resolve blood stasis, which contributes to its remarkable efficacy in managing decompensated hepatitis B cirrhosis. In this regard, a combination of Yiqi Yangxue Jiedu Decoction with Entecavir exhibits a synergistic effect and achieves superior therapeutic outcomes compared to Entecavir alone for treating decompensated hepatitis B cirrhosis.

Differences in disease severity and viral load have a significant impact on treatment efficacy. For instance, patients with moderate liver cirrhosis generally exhibit better liver function, which supports stronger regenerative and compensatory abilities and contributes to a more favorable response to treatment. In contrast, patients with severe cirrhosis experience extensive liver damage and functional failure, leading to a diminished response to medication and a reduced clinical efficacy of treatments. Viral load also plays an important role in treatment outcomes, as a low viral load reflects a reduced viral burden, which facilitates the immune system's capacity and enhances the efficacy of therapeutic agents in clearing the virus, which results in improved treatment outcomes. Conversely, patients with a high viral load often present with more active viral replication, which contributes to severe liver damage and reduced treatment effectiveness. Yiqi Yangxue Jiedu Decoction, a TCM formula, may further enhance treatment outcomes in patients with moderate cirrhosis and low viral load by improving the overall condition, boosting immunity, and promoting liver repair and regeneration. The regulatory role of TCM in improving systemic function and alleviating symptoms appears to be more pronounced in these patients. Furthermore, moderate cirrhosis patients are less likely to present with comorbidities, whereas severe cirrhosis is often accompanied by multiple complications such as hepatic encephalopathy, ascites and esophageal varices. These complications exacerbate the underlying condition and interfere with treatment efficacy, further emphasizing the challenges in managing patients with severe cirrhosis.

After treatment, the levels of ALT and TBIL in the observation group were significantly lower, while ALB levels were significantly higher compared to the control group, which indicates that the combination of TCM and Western medicine could be more effective in improving liver function in patients with decompensated liver cirrhosis caused by hepatitis B. These biomarkers provide essential insights into the extent of hepatocyte damage and the restoration of liver synthetic function. For instance, a decrease in ALT, a marker of hepatocyte injury, suggests reduced inflammation and improved liver cell recovery. Similarly, a reduction in TBIL reflects enhanced liver metabolic function, while an increase in ALB indicates the restoration of the liver's synthetic capacity. The therapeutic effects of Yiqi Yangxue Jiedu Decoction can be attributed to its various herbal components, which exhibit complementary mechanisms of action. Raw Astragalus and Angelica sinensis play a role in tonifying Qi and nourishing blood, which enhances immune function, improves hepatic blood flow, and delivers essential nutrients to facilitate hepatocyte repair. Herbs such as Hedyotis diffusa and Scutellaria barbata clear heat and possess detoxifying properties, which reduce viral load and alleviate liver inflammation. Additionally, the decoction supports liver recovery by modulating immune responses and reducing hepatic inflammation. Specific components, including Scutellaria baicalensis and Salvia miltiorrhiza, inhibit inflammatory mediators such as Interleukin 6 (IL-6) and Tumor Necrosis Factor-α (TNF-α), further mitigating liver inflammation. Furthermore, the herbal components promote hepatocyte regeneration and repair, which enhances liver synthetic function and improves liver function indicators. Entecavir, an antiviral drug, complements these actions by targeting HBV DNA synthesis. Its mechanisms include inhibiting HBV replication through competitive inhibition of HBV polymerase, which reduces viral replication, lowers viral load and alleviates the liver's viral burden. Additionally, Entecavir may modulate the immune response, potentially restoring immune surveillance against the virus. The combination of Yiqi Yangxue Jiedu Decoction and Entecavir provides synergistic therapeutic benefits. The Qi-tonifying effects of the decoction, combined with the antiviral properties of Entecavir, create a comprehensive treatment approach that not only inhibits viral activity but also improves the liver microenvironment. This combination enhances liver function, reduces markers of liver fibrosis, and promotes liver repair and recovery. Taken together, these results highlight the potential of integrating TCM and Western medicine to achieve superior therapeutic outcomes in patients with decompensated hepatitis B cirrhosis.

