Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i18.3374

HEPATORENAL SYNDROME IN ASSOCIATION WITH ALCOHOLIC LIVER DISEASE.

Santiago David Maldonado Peñafiel[1*], Andrés Santiago Bueno Castro[2]

[1*]Estudiante de la carrera de Medicina de la Universidad Católica de Cuenca, Email: sdmaldonadop52@est.ucacue.edu.ec, Orcid: 0009-0001-3630-8264
[2]Docente Universidad Católica de Cuenca, Email: andres.bueno@ucacue.edu.ec, Orcid: 0009-0008-7581-4312

***Corresponding Author:** Santiago David Maldonado Peñafiel
*Estudiante de la carrera de Medicina de la Universidad Católica de Cuenca, sdmaldonadop52@est.ucacue.edu.ec, Orcid: 0009-0001-3630-8264

Abstract
Hepatorenal syndrome is an acute renal lesion in which histologically there is no evidence of structural abnormalities in the kidneys, as a consequence of acute decompensation of cirrhosis, mainly of alcoholic etiology. Its pathophysiology is not yet fully defined; however, its progression is of rapid onset and is associated with complications which, if not treated promptly, have high morbimortality. In Ecuador, local studies show that emergent care for hepatorenal complications secondary to alcoholic etiology are frequent in the clinical area. The definitive treatment for hepatorenal syndrome, both type 1 and 2, is liver transplantation. Currently, medical progress has given way to the study of other therapeutic alternatives such as terlipressin and even the use of probiotics for regenerative purposes.
General objective: To describe hepatorenal syndrome in association with alcoholic liver disease.
Methods: A narrative literature review study was conducted in a broad literature review of hepatorenal syndrome in association with alcoholic liver disease. As part of the PRISMA strategy, information is collected in scientific databases, mainly Cochrane, Pub Med, Science Direct and Scielo.
Results: Alcoholic liver disease represents the main cause of liver damage and hospital admission in Ecuador, being represented in 33% of all cases, being directly related to the generation of kidney injury subsequent to liver damage in 16.7% of cases. On the basis of the diagnosis, hepatorenal syndrome is characterized by elevation of azoates in the context of a patient with liver damage and ascites that does not improve after 48 hours of discontinuation of diuretics and volume expansion with albumin. The main pharmacological treatment is the use of terlipressin to improve kidney function during the first 14 days, although if there is no timely correction, the definitive treatment is still liver transplantation.
Conclusions: In Ecuador, local studies show that emergent care for hepatorenal complications secondary to alcoholic etiology is frequent in the clinical area. The definitive treatment for both type 1 and 2 hepatorenal syndrome is liver transplantation. Currently, medical advances have given way to the study of other therapeutic alternatives such as terlipressin and even the use of probiotics for regenerative purposes.

Key words: "Alcoholic Hepatitis"; "Hepatorenal Syndrome"; "Alcohol Induced Disorders".

INTRODUCTION

RHS is a pathology that usually occurs in the context of liver disease in an advanced stage or when acute liver failure occurs, related to high mortality and manifests as an alteration in renal function accompanied by a decreased glomerular filtration rate as well as an elevation of creatinine without the presence of important histological alterations in the nephron. Therefore, the association of hepatorenal syndrome and alcoholic liver disease is of great relevance for the scientific-medical study, which will provide us with the tools and knowledge for the adequate management of the patient, seeking to reduce the mortality and morbidity of this pathology (11).

RHS is characterized by acute kidney injury that generally occurs in patients suffering from cirrhosis and ascites, and is prevalent in 20% of the hospitalized population due to decompensation of these pathologies (12). This pathological disorder is based on the deterioration of renal function mainly as a result of systemic dysfunction of circulatory function as a result of the complications of cirrhosis, so hepatorenal syndrome will be characterized by having the worst survival rates, since it can present great complications such as spontaneous bacterial peritonitis, systemic inflammation, cardiomyopathy and chronic renal failure. (13).

For the above reasons, it is important to make a prompt diagnosis, as well as the correct and timely therapeutic implementation according to the context of each of the patients, which will improve the prognosis that will go hand in hand with assistance

It has been shown that with the appropriate therapeutic application this pathology is potentially reversible (14). For the evaluation of renal function in a context of acute kidney injury, the parameters should be interpreted especially in patients with liver cirrhosis, the use of evidence-based protocols has improved patient survival, and it has also been defined that among therapeutic treatments the use of vasoconstrictor therapies such as terlipressin plus albumin compared to the effectiveness of midodrine and octreotide improves the patient's prognosis and reduces its complications (15).

MATERIALS AND METHODS

Type of Study: Narrative literature review.

Study Design: As part of the narrative literature review of the present study, a literature review on hepatorenal syndrome in association with alcoholic liver disease was developed. Information was collected from original articles, case reports, and randomized controlled trials (RCTs), both in primary and secondary sources, published in the last five years in different nations around the world, in Spanish and English in reference to hepatorenal syndrome in association with alcoholic liver disease. Using keywords: "Hepatorenal Syndrome"; "Alcoholic Hepatitis"; "Alcohol-Induced Disorders." The main databases for searching the medical literature were Scopus, EMBASE, Web of Science, Science Direct and PubMed.

Inclusion Criteria

- Scientific articles referring to hepatorenal syndrome in association with alcoholic liver disease.
- Spanish and English language articles.
- Clinical practice guidelines.
- Studies of journals that are between quartile 1 and 4 according to the Scimago Journal Rank quality range.
- Articles with different methodological studies such as analytical, cohort studies, experimental studies and quasi-experimental studies.

Exclusion Criteria

- Qualitative studies.
- Scientific articles without open access.

Search strategy: Descriptor terms were searched using the Boolean operators "AND", "OR" and "NOT". The multilingual thesaurus of Health Sciences/Medical Subject Headings (DeCS/MeSH)

descriptors was used. Four criteria were used to select the studies: the first was to search for all clinical trials in the proposed databases; the second, to filter out duplicate entries in the databases; the third, to discard documents that were accessible for a fee. And as a fourth criterion, we did not include documents published in journals without a quartile classification, determined by the Scimago Journal Rank.

Data Extraction and Collection

To facilitate the search and synthesis of results, a database table was created for the compilation of the articles chosen in the statistical program Excel 2019 with the title of the article, the year of publication, the name of the journal, the DOI link and the included objective. The statistical application Excel 2019 was used to establish a database once the clinical trials were chosen, where a summary of each article was made, including the author, year, type of study and population in relation to hepatorenal syndrome in association with alcoholic liver disease. The metric that was used was determined by the Scimago Journal Rank, Enel, in which the quality ranking of the journal and studies correspond to quartiles ranging from 1 to 4. In the initial search, we found 70 articles; 12 were removed as they were duplicates and 8 due to revision of the title and/or abstract. From this group, we used 44 research studies that met the inclusion and exclusion criteria; 6 publications were omitted because they were not open access, and a total of 44 studies were used.

