

Experimental Investigation of Hepatoprotective Agents and Antimicrobials for the Management of Liver Disorders: A Cross-Sectional Study

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ABSTRACT

Background: One of the world's leading causes of mortality, liver illnesses have far-reaching repercussions in society, the economy, and medicine. Our primary objective is to raise awareness of liver disease symptoms and consequences while simultaneously decreasing the likelihood of illness and assessing the efficacy of hepatoprotective medicines and antimicrobials. Research Tools and Procedures: This 55-patient cross-sectional research took place over the course of six months in a tertiary care teaching hospital. Information was gathered using the patient profile, a questionnaire, and laboratory testing. The results show that among 55 patients treated between the ages of 40 and 70, the most prevalent types of liver disease were alcoholic liver disease (36.36%), chronic liver disease (34.54%), decompensated liver disease (12.72%), and liver abscess (16.36%). Males (87.27%) and females (12.72%) were the most afflicted. While 14.54% do not drink, 85.45% have a drinking habit. Ascites develops in around 60% of cases. Cephalosporins (78.18%) and ursodeoxycholic acid (80%) are the most often recommended hepatoprotective agents and antibiotics, respectively. In patients treated with hepatoprotective drugs for one week, serum bilirubin, aspartate transaminase, and alanine transaminase levels decreased by 42%, 58%, and 65%, respectively, according to this research. Researchers concluded that alcohol abstinence, in conjunction with antimicrobial and hepatoprotective symptom care, may assist to avert further problems.

Key words: Liver diseases caused by alcohol, liver infections, chronic liver disease, decompensated liver disease, Antibiotics, hepatoprotective medications.

INTRODUCTION

Another name for liver illness is hepatic disease. When the liver's normal functions are impaired, it leads to illness, which is called liver disease. Common symptoms of liver illness include jaundice, swelling, abdominal discomfort, edema, itchy skin, dark urine, pale, bloody, or tar-colored feces, chronic lethargy, nausea, vomiting, anorexia, and an easy bruising propensity.¹ Liver disease testing involves looking for signs of liver damage, finding out how bad it is, finding out what caused it, and monitoring the liver's health over time. Laboratory testing includes a complete blood count (CBC), liver tests, and liver biopsies. A few examples of non-laboratory tests include ultrasound, computed tomography, MRI, and magnetic resonance cholangiopancreatography.² Common medications used to treat liver problems include hepatoprotective medicines, such as silymarin, ursodeoxycholic acid, and Hepamerz. Patients with liver illnesses are at increased risk of infection due to the suppression of immunity; hence, antibiotics are prescribed to treat bacterial infections.³

Alcoholic liver disease (ALD) refers to the liver's damage and dysfunction brought on by drinking too much alcohol. The disease may develop in people who drink alcohol regularly, although the amount of alcohol they drink each day varies widely from person to person.⁴ The three most common types of alcoholic liver disease are alcoholic cirrhosis, acute alcoholic hepatitis, and alcoholic fatty liver (steatosis).⁵

The severity of steatosis, also known as alcoholic fatty liver, may vary from moderate inflammation to complete liver failure.⁶ Heavy alcohol use over an extended period of time (mean intake, around 100g

per day) causes alcoholic hepatitis, a clinical illness characterized by jaundice and liver failure. There are a number of ways in which liver damage may lead to cirrhosis, including necroinflammation and fibrogenesis. The disease can also be categorized into two stages, compensated and decompensated, and each has its own unique symptoms, outlook, and mortality projections. There are two distinct subgroups within the compensated stage, and their respective prognoses are determined by whether or not varices are present.⁹ The development of complications such as ascites, variceal bleeding, hepatic encephalopathy, or jaundice as a result of portal hypertension or liver insufficiency is referred to as decompensated cirrhosis. Liver abscesses may cause hypochondria, epigastric, or left upper quadrant stomach pain, among other symptoms. ¹¹