After treatment, the levels of PC III, IV-C, LN and HA were significantly lower in the observation group compared to the control group, indicating that the combined therapy is more effective in inhibiting the progression of liver fibrosis. Relevant studies suggest that the degree of liver fibrosis is closely correlated with the severity of decompensated liver

cirrhosis caused by hepatitis B [25]. These biomarkers are important indicators of liver fibrosis. For instance, a reduction in PC III and IV-C reflects an improvement in liver fibrosis, potentially attributable to the regulatory effects of Yiqi Yangxue Jiedu Decoction on liver repair and collagen synthesis [26]. Similarly, LN and HA, which typically increase during the progression of liver fibrosis [27], were reduced, suggesting that the combination therapy may inhibit hepatic stellate cell activation or regulate the liver microenvironment. The mechanism of action of Yiqi Yangxue Jiedu Decoction in addressing liver fibrosis involves several pathways. The anti-fibrotic effects of certain components, such as Salvia and Scutellaria, are mediated by their ability to inhibit hepatic stellate cell activation and collagen deposition, thereby alleviating liver fibrosis. Additionally, the components of the formula may modulate key signaling pathways, such as TGF-β and NF-κB, to influence liver inflammation and fibrosis progression. The pharmacological effects of the formula are derived from its diverse herbal composition. Raw Astragalus enhances immunity, alleviates liver burden, and protects liver function, promoting recovery [28]. Hedyotis diffusa and Scutellaria barbata possess heat-clearing and detoxifying properties, which help suppress HBV and reduce liver inflammation [29]. Alisma orientalis alleviates edema and ascites associated with cirrhosis [30]. Herbs such as Angelica sinensis, Paeoniae Radix Rubra, and Salvia miltiorrhiza improve blood circulation and promote liver regeneration [31]. Chicken gizzard membrane supports digestion and bile secretion, aiding liver function and metabolism. Vinegar-treated turtle shell helps alleviate liver cirrhosis and nodulation. Other components, including Radix Curcumae, Eupatorium, Atractylodes macrocephala, Scutellaria baicalensis, Curcuma longa, Bupleurum chinense, and Smilax glabra, clear heat, detoxify, reduce inflammation, and regulate blood circulation, thereby alleviating the symptoms of liver cirrhosis [32]. Licorice harmonizes the effects of the other herbs, enhancing their efficacy and ensuring the overall safety of the treatment [33]. Collectively, Yiqi Yangxue Jiedu Decoction significantly improves clinical symptoms, reduces liver inflammation, protects liver function and promotes liver repair. Entecavir complements this by inhibiting HBV DNA synthesis, reducing viral replication, lowering viral load, alleviating the viral burden on the liver and improving patient prognosis. Additionally, Entecavir enhances the immune response, potentially restoring immune surveillance against the virus. The synergistic effects of this combination of traditional Chinese and Western medicine improve immunity, reduce complications, and enhance the overall quality of life for patients with decompensated liver cirrhosis caused by hepatitis B.

This study demonstrates that, compared to entecavir monotherapy, the combination of Yiqi Yangxue Jiedu Decoction and entecavir significantly shortens PT and increases PTA. These effects may be attributed to the ability of Yiqi Yangxue Jiedu Decoction to improve hepatocyte function, which facilitates the liver's synthesis of coagulation factors and enhances overall coagulation function [34]. This observation aligns with findings by Wu X *et al*. [35], who highlighted the importance of a multi-drug combination strategy in the treatment of liver cirrhosis and demonstrated that entecavir-based combination therapy improves coagulation function. As a natural remedy, Yiqi Yangxue Jiedu Decoction is notable for its relatively low toxicity to the human body, making it a safe option for effectively regulating biological functions.

The incidence of adverse reactions was comparable between the two groups, indicating that Yiqi Yangxue Jiedu Decoction is safe for clinical use. In addition, the safety of this formula can be attributed to its mechanisms, which include promoting blood circulation, improving blood supply, reducing vascular inflammation and minimizing the risk of adverse effects. Moreover, as a traditional Chinese herbal formula, its components are inherently safe and are not associated with significant damage to multiple organs, which ensures a high safety profile, making it a suitable option for clinical practice.