EPIDEMIOLOGY

According to statistics, 10% of patients who suffer from alcoholic cirrhosis in advanced stages or who have a diagnosis of acute liver failure will generate a hepatorenal syndrome, while patients who, in addition to cirrhosis, have a concomitant ascites will have an 18% probability of developing RHS in the first year. while in the 5 years this figure rises to 39% (16). In relation to sex, males are predominant for this pathology, accounting for 66.4% of patients with liver cirrhosis (17). In addition, the main etiology of cirrhosis is alcohol consumption with 72.75% of the total prevalence, these patients who present this pathology may present abdominal distension in 80.48%, infections in 53.39%, hepatic encephalopathy in 43.82%, hepatorenal syndrome in 16.3% and complications of ascites in 80.48% of these patients. In addition, this research shows that mortality in this study was around 32.8%, which reveals the importance of correct management of this disease and the serious repercussions it can have (18).

In another observational, analytical study of cases and controls at the Dr. Salvador Allende University Hospital in the period between 2015 and 2019, where 77 patient cases were included, demonstrated and confirmed that the predominance of the disease rests on the male population with 68.8% of all cases and 72.7% of all controls. The most frequent cause of this disease was alcoholism, with 46.8% of cases and 62.3% of controls, above hepatitis B, which was the etiology in 11.7% of cases and 7.8% of controls, and hepatorenal syndrome was defined as a risk factor that considerably increases mortality in these patients (19).

PHYSIOPATHOLOGY

The natural history of cirrhotic liver disease presents an asymptomatic phase in which liver function progressively deteriorates until severe systemic complications finally occur (19).

In order to explain the pathophysiology of hepatorenal syndrome, there are different hypotheses, among which we will find:

Splanchnic vasodilation

After the patient has developed cirrhosis as a result of this hepatic structural remodeling, portal hypertension will occur, followed by changes in the intestinal mucosa producing congestion of the portal system which in turn is related to a decrease in intestinal peristalsis favoring bacterial overgrowth and the production of endotoxins, these bacteria usually enter the portal circulation to be eliminated through the action of hepatocytes and Kupffer cells, which make up the phagocytic-mononuclear system of the liver organ (20). At the level of the mucosal barrier of the intestine,

translocations of microorganisms can be generated, which translates into an inflammatory response mediated by pro-inflammatory cytokines and an increase in tumor necrosis factor (TNF-α) and interleukin 6 (IL-6), as well as vasodilator factors such as nitric oxide, prostacyclins, epoxyicocosatrienoic acids, carbon monoxide (CO), glucagon, endogenous cannabinoids among other substances such as nitric oxide that will produce a vasodilation is related to the inhibition of leukotriene production, while prostacyclins will contribute to the relaxation of the vascular wall producing vasodilation that In the long term, there is a decrease in effective circulatory volume and, therefore, acute kidney injury (20).

Systemic inflammation

In patients with systemic inflammation, it has been shown that they maintain a higher probability of developing acute kidney injury regardless of whether or not there is infection, this systemic inflammation will cause an elevation of pro-inflammatory cytokines in the blood plasma such as interleukin 6 (IL-6) and interleukin 8 (IL-8) in addition to TNF-α and adhesion proteins 1. These substances in the bloodstream will also cause inflammation in the renal system, leading to damage to the functional renal unit known as the nephron (21).

Vasoconstrictor mechanisms

By activating the renin-angiotensin-aldosterone system, which is a neurohormonal mechanism that occurs in 80% of patients with decompensated liver cirrhosis and more intensely in patients who develop hepatorenal syndrome, through the secretion of vasopressin, they will counteract the hypovolemia that is accessory to vasodilation of the spleen in a compensatory act of circulatory blood volume homeostasis. The renin-angiotensin-aldosterone system will initially cause selective vasoconstriction of arterioles at the level of the glomerulus in the efferent renal ducts, thus increasing the pressure of the glomerular filtration rate (21).

Adrenal insufficiency

Approximately 25 to 30% of patients with decompensated cirrhosis develop adrenal insufficiency, which will cause a decreased vascular response, as well as hemodynamic instability that can greatly affect vasculature and renal perfusion, which can contribute to the onset of hepatorenal syndrome and acute kidney injury. Importantly, adrenal insufficiency is often associated with circulatory dysfunction and, therefore, a worse survival rate (22).

Cholemic nephropathy

Also called biliary casts secondary to a probable hepatorenal syndrome caused by the formation of casts that are composed of intratubular bile acids that cause obstructive tamponade and direct toxicity on the tubular cells of the kidney, triggering irreversible acute kidney injury in patients with chronic liver disease or in turn in patients with intense cholestasis; however, in patients with less severe forms, proximal tubulopathy similar to that occurring in Fanconi syndrome will occur (23).

Renal dysfunction without acute kidney injury

Patients with cirrhosis may also have organic renal failure that manifests as a result of glomerulonephritis related to the hepatitis B or C virus, or in turn with patients who have nonalcoholic steatohepatitis, presenting an increased risk of developing chronic renal failure. In cases where glomerulonephritis is present, the diagnosis will be guided by the appearance of urinary sedimentation such as proteinuria or hematuria. In these cases, patients may develop acute kidney injury as a result of diuretic abuse, gastrointestinal bleeding, or fluid loss that alters hemodynamic balance or renal factors such as acute tubular necrosis or acute interstitial nephritis (24).

Pathophysiology of alcohol-associated liver cirrhosis

At the hepatic level, it should be considered that the metabolism of alcohol is carried out by the microsomal oxidizing enzyme system, this triggers a metabolic response characterized by the binding

of phospholipids, whose residues of amino acids and hydrogen sulfide groups produce depolymerization of plasma membrane proteins, favoring lipoperoxidation that, in the long term, predisposes to fatty liver. which is secondary to the peripheral mobilization of fatty acids and to the increase in synthesis and less degradation at the hepatic level (25). In addition, these lipoperoxidation-derived free radicals bind to tubulin, damaging the microtubules of the cytoskeleton and in turn stimulate the synthesis of a protein called procollagen type I from liver cells. It should be noted that chronic alcohol ingestion increases oxygen expenditure by re-oxidation of NADH (nicotinamide adenine dinucleotide) and in turn increases oxygen requirements producing a steeper oxygen gradient along the acine (26).