Complications

Injuries to the liver caused by alcohol use may manifest as Portal hypertension causes dilated oesophageal veins, which may lead to oesophageal variceal hemorrhage. Ascites occurs when fluid collects in the abdominal cavity, namely between the peritoneal membrane and the peritoneal effusion.¹² In individuals with cirrhosis and ascites, spontaneous bacterial peritonitis (SBP) arises when an ascitic fluid infection occurs without a clear intra-abdominal medically treatable etiology.¹³

Renal failure occurs in patients with hepatorenal syndrome (HRS), a form of severe liver illness. Patients suffering from severe liver failure may develop hepatic encephalopathy, which is a reversible disorder affecting brain function. This condition is also called portosystemic encephalopathy (PSE). The majority of cases of hepatocellular carcinoma (HCC) occur in patients with cirrhosis or chronic liver disease. An elevation in pressure within the portal venous system is called "portal hypertension." Ten millimeters of mercury is the standard for portal venous pressure. Typical symptoms include ascites, gastrointestinal hemorrhage (which may be fatal), and splenomegaly.¹⁴

In order to treat alcoholic liver damage, abstinence from alcohol is crucial. Addiction to alcohol may be treated with the use of medications like disulfiram, naltrexone, and acamprosate. Deficiencies in vitamins and trace minerals (such as zinc, thiamine, folate, pyridoxine, and vitamin A) should be addressed in order to optimize nitrogen balance. A daily consumption of 35-40 kcal/kg of protein should also be maintained. "Hepatoprotective

agents" are those that keep the liver healthy. Despite having little effect on long-term survival, ursodeoxycholic acid decreases serum alanine transaminase by 35% and aspartate transaminase by 33%, and blood bilirubin by 25%. Because of this, it is used for the treatment of alcoholic liver disease in an off-label manner.¹⁵ For the treatment of hepatic encephalopathy, the amino acid combination of ornithine and aspartate is administered as Hepamerz.¹⁶ Antibiotics are prescribed to patients with liver disease in order to combat bacterial infections, since their immune systems are already compromised, making them more vulnerable to these diseases. Because antibiotics may cause abrupt liver failure, they should be given with care.

MATERIALS AND METHODS

A Cross-sectional study was performed in the Department of General Medicine, GSL General Hospital, Rajahmundry between September 2019 and February 2020. Over six months, 55 patients were monitored. Before being included in the study, each participant was given oral information and a written informed consent form. Patients' case sheets, as well as questionnaires from patients or patient representatives about their alcohol intake, previous health problems, and co-morbidities, were used to collect data. Age, gender, illness prevalence, and medication treatment care offered to patients, particularly antibiotic and hepatoprotective agent use, have all been deemed significant for this research. The information gathered was organized into spreadsheets and evaluated for evaluation and interpretation.

Inclusion Criteria: This research includes patients of both sexes who have been diagnosed with liver disease and are above the age of 20.

Exclusion Criteria: Patients under the age of 20 and those who refuse to comply are excluded from the study.

Statistical Analysis

Numbers and percentages are used to represent categorical data. Microsoft Excel was used to produce the data analysis and graphics. To demonstrate the efficiency of hepatoprotective drugs, the collected data were examined using the statistical techniques mean and

paired *t*-test, and the findings were presented.

RESULTS

During the six-month research period, a total of 55 individuals were evaluated. The findings reveal that

Disease wise distribution

The majority of the patients in this study are males (87.27%) and females (12.73%) alcoholic liver disease (36.36%, $n=20$), chronic liver disease (34.54%, $n=19$), decompensated liver disease (12.72%, $n=7$), liver abscess (16.36%, $n=9$).

Gender wise distribution

This study includes both sexes in which the majority of the patient are males (87.27%) and females (12.73%).

Age-wise distribution

Patients aged 21-30 ($n=5$), 31-40 ($n=13$), and over 40 ($n=37$) had the highest prevalence of liver disease, with the bulk of cases occurring between the ages of 40 and 80.