During the six-month follow-up period, the incidence of delayed adverse reactions in the observation group was significantly lower than in the control group, and this could be due to several factors. First, the treatment protocols differed between the two groups. The observation group received combination therapy with Yiqi Yangxue Jiedu Decoction and entecavir, which appears to have contributed to improved outcomes. The components of Yiqi Yangxue Jiedu Decoction, known for tonifying Qi and blood, detoxifying and promoting bile secretion, may have enhanced overall patient health, strengthened resistance, and promoted the liver's self-repair capabilities, which likely reduced liver damage and slowed the progression of liver fibrosis. Second, the drugs' synergistic effects may have played a role. Entecavir, an antiviral agent, primarily inhibits the replication of HBV, and when combined with Yiqi Yangxue Jiedu Decoction, the therapy may enhance immune function and improve liver function, increasing the efficacy of antiviral treatment. This synergy likely reduced the risk of liver function deterioration and complications associated with persistent viral infection. Third, the safety profile of Yiqi Yangxue Jiedu Decoction likely contributed to the favorable outcomes. TCM, including this formula, is generally associated with fewer side effects and can be relatively safer to be used alongside Western medicines without significant drug interactions. This reduced the risk of adverse reactions such as liver and kidney damage or allergic responses in the observation group compared to the control group. Fourth, the treatment protocol in the observation group included comprehensive symptomatic management tailored to individual patient needs, which addressed complications such as ascites, cholestasis, and hypoalbuminemia. By alleviating symptoms and improving quality of life, this comprehensive care likely reduced the incidence of complications, including ascites and esophageal varices. Lastly, follow-up and monitoring likely contributed to the observed outcomes. Patients in the observation group may have received more detailed follow-up care, including regular assessments of liver function, viral load, and imaging studies. Thus, close monitoring enables the early detection of potential complications and facilitates timely interventions, further reducing the incidence of adverse reactions.

This study has several limitations that should be addressed. First, the sample size was relatively small, and patient baseline conditions were not sufficiently accounted for, which may limit the generalizability of the findings. Second, the single-

center design may restrict the applicability of the results to broader patient populations. Third, this study did not investigate the recurrence rate or associated risk factors, leaving gaps in understanding the long-term outcomes of the treatment. Fourth, the retrospective nature of the study introduces inherent limitations such as potential sample selection bias due to reliance on existing case data. In addition, retrospective designs can also be prone to confounding factors, as uncontrolled variables may influence the results and lead to misinterpretation of the relationship between exposure and outcomes. Moreover, the absence of randomization decreases internal validity, further limiting the robustness and generalizability of the findings. Lastly, the risk factors contributing to patient complications should be further analyzed to enhance clinical management strategies.

Future studies should include larger sample sizes and multicenter designs to ensure broader applicability and enhance the accuracy of the findings. A comprehensive investigation of risk factors for complications and recurrence is essential to improve the precision and depth of the results. Prospective cohort studies or randomized controlled trials (RCTs) should be conducted to overcome the inherent limitations of retrospective studies. These designs would help establish causal relationships, reduce bias, and provide more definitive evidence for the effectiveness of the combination therapy.

5. Conclusions

In conclusion, the combination of Yiqi Yangxue Jiedu Decoction and Entecavir significantly improves treatment outcomes by promoting liver function recovery and alleviating liver fibrosis. With its favorable safety profile, this combination therapy represents a promising approach for the management of decompensated hepatitis B cirrhosis. However, further clinical studies are warranted to confirm these findings and expand on understanding its therapeutic potential.

AVAILABILITY OF DATA AND MATERIALS

The author declares that all data supporting the findings of this study are available within the paper, and the raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

MLJ—designed and conducted the study; supervised data collection; analyzed and interpreted the data; prepared the manuscript for publication; and reviewed the manuscript draft. The author has read and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Fourth Affiliated Hospital of Harbin Medical University (Approval no. 2024-008). Written informed consent was obtained from a legally authorized representatives for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

[1] Jin Y, Wang S, Tang K, Zhan P, Liu X. Recent advances in screening methods enabling the discovery of novel anti-hepatitis B virus drug candidates. European Journal of Medicinal Chemistry. 2025; 282: 117093.

[2] Iannacone M, Guidotti LG. Immunobiology and pathogenesis of hepatitis B virus infection. Nature Reviews Immunology. 2022; 22: 19–32.

[3] McMahon BJ. Natural history of chronic hepatitis B. Clinics in Liver Disease. 2010; 14: 381–396.

[4] Shan S, Zhao X, Jia J. Comprehensive approach to controlling chronic hepatitis B in China. Clinical and Molecular Hepatology. 2024; 30: 135–143.