CHARACTERISTICS OF THE DISEASE

Patients with hepatorenal syndrome have clinical manifestations or characteristics of the disease that are compatible with cirrhosis, since RHS is related to alcoholic liver disease in most cases, which in this specific case is cirrhosis due to indiscriminate and chronic alcohol consumption that damages hepatocytes by oxidation, causing death and fibrosis of liver tissue, which will complicate the normal metabolic functioning of the liver. increasing the probability of acute renal failure, known in this context as hepatorenal syndrome (24).

Among the clinical findings that we will find in alcoholic cirrhosis we will have that in 81.3% of patients abdominal distension will be shown, in 75% of these patients will be observed displaceable dullness, ascites that is the result of decompensated cirrhosis will be present in about 71.3%, jaundice can also manifest in 59.3% of the population, In addition, peripheral edema can be evidenced in 45.4% of these patients, the wave sign will represent 38.9% of the clinical manifestations, while ecchymosis will be present in 25%, hepatomegaly will occur in 13.9% while periumbilical spider veins will occur in 11.1% of the population with cirrhosis (26).

CLASSIFICATION OF HEPATORENAL SYNDROME

TIPO	CARACTERÍSTICAS
SHR 1	• Duplicación de la creatinina sérica hasta una concentración ≥ 2,5 mg/dl en dos semanas. • Sin respuesta a la abstinencia de diuréticos y desafío de dos días con líquidos con 1 gr/kg/día de albúmina 20-25 %. • Cirrosis con ascitis. • Ausencia de shock. • Sin uso actual o reciente de fármacos nefrotóxicos. • Sin signos de lesión renal estructural. • Ausencia de proteinuria (>500 mg/día). • Ausencia de hematuria (>50 RBCs por campo de gran aumento). • Hallazgos normales en la ecografía renal.
SHR 2	• Aumento gradual de la creatinina sérica que no cumple los criterios anteriores.

Table No. 1: Classification of Hepatorenal Syndrome (25)
Source: Kweput et al (27)

WARNING SIGNS

Cirrhosis being the most frequent alcoholic liver disease, we must focus on the different complications and warning signs that can mean a considerable increase in patient mortality, one of the most common complications in patients who have decompensated cirrhosis is acute renal failure, so we will always be expectant of the glomerular filtration rate (GFR), which is a predictive marker very easy to interpret

and practical in terms of diagnosis of renal insufficiency in these patients and even in patients who do not suffer from cirrhosis; However, there may be certain limitations that will vary the results such as the weight, age, sex and ethnicity of the patient, it is also important to note that patients diagnosed with cirrhosis will decrease the levels of muscle creatinine production as well as an increase in tubular renal secretion, while these altered data can be observed in laboratory tests. Elevated bilirubin concentrations may interfere with the results, or an increase in the volume of distribution may dilute the filtrate (28).

The criteria for ICA-AKI should be used as the primary predictor of death, and a sudden increase in creatinine can be used as a warning indicator for initiating therapeutic therapy. which can vary from the use of vasopressors plus albumin or other treatments such as TIPS, peritoneal dialysis or even the planning of a liver transplant, so we can also say that an alarm sign in patients with cirrhosis who concomitantly present ascites will have a higher risk of developing hepatorenal syndrome, in addition all the causes or etiologies described above in this section must be taken into account at the time of the decision-making about these patients (29).

CLASSIFICATION OF CHILD PUG

The modified Child-Pugh classification of ascites by assessing the degree of ascites, plasma bilirubin and albumin concentrations, prothrombin time, and encephalopathy is a predictor of liver disease severity in patients with liver cirrhosis (30).

Parámetro	**A (1 punto c/u)**	**B (2 puntos c/u)**	**C (3 puntos c/u)**
Ascitis	No	Fácilmente controlable	Mal controlada
Bilirrubinas (mg)	< 2.0	2.0 - 3.0	> 3.0
Albúmina (gr)	> 3.5	3.0 a 3.5	< 3.0
Tiempo de protrombina	1-3	4-6	>6
Encefalopatía	No	Mínimo	Avanzada (coma)
Total	5 a 6 puntos **GRADO A DE CHILD**	7 a 9 puntos **GRADO B DE CHILD**	10 a 15 puntos **GRADO C DE CHILD**

Table No:2. Child Pug Scale (30)
Source: Louvet A, et al (31)

TREATMENT

In recent decades, great advances have been made in terms of the pathophysiology and treatment of hepatorenal syndrome, so there are currently different options and therapeutic possibilities that can be applied in patients with the clinical manifestations of this syndrome in which we can implement pharmacological treatments, among which we will find transjugular intrahepatic portosystemic shunt (TIPS). liver transplantation, as well as the therapeutic criteria of the International Ascites Club (ICA) (28). It is important to distinguish the hepatorenal syndrome of type I, which will require a hospital therapeutic implementation within the intensive care unit due to the severity and complications that manifest in this type of HRS, while in type II the management may be ambulatory, contemplating the possibility of a central venous access that represents a great utility in the evaluation of intravascular volume status. In addition to these measures, diuretic and nephrotoxic drugs should be discontinued (28). In hepatorenal syndrome, different pharmacological therapies can be implemented according to the clinical context and the particular case of each individual, so we will have different therapeutic options:

Vasoconstrictor therapy

• The most commonly used vasoconstrictor drugs in hepatorenal syndrome, according to a study of the literature on therapeutic alternatives, are terlipressin, noradrenaline, octreotide and vasopressin. To increase the survival rate of patients with hepatorenal syndrome, these drugs should be used immediately (29). The use of vasoconstrictors as systemic treatment to reverse some of the features associated with decreased kidney function as a result of cirrhosis was first discovered in the 1960s, but they are now commonly used in conjunction with albumin, midodrine, and octreotide for the treatment of hepatatorrenal syndrome type I. (30).