Habit wise distribution

Alcoholic patients are more prone to liver disease than non-alcoholics. In our study alcoholic percentage is 85.45% and the non-alcoholics percentage is 14.54%.

Symptoms wise distribution

The most commonly observed symptom among liver diseases are jaundice (65.45%), ascites (60%), edema (52.72%), fever and shivering (45.45%), altered sleep pattern (45.45%), breathlessness (32.72%), GI symptoms (26.46%), early bruising/ bleeding (5.45%), confusion (3.63%), clubbing (3.63%).

Complications wise distribution

The most commonly observed complications in liver diseases were ascites (60%), followed by portal hypertension (25.45%), splenomegaly (23.63%), hepatomegaly (20%), hepatic encephalopathy

(16.36%), bleeding disorders (12.72%), oesophageal varices (10.90%), hepatorenal syndrome (5.45%), bacterial peritonitis (3.63%), hepatocellular carcinoma (0%).

Drug wise distribution

The most prescribed drugs in liver diseases are antibiotics (80%), hepatoprotective agents (78.18%), proton pump inhibitors (72.72%), beta blockers (56.36%), vitamins

(50.90%), analgesics (45.45%), anti-hemorrhagic (38.18%), 25% dextrose (27.27%), antiemetics (20%), minerals (18.18%), oral glucose (16.36%), vasoactive agents (12.72%) and represented in (Figure 1).

Utilization of hepatoprotective agents

Among hepatoprotective agents the utilization of silymarin (1.81%, $n=1$), l-ornithine, -l- aspartate (72.72%, $n=40$), ursodeoxycholic acid (76.36%,

$n=42$) depicted in Table 1.

Effects of hepatoprotectives on serum bilirubin, Aspartate Transaminase (AST), and Alanine Transaminase (ALT)

The study showed a drop of 42% of serum bilirubin and 58% of aspartate transaminase and 65% of alanine transaminase in patients having hepatoprotective agents in a time gap of one week. This is shown in Figures 2-4 for serum bilirubin, aspartate transaminase, alanine transaminase and represented in Tables (2-4).

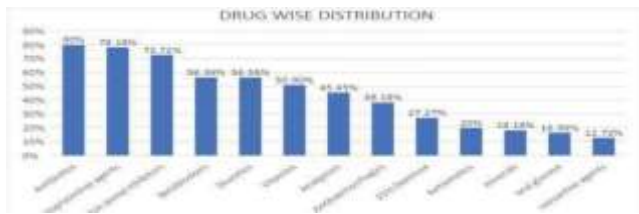


Figure 1: Drug wise distribution.

Hepatoprotective agents	Liver abscess	Alcoholic liver disease	Chronic liver disease	Decompensated liver Disease	Percentage of patients (n=55)
Silymarin	0	1	0	0	1.81% ($n=1$)
L-Ornithine, L-aspartate, L-pancreatin	3	16	15	6	72.72% ($n=40$)
ursodeoxycholic acid	2	20	14	6	76.36% ($n=42$)



Figure 2: Effect of hepatoprotective agents on serum bilirubin level.

Table 2: Analysis of serum bilirubin values before and after administration of hepatoprotective agents.

Table Analyzed	Paired t test data
Column B	After
Vs	Vs
Column A	Before
Paired t test	
P value	< 0.05
Was the pairing significantly effective?	Yes

Table 4: Analysis of alanine transaminase values before and after administration of hepatoprotective agents.

Table Analyzed	Paired t test data
Column B	After
Vs	Vs
Column A	Before
Paired t test	
P value	< 0.05
Was the pairing significantly effective?	Yes

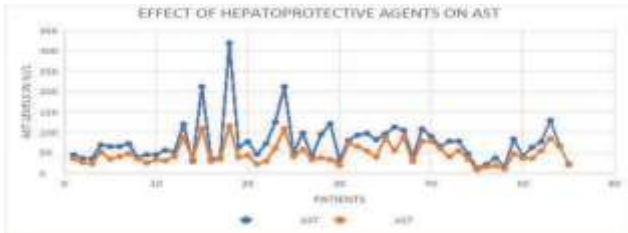


Figure 3: Effect of hepatoprotective agents on aspartate transaminase.