[5] Gülcicegi DE, Hannemann J, Bürger M, Allo G, Dittmann E, Martin A, *et al*. Spleen stiffness measurements during recompensation in patients with acutely decompensated liver cirrhosis: preliminary findings of a pilot study. Frontiers in medicine. 2024; 11: 1475997.

[6] Lan Y, Yu Y, Zhang X, Xu X, Yu X, Tu H, *et al*. Risk factors and prognostic impact of new decompensated events in hospitalized patients with decompensated cirrhosis. BMC Gastroenterology. 2024; 24: 408.

[7] Wang Z, Wang X, Zhou L, Shi S, Hua Y, Feng Y. Safety and efficacy of 48-week pegylated interferon-α-2b therapy in patients with hepatitis B virus-related compensated liver cirrhosis: a pilot observational study. Frontiers in Medicine. 2024; 11: 1489671.

[8] Wang H, Wu L. A comparison of the therapeutic efficacy of Tenofovir Disoproxil Fumarate and Entecavir in patients with chronic Hepatitis-B. Pakistan Journal of Medical Sciences. 2024; 40: 2390–2394.

[9] Tu A, Zhu X, Dastjerdi PZ, Yin Y, Peng M, Zheng D, *et al*. Evaluate the clinical efficacy of traditional Chinese Medicine as the neoadjuvant treatment in reducing the incidence of hepatocellular carcinoma in patients with hepatitis B-related cirrhosis: A systematic review and meta-analysis. Heliyon. 2024; 10: e24437.

[10] Eduku A, Dogbey VES. Seroprevalence of hepatitis B virus infection (HBsAg) and associated factors among antenatal clinic attendees in a secondary-level facility in southern Ghana. Clinical Epidemiology and Global Health. 2024; 26: 101553.

[11] Debsikréo N, Mankréo BL, Moukénet A, Ouangkake M, Mara N, Moussa AM, *et al*. Prevalence of hepatitis B virus infection and its associated factors among students in N'Djamena, Chad. PLOS ONE. 2024; 19: e0273589.

[12] Chinese Society of Hepatology of Chinese Medical Association. Chinese guidelines on the management of hepatic encephalopathy in cirrhosis (2024). Chinese Journal of Hepatology. 2024; 32: 799–812.

[13] Li S, Xiao W. General expert consensus on application of network pharmacology in research and development of new traditional Chinese medicine drugs. China Journal of Chinese Materia Medica. 2024; 49: 5055–5068. (In Chinese)

[14] Domínguez A, Avellón A, Hernando V, Soldevila N, Borràs E, Martínez A, *et al*. Hepatitis B virus-related cirrhosis and hepatocellular carcinoma hospital discharge rates from 2005 to 2021 in Spain: impact of universal vaccination. Vaccines. 2024; 12: 1254.

[15] Hong Y. Impact of nursing interventions based on self-efficacy theory on

HAMA and HAMD scores in patients with hepatitis B cirrhosis. Journal of Clinical and Nursing Research. 2024; 8: 129–134.

[16] Cai X, Peng S, Xiao X, Huang Z, Zhang P. Serum ApoB/ApoA1 ratio in patients with CHB and the occurrence of HBV related cirrhosis and HBV related hepatocellular carcinoma. Scientific Reports. 2024; 14: 10996.

[17] Amal Mohammed AM, El-Hennawy AY, Hassan EH, Mohamed B, Abdelraouf A, Abdelhaleem A, *et al*. Detection of H-Pylori in the explanted liver tissue and the enlarged perihepatic lymph nodes of cirrhotic patients with decompensated end-stage liver disease recruited for liver transplantation. Asian Pacific Journal of Cancer Prevention. 2025; 26: 181–187.

[18] Fan LY. Impact of ALT changes on the risk of HCC in hepatitis B—compensated cirrhotic patients with low viremia. The American Journal of Gastroenterology. 2023; 118: 1701.

[19] Wang Y, Sun Y, Zhang W, Yao Y, Bian Z, Qian X. Relieving effect of jiao-tune of 5-element music on negative emotions in patients with decompensated hepatitis B virus cirrhosis: a randomized and controlled experiment study. Medicine. 2024; 103: e39556.

[20] Deng Y, Zheng H, Xiang H, Nan Y, Hu J, Meng Q, *et al*. On-treatment factors predict recompensation in entecavir-treated hepatitis B patients with decompensated cirrhosis. Journal of Hepatology. 2023; 78: S243.