Albumin

• In patients with infection or cirrhosis, therapeutic treatment with albumin plays a fundamental role beyond the function of a simple intravascular volume expander, generating greater benefit, especially in patients with renal dysfunction or who have severe decompensated liver disease, so the therapeutic implementation with albumin in these patients will be relevant to improve their prognosis and prevention of acute kidney injury (AKI) (31). The steps for diagnosis may include, firstly, the evaluation of the patient according to the prerenal or structural clinical manifestations and etiology, in addition to a urinary sedimentation examination and biomarkers that can alert us to an Acute Tubular Necrosis (ATN), which will differ from a hepatorenal syndrome when there is a fractional excretion of sodium less than 1%. Following these steps, the answer will be considered on the management of pharmacological factors that may cause complications such as the suspension of nephrotoxic drugs, diuretics, as well as the reduction of risk factors, detecting and treating infections if they occur in the patient, it is also important that a replacement of volumes with 5% albumin or in turn with crystalloids is performed, especially in situations where renal depletion is severe (32). The third step in the management of hepatorenal syndrome will focus on the patient's response after administration of albumin infusion, evaluating the possibility of implementing vasoconstrictors in patients with a creatinine >1.5 mg/dL, which usually occurs in patients with hyponatremia or refractory ascites (32). Finally, it has been investigated that the therapeutic treatment of type I hepatorenal syndrome through the implementation of albumin accompanied by some type of vasoconstrictor is considered the Gold Standard for the treatment of this pathology, in addition to being the least invasive therapy improving survival; However, it is necessary to consider the patient's context, especially in renal replacement or renal replacement therapies where cardiac decompensations may occur, which will increase the patient's hospitalization time (33).

Terlipressin

- The Clinical Practice Guidelines of the European Association for the Study of the Liver (34), which are the preferred pharmacological treatment for hepatorenal syndrome, propose treating albumin in combination with terlipressin. This medication is a long-acting analog of vasopressin that has fewer side effects. As such, it is the vasoconstrictor of choice in hepatorenal syndrome and will effectively restore kidney function in people over the age of 65. (35).
- In hospital care, patients with liver cirrhosis with hepatorenal syndrome who do not improve after the implementation of albumin plus terlipressin treatment usually produce irreversible acute kidney injury, so the therapeutic protocol will indicate that renal replacement therapy will be necessary before liver transplantation. In addition, in patients with end-stage liver disease, treatment with terlipressin will be limited by the serious side effects that can occur in these patients, including digital ischemia, loose stools, and particularly cardiorespiratory failure. On the other hand, it is important to consider the high costs of terlipresin, which are not available worldwide, including Ecuador, so in these cases norepinephrine can be implemented as an alternative treatment for the management of hepatorenal syndrome type I (35).

Midodrine

● This anti-hypotensive vasopressor drug has been shown to serve as secondary prophylaxis in combination with albumin in patients with acute kidney injury, as well as liver cirrhosis and ascites. Through different studies and research on the effects and benefits of this drug, daily infusions of 15 mg have been defined in patients with hepatorenal syndrome, the presence of acute kidney injury was lower in these patients than in those who only used albumin, it has also been shown that the therapeutic implementation of this drug has a positive impact on the reduction of ascites punctures, which suggests a lower mean arterial pressure. however, there has been no evidence of a decrease in the recurrence of type II SHR (36).

Peritoneal dialysis

- It is a type of clinical treatment in which the use of a cycler or machine is used in which the patient is connected daily in order to reduce the levels of urea, creatinine, calcium and phosphorus, as well as a decrease in the production of ascitic fluid with a range of less than 500 cc. This will help us to have a higher quality of life and a better patient prognosis (33).

Transjugular intrahepatic portosystemic shunt

- Different studies where this type of procedure is used as a main treatment for hepatorenal syndrome have shown an improvement in short-term survival, while the one-year rate was 72% for patients with type I hepatorenal syndrome and 86% in patients with type II hepatorenal syndrome (25).
- Under this therapeutic technique, no lethal complications were observed, however, hepatic encephalopathy was present in 49% of cases, while, on the other hand, renal function improved in 93% of patients in study with type I SHR and 83% in other types of SHR. According to studies in which this technique is applied, there is a reduction in mortality from 44% to 24% (26).

Liver Transplant Therapy

● This surgical transplant is the definitive therapeutic procedure of choice, since it presents a guaranteed improvement in the patient's quality of life, however, complications can occur as a result of the availability of the quality and quantity of organs available by the donor population, in addition to *de novo* neoplasms, post-surgical infections, so the evaluation of certain prognostic factors such as serum sodium, as well as the use of the objective mortality prognostic index, also called Model for End-stage Liver Disease (MELD), will give us a clear idea of the patient's post-surgical health status after liver transplantation (27).

It is important that, within the therapies mentioned above in this section, the limitations are differentiated, as well as the objectives to be met in patients according to each of the treatments, so that, in vasoconstrictor therapy with albumin, it will be observed as a limitation that this treatment does not present feasibility and effectiveness when renal replacement therapy is underway. However, as a therapeutic objective we have that this type of treatment is the first stabilization, as well as the therapy with greater control of progression for hepatorenal syndrome, so also in vasoconstrictor therapy with the use of terlipressin we will have as limitations the high cost of such therapy, in addition to the fact that if there is no improvement in the patient, The next step will be renal replacement therapy with aspirations to a liver transplant, while among the outstanding effects of this treatment will be the greater therapeutic efficacy when terlipressin is combined with albumin, especially in patients over 65 years of age (34).

On the other hand, vasoconstrictor therapy with midodrine has as a limitation the ineffectiveness of the treatment for the control of recurrences in hepatorenal syndrome type II, while this therapy has been useful in the secondary prophylaxis of hepatorenal syndrome causing acute renal injury. While peritoneal dialysis will help us in the elimination of ascitic fluid on a daily and constant basis, however, there are limitations due to the complications that can occur, as well as in the transjugular intrahepatic portosystemic shunt (TIPS) it can be observed as a highlight that survival rates improve in the short and long term. however, there is a high incidence of treatment-adjacent complications

(35). Finally, we will observe that liver transplantation in the SHR will be the best therapeutic option, as well as the definitive treatment of choice, however, this surgical procedure has limitations in terms of the availability of grafts, waiting times, as well as a high probability of generating de *novo neoplasms* (34).

PREVENTION METHODS

Hepatorenal syndrome is one of the complications with the highest mortality that develop in the context of patients with alcoholic liver disease, so toxic habits such as alcohol consumption and other hepatotoxic or nephrotoxic drugs should be avoided, it is also necessary to inquire among the patient's history if there is any contact with hepatitis B or C viruses that are also other etiological hypotheses for the development of RHS and therefore Finally, it is important to be expectant about any possible infection, especially at the level of the urinary tract, which, by activating the mechanisms of inflammation, can also cause RHS with an unfavorable outcome due to its high morbidity and mortality of the disease in these patients (26).