Table 3: Analysis of aspartate transaminase values before and after administration of hepatoprotective agents.

Table Analyzed	Paired t test data
Column B	After
Vs	Vs
Column A	Before
Paired t test	
P value	< 0.05
Was the pairing significantly effective?	Yes

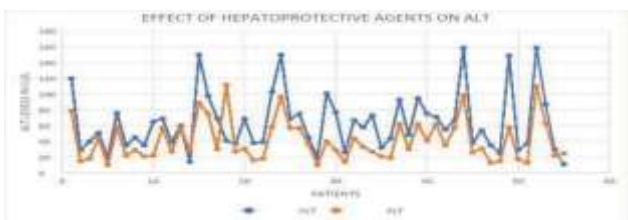


Figure 4: Effect of hepatoprotective agents on alanine transaminase.

DISCUSSION

Patients with liver disease at the GSL hospital in Rajahmundry were surveyed to determine their experiences with liver sickness, antibacterial and hepatoprotective medication usage, and the effectiveness of these medications. The research is a cross-sectional analysis of 55 patients that used alcohol use, health status, and comorbidities questionnaires in addition to patient case sheets.

The results show that alcoholic liver disease, which is mostly caused by excessive alcohol consumption and is the top cause of high mortality and morbidity, is the most common liver illness (36.36%). Hepatic abscess (16.36%), decompensated liver disease (12.72%), and chronic liver disease (34.54%).

Despite the fact that several studies show that women acquire liver disease at a lower alcohol consumption rate and for a shorter duration than males. However, our research only found 12.72 percent females and 87.27 percent men. It is evident that men consume alcohol at a higher rate than women do. People with a history of alcoholism (85%) and those without a drinking problem (15%) were also studied; the former group includes those with a higher risk of liver disorders due to conditions like fatty liver and parasite infections or hepatitis viruses. Additionally, the majority of individuals with liver problems are between the 40-70 age bracket. This makes sense when we consider the patient's history of alcohol use, which begins at a young age (around 10 to 15 years old).

A prospective study evaluating the clinical characteristics of alcoholic liver disease and alcoholic hepatitis was carried out by Christena James et al. Constipation and yellowing of the skin were shown to be prevalent symptoms in patients with alcoholic liver disease.¹⁷ Similarly, our study found that the most common symptoms were fever, chills, swelling, abnormal sleep patterns, shortness of breath, and gastrointestinal symptoms like gas, bloating, pain, nausea, vomiting, constipation, diarrhea, and blood in the stool. Among the least common symptoms, you can notice clubbing or be confused.

In our study, the most commonly observed complications were ascites (60%), portal hypertension (25.45%), splenomegaly (23.63%), hepatomegaly (20%), hepatic encephalopathy (16.36%), bleeding disorders (12.72%), oesophageal varices (10.90%), hepatorenal syndrome (5.45%), bacterial peritonitis (3.63%), and the least observed complication in hepatocellular carcinoma (0%).

Prescription trends in alcoholic liver disease were the subject of a retrospective observational study reported by Kolasani et al. Results showed that antibiotics and hepatoprotectives were most often prescribed, followed by diuretics, intravenous fluids, analgesics, multivitamins, alcohol withdrawal treatments, and propranolol for symptomatic relief.¹⁸ Eighty percent of the prescriptions provided in our research were antibiotics. The most common drugs given to patients depending on their condition were Ceftriaxone, ciprofloxacin, metronidazole, sulbactam + cefoperazone, rifaximin, piperacillin + Tazobactam, and levofloxacin. The second most common kind of medication recommendation is for a hepatoprotective agent, with the most common

ones being ursodeoxycholic acid (76.36%), l-ornithine-l-aspartate (72.72%), and silymarin (1.81%). The proton pump inhibitor pantoprazole is effective in treating acid reflux. Portal hypertension is treated with beta-blockers such as propranolol. Spironolactone and furosemide are examples of diuretics used to treat edema and ascites.