[21] Zhang X, Zheng D, He L, Li W, Zhou W, Pang Z, *et al*. A clinic study on long-term efficacy and safety of autologous peripheral blood stem cell transplantation in patients with decompensated hepatitis B cirrhosis. Alternative Therapies in Health and Medicine. 2024; 30: 160–166.

[22] Zheng S, Xue C, Li S, Zao X, Li X, Liu Q, *et al*. Liver cirrhosis: current status and treatment options using western or traditional Chinese medicine. Frontiers in Pharmacology. 2024; 15: 1381476.

[23] Wang X, Zeng X, Wang G. External treatment of refractory ascites induced by liver cirrhosis by traditional Chinese medicine. Asian Journal of Surgery. 2024; 47: 4429–4430.

[24] Ding R, Xie W, Jia J, Wang Q. FRI-114 Entecavir can significantly improve the prognosis of patients with first decompensated hepatitis B cirrhosis. Journal of Hepatology. 2024; 80: S228–S229.

[25] Li Y, Zhu Y, Gao D, Pan Y, Wang J, Zhang S, *et al*. HBeAg-positive CHB patients with indeterminate phase associated with a high risk of significant fibrosis. Virology Journal. 2024; 21: 287–287.

[26] Xu T, Lu Z, Xiao Z, Liu F, Chen Y, Wang Z, *et al*. Myofibroblast induces hepatocyte-to-ductal metaplasia via laminin-α$v\beta$6 integrin in liver fibrosis. Cell Death & Disease. 2020; 11: 199.

[27] Gong L, Zhou H, Zhang Y, Wang C, Fu K, Ma C, *et al*. Preparation of Phillygenin-Hyaluronic acid composite milk-derived exosomes and its anti-hepatic fibrosis effect. Materials Today Bio. 2023; 23: 100804.

[28] Liu Y, Wang Z, Qin X. Metabolomics and molecular docking to compare of the efficacies of wild-simulated and transplanted Astragali Radix based on its compatibility with Angelicae Sinensis Radix against blood deficiency. Journal of Chromatography B. 2021; 1173: 122682.

[29] Bai Y, Chen R, Sun J, Guo Y. Evaluation of therapeutic mechanism of hedyotis diffusa willd (HDW)-scutellaria barbata (SB) in clear cell renal cell carcinoma via singlecell RNA sequencing and network pharmacology. Combinatorial Chemistry & High Throughput Screening. 2024; 27: 910–921.

[30] Dai MX, Shi QX, Xiang XL, Zhao XY, Zeng ZX, Jin SN, *et al*. Metabolomics study of lipid lowering effect and lysophospholipids regulation by *Alismatis rhizoma* and processed forms in hyperlipidemia mice. Chinese Journal of Analytical Chemistry. 2024; 52: 100431.

[31] Huang Y, You J, Jing R, He Y, Li X, Wen Y, *et al*. Mechanisms of Salvia miltiorrhiza and Angelica sinensis herbal pair in intervening ischemic stroke based on network pharmacology and molecular docking. Frontiers in Medical Science Research. 2023; 5: 1–11.

[32] Zhan D, Li Y, Xu L, Li Y, Song M, Yi W, *et al*. Fuling Guizhi Baizhu Gancao Decoction combined with traditional Chinese medicine and acupoint injection in the treatment of refractory ascites in patients with hepatitis B-related cirrhosis. Panminerva Medica. 2024; 66: 207–209.

[33] Li Z, Dong M, Chen Z, Zhang C, Jiang J, Liu M, *et al*. Combining virus-based affinity ultrafiltration method with serum pharmacochemistry to identify the antiviral pharmacodynamic substances in licorice. Journal of Ethnopharmacology. 2024; 338: 118978.

[34] Liu A, Sun J, Tiwari S, Wong J, Wang H, Tang D, *et al*. Effect of Chinese herbal formulae (BU-SHEN-YI-QI granule) treatment on thrombin expression after ischemia/reperfusion. All Life. 2023; 16: 2173311.

[35] Wu X, Zhou J, Xie W, Ding H, Ou X, Chen G, *et al*. Entecavir monotherapy versus de novo combination of lamivudine and adefovir for compensated hepatitis B virus-related cirrhosis: a real-world prospective multicenter cohort study. Infect Drug Resist. 2019; 12: 745–757.

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