WARNING SIGNS

It is important to implement the ICA-AKI criteria as a great predictor of mortality, while an abrupt increase in creatinine can be considered a warning sign to start with the implementation of a therapeutic treatment that can range from the use of vasopressors plus albumin or other treatments such as TIPS, peritoneal dialysis or even the planning of a liver transplant, Thus, we can also say that a warning sign in patients with cirrhosis who concomitantly present ascites will have a higher risk of developing hepatorenal syndrome, in addition to taking into account all the causes or etiologies described above in this section to take into account when making decisions about these patients (27).

RESULTS

Prevalence of hepatorenal syndrome in Ecuador							
Auto r	**Country**	**Title of the Study**	**Year**	**Design of the Study**	**Participants**	**Results**	**Quadrile**
Sanc hez et al (36)	Ecua dor	**Analysis of etiologies, complications, in-hospital mortality and survival in patients with cirrhosis admitted to the services of Gastroenterology of two tertiary hospitals in the city of Quito since January 2012 as of December 2017**	**20 18**	Study Academi co	389 patients	In 33% of cases, cirrhosis due to alcoholism was the main cause. Ascites was present in 56% of patients. 48% of admissions had Child B and 69% of deaths had Child C, with a mean MELD at admission of 15 and death of 20. 52% of the 169 deaths occurred during the first admission. In-hospital mortality was 31%. A direct complication of cirrhosis was not the leading cause of mortality. Hepatorenal syndrome (HRS) and spontaneous bacterial peritonitis (SBP) cause changes in functional status. Ascites, PBS, HRS, encephalopathy, and varicose hemorrhage cause changes in the MELD. NASH was associated with higher in-hospital mortality but had no effect on survival time.	

Bismarck et al (37)	Ecuador	**Prevalence of Hepatorenal Syndrome in Patients With Liver cirrhosis at the Dr. Abel Gilbert Ponton from January 2015 to December 2017**	**2018**	Study Academico	150 patients	According to the place of admission of these patients, 83.3% went to the emergency room, but did not do so specifically because of their pathology, but for another reason. During their stay, they were diagnosed with hepatorenal syndrome. The remaining 16.7% were admitted from the outpatient clinic because they presented some symptoms or changes during the control that suggested that they should be admitted for observation.	
Cantos et al (38)	Ecuador	**"Prevalence of ascites and Clinical Epidemiological Characterization of Patients with Chronic Liver Disease From the hospital General Enrique Garcés of Quito, during the period May 2018-April 2019."**	**2019**	Study Academico	165 patients	The prevalence of ascites was 36.4%, as a result of chronic liver disease due to portal hypertension, among the most frequent etiology of cirrhosis we find alcoholic liver disease and generation of a hepatorenal syndrome in it. (85,5%).	
Clinical features, diagnosis and treatment of hepatorenal syndrome in association with alcoholic liver disease.							
Car r	**Country**	**Title Study of the**	**Year or**	**Design "We don't of the Study**	**Participants**	**Results**	**Cuartil**
Wang et al (39)	On Jap	Establishment and evaluation of anearly prediction model of hepatorenal syndrome in patients with decompensate for hepatitis B cirrhosis	2023	Ensayo Clínico	255 patients	This study included 255 patients with decompensated hepatitis B cirrhosis, including 184 in the training group and 71 in the validation group. The multivariate logistic regression model was established in the training group and verified in the validation group. Logistic regression showed that hemoglobin (OR 0.938, CI 95% 0.908-0.969), total bilirubin (OR 1.014, 95% CI 1.008-1.021) and creatinine (OR 1.079, 95% CI 1.043-1.117) were independent risk factors for hepatorenal syndrome. (P<0.05). These were used to establish the model. In the training group and in the validation group, the area under the ROC curve of the nomogram for the diagnosis of Hepatorenal syndrome was 0.968 and 0.980, respectively.	
						The patients' cognition improved significantly after treatment with Probiotics. The	

Xia et to (40)	US To	Role of Probiotics in the treatment of minimal hepatic encephalopath and in patients with HBV-induced liver cirrhosis	2018	Ens ayo Clínico Co ntrolad o	67 patients	Predominant bacteria (Clostridium cluster I and Bifidobacterium) were significantly enriched in the group treated with probiotics, while Enterococcus and Enterobacteriaceae decreased significantly. Probiotic treatment was also associated with an evident reduction in venous ammonia. In addition, intestinal mucosal barrier parameters obviously improved after treatment with probiotics, which could have contributed to improved cognition and decreased ammonia levels. Conclusion: Treatment with probiotics containing C. butyricum and B. infantis represents a novel adjuvant therapy for the treatment of HBV induced HCM in patients with HBV-induced cirrhosis. Probiotic treatment was also associated with an evident reduction in venous ammonia. In addition, intestinal mucosal barrier parameters obviously improved after treatment with probiotics, which could have contributed to improved cognition and decreased ammonia levels.	Q3
Wa Ng et al (41)	US To	Compariso n of the effects of probiotics, rifaximin, and lactulose in the treatment of minimal hepatic encephalopath and and Gut Microbiota	2023	Case Study and Control is	323 patients	Of 323 patients with liver cirrhosis, 74 were diagnosed with MHE. A total of 54 patients were enrolled and 52 who accepted follow-up were included in the analysis. The recovery rates of patients with MHE who received probiotics, rifaximin, and lactulose were 58.8% (20/34), 45.5% (5/11), and 57.1% (4/7), respectively. Probiotics and rifaximin improved liver function to some extent in patients with EHM. The taxonomic compositions of the gut microbiota in patients with EHM were different from those of healthy people before treatment; The differences were significantly reduced after treatment and the gut microbiota gradually resembled the structure of healthy individuals. We found that the relative abundance of specific taxa associated with anti-inflammatory functions and good cognitive functions increased in patients with MHE after of the treatment. Respectively, metabolic	Q1