Since nutritional deficiency is common among these people, it is advised that they take multivitamins, thiamine, folic acid, and sodium chloride, among other minerals and vitamins. Analgesics, like paracetamol, alleviate pain. An anti-hemolytic agent is tranexamic acid with vitamin K. One quarter of a percent dextrose is the intravenous fluid most often given. Ondansetron and other anti-emetics are used to treat nausea and vomiting. It is advised to take norepinephrine, octreotide, or terlipressin, which are vasoactive medications.

Hanan Fathima Ahmed used prospective observational study to look at the impact of hepatoprotective drugs in alcoholic liver disease. Ursodeoxycholic acid decreases blood bilirubin by 25%, aspartate transaminase by 33%, and alanine transaminase by 35% in a week. Patients treated with hepatoprotective drugs had a 42% decrease in blood bilirubin, a 58% decrease in aspartate transaminase, and a 65% decrease in alanine transaminase after a week, according to comparable studies.

Limitation

Although our study yields important results, it has limitations. It is a study institution of a relatively uncommon patient group with a smaller number of samples. So, a large group and multi-center study would be valuable to evaluate mortality and quality of life.

CONCLUSION

Liver illnesses, such as alcoholic fatty liver, parasite infection, and hepatitis viruses that infect the liver, are more common in people who have been drinking for a long period, according to the present research. Among all liver diseases, alcoholic liver disease is the most common. It is possible that men's higher alcohol consumption makes them more prone to liver disorders than women, as seen in the results. Most of the people taking part are in their forties and eighties. Because most people with gastrointestinal issues also have similar symptoms, such as fever, chills, shivering, ascites, oedema, shivering, and stomach pain or distension. Ascites,

the most common consequence, and liver carcinoma, the least common complication, are both significantly influenced by the duration of alcohol use. The most effective way to treat liver disease is to make therapeutic lifestyle changes, such as giving up alcohol, as this increases the likelihood of survival throughout the disease's progression. The patient's treatment is centered on managing the symptoms and severity of their disease, while also providing support with alcohol abstinence and dietary needs. The majority of antibiotic prescriptions are for cephalosporins. Because liver disease impairs liver function, hepatoprotectives are also utilized to improve liver function. Researchers found that after one week of using hepatoprotective medicine, serum bilirubin levels dropped 42%, aspartate transaminase levels dropped 58%, and alanine transaminase levels dropped 65%.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATION

Alcoholic Steatohepatitis (ASH), Alkaline Phosphatase (ALP), Alanine Amino Transferase (ALT), Complete Blood Count (CBC), Chronic Liver Disease (CLD), Computerized Tomography (CT), Decompensated Liver Disease (DLD), and the Food and Drug Administration (FDA) are all acronyms that stand for various liver diseases. SGOT and SGPT are acronyms for serum glutamic acid oxidase and serum glutamic pyruvate transaminase, respectively, and they stand for hepatocellular carcinoma (HCC), hepatitis C virus (HCV), hepatic encephalopathy (HE), hepatic renal syndrome (HRS), spontaneous bacterial peritonitis (SBP), and other liver diseases.

SUMMARY

The goal of the study was to determine the

consequences of alcoholic liver disease, as well as the use of antimicrobials and hepatoprotective agents, as well as the efficacy of hepatoprotective drugs in the treatment of liver disorders. 55 patients of both sexes attending a tertiary care center were screened and analyzed, and we found that ascites as the most common complication. We also noticed that cephalosporins are the most commonly used antibiotic and that using hepatoprotective agents for a week results in a decrease in serum bilirubin, aspartate transaminase, and alanine transaminase.

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