						pathways in patients with MHE were altered before and after treatment. Pathways downregulated after probiotic treatment included glycometabolism and degradation of Aromatics. After treatment with lactulose, the degradation pathways of arginine and ornithine showed a downward trend.	
Wo ng et al (42)	JA PON	Terlipressin plus Albumin for The Treatment of Type 1 Hepatorenal Syndrome	2 021	Ens ayo Clínico Co ntrolad o	300 patients	A total of 300 patients were randomized, 199 of whom received terlipressin and 101 placebo. In the terlipressin group, 63 patients (32%) and 17 patients (17%) experienced a verified HRS reversal (p = 0.006). In terms of predetermined secondary endpoints, reversal of SHR – defined as any serum creatinine level equal to or less than 1.5 mg per deciliter during the first 14 days – was reported in 78 patients (39%) in the terlipressin group and 18 patients (18%) in the placebo group (P = .001); reversal of RHS without renal replacement therapy at day 30 was reported in 68 patients (34%) and 17 patients (17%), respectively (P = 0.001); and reversal of RHS without renal replacement therapy at day 30 was reported in 68 patients (34%) and 17 patients (17%), respectively (P = .001); and reversal of RHS without renal replacement therapy at day 30 was reported in 68 patients (34%) and 17 patients (17%), respectively (P = .001).	Q1
Coll ETA et al (43)	US To	The progression of hepatorenal syndrome-acute kidney injury in acute alcohol- associated hepatitis: renal outcomes after liver transplant	2 023	Ens ayo Clínico Co ntrolad o	210 patients	A total of 210 subjects underwent LTE; 25% were evaluated for AAH and 75% were evaluated for CLD. Hepatorenal syndrome was more common in subjects evaluated for AAH (37/47) than CLD (104/163) (78,7 *versus* 63,8%, *p* = 0.04). For the primary outcome, subjects with HRS AAH required approximately 30 days of renal replacement therapy (RRT) after LT more frequently than subjects with HRS CLD (p = 0.02) and non-HRS *CLD* (p< 0.01). There were no significant differences	

						in other forms of long-term kidney outcomes, including kidney transplant bypass and kidney transplantation between cohorts. In subgroup analysis, RRR 30 days after LT was more common in AAH HRS than in A-CLD HRS (*p* = 0.08). Logistic regression showed What AAH HRS Conferred 20 × odds and 3.3 × of requiring □30 days post-LT RRT compared with CLD without HRS and UNCCD HRS , respectively. Postoperative complications were similar across cohorts, but had an effect significant renal outcome at 30 days after HT.	
Wo ng et al (44)	US To	Outcomes of patients with cirrhosis and hepatorenal syndrome type 1 treated with liver transplantation	2019	Cohort and transv ersal study	45 patients	Patients without HRS reversal had significantly higher pre-transplant serum creatinine levels (3.81 ± 0.34 versus 3.23 ± 0.14 mg/dL, P = 0.06), longer duration of HRS1 {25 days (95% confidence interval (CI) 16-42 days) versus 10 days (CI 95%, 10-18 days), P = 0.02}, longer duration of pre-transplant dialysis [27 days (95% CI, 13-41 days) versus 10 days (95% CI, 13-41 days), 6-14 days), P = 0.01], and higher post-transplant mortality (P = 0.0045) compared with those whose kidney function recovered. The only predictor of HRS1 non-reversal was the duration of pre-transplant dialysis, with a 6% increase in the risk of non-reversal with each day Additional dialysis	Q1

DISCUSSION

In relation to hepatorenal syndrome associated with alcoholic liver disease in Ecuador, a study conducted by Sanchez et al (36) found that alcoholism represents 56% of the initial causes of cirrhosis, in which it was observed that 18% will develop RHS in 1 year and 39% in 5 years and changes in functional status. Similar data were found in the study by Bismarck et al. (37) in which it was shown that 83.3% of patients who attend the emergency room in the clinical area, 16.7%, will be diagnosed with some complication associated with hepatorenal syndrome. It should be noted that in patients with alcoholic liver disease, a predecessor of hepatorenal syndrome, according to Cantos et al (38), is ascites, which was 36.4%, a product of chronic liver disease due to portal hypertension and this is associated with hepatorenal syndrome in 85.5%.

In the study by Wang et al. (39) based on the diagnosis of hepatorenal syndrome characterized by an increase in creatinine concentration > 1.5 mg/dL in a patient with cirrhosis and ascites that does not improve after 48 hours of discontinuation of diuretics and volume expansion with albumin, it was found that hemoglobin (OR 0.938; 95% CI: 0.908-0.969), total bilirubin (OR 1.014; 95% CI: 1.008-1.021) and creatinine (OR 1.079, 95% CI 1.043-1.117) were independent risk factors for HRS, as they significantly increased mortality (P<0.05).

In relation to treatment, the study by Xia et al (40) evaluated the effect of certain probiotics such as lactobacillus acidophilus against probiotics, the results of which have corroborated that in patients with liver cirrhosis and hepatorenal syndrome, showing an evident reduction in venous ammonia. In addition, intestinal mucosal barrier parameters were significantly improved, which could have contributed to improved cognition and decreased ammonia levels. Similar data were found in the study by Wang et al (41) in which they started from a sample of 323 patients with liver cirrhosis, in which a recovery rate after the administration of probiotics of 58.8% was evidenced, followed by rifaximin 45% and lactulose in 57%, it was also evidenced that liver function improved considerably with probiotics. In the same study, it was evidenced that the long-term intestinal microbiota obtained significant changes characterized by glycometabolism and the degradation of certain aromatic compounds, it should be noted that the final histological analysis showed that the microbiota after the use of probiotics had an appearance similar in 60% to normal individuals.

Another treatment is terlipressin. The study by Wong et al. (42) showed that, out of 300 randomized patients, 199 were assigned to the terlipressin group in which improvement in serum creatinine levels was evidenced during the first 14 days in 78 patients (39%) in the terlipressin group and 18 (18%) in the placebo group. On day 30, renal replacement therapy was administered to 68 (34%) and 17 (17%) patients. In contrast, it was shown that 2 patients (2%) in the placebo group and 22 patients (11%) in the terlipressin group died at 90 days as a result of respiratory problems.

Another therapeutic option in patients with alcoholic liver disease and hepatorenal syndrome in the study by Colleta et al (43) showed that out of 210 patients, hepatorenal syndrome was more common compared to another etiology (78.7% versus 63.8%, $p = 0.04$). For the primary outcome, subjects with alcoholic liver disease and hepatorenal syndrome required 30 days of renal replacement therapy after liver transplantation compared to other causes. There were no significant differences in other forms of long-term renal outcomes, including kidney transplant referral and kidney transplantation between cohorts, in this study we concluded that the etiology of liver decompensation and postoperative complications affect post-liver transplant renal recovery. The systemic inflammation of alcoholic liver disease, in addition to conditions that favor renal hypoperfusion, may contribute to unfavorable outcomes of hepatorenal syndrome after transplantation. Similar data were found in the study by Wong et al (44) in which patients without reversal of hepatorenal syndrome had significantly higher pretransplant serum creatinine levels (3.81 ± 0.34 versus 3.23 ± 0.14 mg/dL, $P = 0.06$), longer duration of illness (25 days [95% confidence interval (CI)] 16-42 days) versus 10 days (95% CI, 10-18 days), $P = 0.02$}, longer duration of pre-transplant dialysis [27 days (95% CI, 13-41 days) versus 10 days (95% CI, 13-41 days), 6-14 days), $P = 0.01$], and higher post-transplant mortality ($P = 0.0045$) compared with those whose kidney function was preserved.

CONCLUSIONS

- Regarding the prevalence of hepatorenal syndrome in Ecuador, local studies show that emergent care for hepatorenal complications secondary to alcoholic etiology is frequent and represents 10% of emergencies in the clinical area.
- The clinical features, diagnosis and treatment of hepatorenal syndrome in association with alcoholic liver disease have been clearly defined and are based on criteria that exclude other causes of renal damage, such as the presence of renal damage, structural damage or obstructive renal damage.
- Liver transplantation is the only therapeutic option associated with improved survival in patients with type 1 and 2 RHS, making it the only effective therapeutic option.
- Currently, medical advances have given way to the study of other therapeutic alternatives such as terlipressin and even the use of probiotics for regenerative purposes.

BIBLIOGRAPHIC REFERENCES

1. Divens LL, Rivera SL. Hepatorenal Syndrome: From the Beginning to Now. Crit Care Nurs Clin North Am. 2022; 34(3):321-9.
2. Habas E, Ibrahim AR, Moursi MO, Shraim BA, Elgamal ME, Elzouki AN. Update on hepatorenal

Syndrome: Definition, Pathogenesis, and management. Arab Journal of Gastroenterology. 2022; 23(2):125-33.
3. Juanola A, Solé C, Toapanta D, Ginès P, Solà E. Monitoring Renal Function and Therapy of Hepatorenal Syndrome Patients with Cirrhosis. Clinics in Liver Disease. 2021; 25(2):441-60.
4. Wilde B, Canbay A, Katsounas A. Clinical and pathophysiological understanding of the hepatorenal syndrome: Still wrong or still not exactly right? World J Clin Cases. 2023; 11(6):1261-6.
5. Jung CY, Chang JW. Hepatorenal Syndrome: Current Concepts and Future Perspectives. Clin Mol Hepatol. 2023;
6. Ayares G, Idalsoaga F, Díaz LA, Arnold J, Arab JP. Current Medical Treatment for Alcohol-Associated Liver Disease. J Clin Exp Hepatol.2022; 12(5):1333-48.
7. Crocombe D, O'Brien A. Diagnosis and management of ascites and hepatorenal syndrome (acute kidney injury) in cirrhosis. Medicine 2023. Available in: https:// www.sciencedirect.com/science/article/pii/S1357303923000774
8. Bera C, Wong F. Management of hepatorenal syndrome in liver cirrhosis: a recent update. Therap Adv Gastroenterol. 2022;15:17562848221102680.
9. Premkumar M, Anand AC. Overview of Complications in Cirrhosis. J Clin Exp Hepatol. 2022; 12(4):1150-74.
10. Krátká K, Libicherová P, Mejzlíková N, Rychlík I. Hepatorenal syndrome - update 2020. Vnitr Lek. 2020; 66(3):71-5.
11. Carrasco L, Rojas J, Zavala J. Hepatorenal syndrome in association with alcoholic hepatitis and Zieve syndrome. Annals of the Faculty of Medicine; 83(3):235–8. Available from:http://www.scielo.org.pe/scielo.php?pid=S1025-55832010000300008&script=sci_arttext&tlng=en
12. O'Brien A. Diagnosis and management of ascites and hepatorenal syndrome (acute kidney injury) in cirrhosis. Medicine 2019; 47(12):828–32. Available from: https:// www.scienceopen.com/document?vid=857a7a16-fb32-4e77-bfc5-89800e41dd56
13. Piano S, Tonon M, Angeli P. Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome. In: Critical Care Nephrology Elsevier; 2019; 487-492.e2. Available from: https:// www.researchgate.net/publication/328703491_Spontaneous_Bacterial_Peritonitis_and Hepatorenal_Syndrome.
14. Ojeda A, Cerda E, Herrero M, Castro G, Piano S. An Integrated Review of the Hepatorenal Syndrome. Ann Hepatol 2022.; 22:100236. Available from: https://pubmed.ncbi.nlm.nih.gov/32846202/
15. Belcher J, Parada X, Simonetto D, Juncos L, Karakala N, Wadei H, et al. Terlipressin and the Treatment of Hepatorenal Syndrome: How the CONFIRM Trial Moves the Story Forward. American Journal of Kidney Diseases 2022; 79(5):737–45. Available from: https://pubmed.ncbi.nlm.nih.gov/34606933/
16. Giraldo C, Jiménez M, Torres J. Hepatorenal syndrome in acute and chronic liver failure: a case report. Colombian Journal of Nephrology 2021; 8(2):E532. Available from: https://revistanefrologia.org/index.php/rcn/article/view/532/859
17. López M. Renal insufficiency in liver cirrhosis. Internal Medicine of Mexico 2019; 35(1):94–103. Available from: https:// www.medigraphic.com/pdfs/medintmex/mim-2019/mim191j.pdf
18. Peralta K. Clinical-epidemiological characteristics of patients with liver cirrhosis at the Cusco Regional Hospital, 2014-2018 Universidad Nacional San Antonio Abad del Cusco; 2020
19. Mero J, Rego J, Saborit A, Fernández W, Blanco R. Factors associated with death in patients with liver cirrhosis. Cuban Journal of Comprehensive General Medicine 2021; Available from: https://aniversariocimeq2021.sld.cu/index.php/ac2021/Cimeq2021/paper/view/249
20. Chancharoenthana W, Leelahavanichkul A. Acute kidney injury spectrum in patients with chronic liver disease: Where do we stand? World J Gastroenterol 2019 Available from: https://pubmed.ncbi.nlm.nih.gov/31391766/
21. Cure I. Pathophysiology and treatment of hepatorenal syndrome. Mexican Association of Hepatology 2021; 1:114–9. Available from: https://hepatologia.org.mx/wp-

content/uploads/2022/11/Cirrhosis-Pediatrica-digital.pdf#page=114
22. Kapoor N, Mehta V, Singh B, Karna R, Kumar S, Kar P. Prevalence of cirrhotic cardiomyopathy and its relationship with serum pro-brain natriuretic peptide, hepatorenal syndrome, spontaneous bacterial peritonitis, and mortality. Indian Journal of Gastroenterology 2020; 39(5):481–6. Available from: https://pubmed.ncbi.nlm.nih.gov/33188455/
23. Calderón W, Ascanio M, Yarinsueca P. Clinical characteristics and complications of liver cirrhosis in a high-altitude population (Huancayo, 3250 m a.s.l.). Medical Horizon (Lima)2020; 20(2):E1186. Available from: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1727-558X2020000200008
24. Angeli P, Garcia G, Nadim M, Parikh C. News in pathophysiology, definition and classification of hepatorenal syndrome: A step beyond the International Club of Ascites (ICA) consensus document. J Hepatol 2019; 71(4):811–22. Available from: https://pubmed.ncbi.nlm.nih.gov/31302175/
25. Kaewput W, Thongprayoon C, Dumancas C, Kanduri S, Kovvuru K, Kaewput C, et al. In-hospital mortality of hepatorenal syndrome in the United States: Nationwide inpatient sample. World J Gastroenterol 2021; 27(45):7831–43. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8661379/
26. Martinez M, Almanza A, Rodriguez T, Imbeth P. Renal insufficiency in cirrhosis. Literature review. Colombian Journal of Nephrology 2022; 9(1):E531. Available from: http://www.scielo.org.co/scielo.php?pid=S2500-50062022000100205&script=sci_arttext
27. Angeli P, Garcia G, Nadim M, Parikh C. News in pathophysiology, definition and classification of hepatorenal syndrome: A step beyond the International Club of Ascites (ICA) consensus document. J Hepatol 2019; 71(4):811–22. Available from: https://pubmed.ncbi.nlm.nih.gov/31302175/
28. Angeli P, Merkel C. Pathogenesis and management of hepatorenal syndrome in patients with cirrhosis. J Hepatol 2018; 48:S93–103. Available from: https://pubmed.ncbi.nlm.nih.gov/18304678/#:~:text=Hepatorenal%20syndrome%20is%20a%20severe,related%20to%20intense%20renal%20vasoconstriction.
29. Sanabria D. HEPATORENAL SYNDROME: REVIEW OF THE LITERATURE. Magazine Colombian of Nephrology 2022. Availafrom: https://revistanefrologia.org/index.php/rcn/article/view/539
30. Adebayo D, Neong S, Wong F. Ascites and Hepatorenal Syndrome. Clin Liver Dis 2019 23(4):659–82. Available from: https://pubmed.ncbi.nlm.nih.gov/31563217/
31. Louvet A, et al. Early liver transplantation for severe alcohol-related hepatitis not responding to medical treatment: a prospective controlled study. Lancet Gastroenterol Hepatol. 2022 416-425. doi: 10.1016/S2468-1253(21)00430-1.
31. Buccheri S, Da B. Hepatorenal Syndrome. Clin Liver Dis 2022; 26(2):181–201. Available from: https://pubmed.ncbi.nlm.nih.gov/35487604/
32. Biggins S, Angeli P, Garcia G, Ginès P, Ling S, Nadim M, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2021 Available from: https://pubmed.ncbi.nlm.nih.gov/33942342/
33. Zhenchuan M, Qianmei C. Predictive factors for the therapeutic effect of terlipressin combined with albumin in hepatorenal syndrome. Journal of Clinical Hepatology [Internet]. 2021. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/wpr-904966
34. Mujtaba M, Gamilla A, Merwat S, Hussain S, Kueht M, Karim A, et al. Terlipressin in combination with albumin as a therapy for hepatorenal syndrome in patients aged 65 years or older. Ann Hepatol 2023 Available from: https://pubmed.ncbi.nlm.nih.gov/37302573/
35. Sharma P, Puri P, Bansal N, Singla V, Kumar A, ShriHari A, et al. Midodrine and albumin versus albumin alone for the secondary prophylaxis of acute kidney injury in a patient with cirrhosis and ascites. Eur J Gastroenterol Hepatol 2021 Available from: https://pubmed.ncbi.nlm.nih.gov/34034268/

36. Louvet A, et al. Early liver transplantation for severe alcohol-related hepatitis not responding to medical treatment: a prospective controlled study. Lancet Gastroenterol Hepatol. 2022 416-425. doi: 10.1016/S2468-1253(21)00430-1.
37 Carrasco U, Eduardo J, Manuel DR, Navarro Chavez R. PAZMIÑO ANTEPARA BISMARCK STIVEN Edu.ec. Available in: http://repositorio.ug.edu.ec/bitstream/ redug/31393/1/PAZMI%c3%91O%20ANTEPARA%20BISMARCK%20STIVEN.pdf
38. De Medicina C, Belén M, Moscoso C, Cornejo F, Gabriel L, Mendoza T, et al. UNIDAD ACADÉMICA DE SALUD Y BIENESTAR Edu.ec. Available in: https://dspace.ucacue.edu.ec/bitstream/ucacue/8662/1/9BT2019-MTI164.pdf
39. Wang S, Zhou Z, Xu C, Chen H, Ren W, Yang X, Yin Q, Zheng W, Pan H. Establishment and evaluation of an early prediction model of hepatorenal syndrome in patients with decompensated hepatitis B cirrhosis. BMC Gastroenterol. 2023 doi: 10.1186/S12876-022-02618-X.
40. Xia X, Chen J, Xia J, Wang B, Liu H, Yang L, Wang Y, Ling Z. Role of probiotics in the treatment of minimal hepatic encephalopathy in patients with HBV-induced liver cirrhosis. J Int Med Res. 2018 doi: 10.1177/0300060518776064.
41. Wang MW, Ma WJ, Wang Y, Ma XH, Xue YF, Guan J, Chen X. Comparison of the effects of probiotics, rifaximin, and lactulose in the treatment of minimal hepatic encephalopathy and gut microbiota. Front Microbiol. 2023. Doi: 10.3389/FMICB.2023.1091167.
42. Wong F, Pappas SC, Curry MP, Reddy KR, Rubin RA, Porayko MK, Gonzalez SA, Mumtaz K, Lim N, Simonetto DA, Sharma P, Sanyal AJ, Mayo MJ, Frederick RT, Escalante S, Jamil K; CONFIRM Study Investigators. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. N Engl J Med. 2021 doi: 10.1056/NEJMoa2008290.
43. Colletta A, Cooper KM, Devuni D. The progression of hepatorenal syndrome-acute kidney injury in acute alcohol-associated hepatitis: renal outcomes after liver transplant. Therap Adv Gastroenterol. 2023. doi: 10.1177/17562848231188813.
44. Wong F, Leung W, Al Beshir M, Marquez M, Renner EL. Outcomes of patients with cirrhosis and hepatorenal syndrome type 1 treated with liver transplantation. Liver Transpl. 2015 doi: 10.1002/lt.24