

# THE IMPACT OF TERLIPRESSIN ON HEPATORENEAL DISEASE: RESULTS OF AN OBSERVATIONAL, DESCRIPTIVE, AND CROSS-SECTIONAL STUDY DISEASE

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## Abstract

In India, liver cirrhosis ranks as the tenth leading cause of death. Sickness absenteeism and lost man-days are significantly influenced by the cost of treatment. The purpose of this study was to evaluate Terlipressin's effectiveness with albumin to albumin's effectiveness when used alone in hepatorenal syndrome patients. There were two groups each with 80 patients. Albumin was given to Group 1, Terlipressin and albumin to Group 2. The social sciences-specific statistical programme IBM SPSS version 20 was used for all data analysis. We used cross-tabulation and frequency distribution to construct the tables. We display our data's mean, SD, and median (minimum–maximum). To compare continuous variables, the Student's t test and the Mann-Whitney U test were applied. We used Fisher's exact test and Pearson Chi-square to assess categorical variables. The cutoff for statistical significance was  $p < 0.05$ . study comparing MELDs (Model for end stage liver disease). The MELD ratings did not vary between treatment groups, as indicated by the  $p$  value of 0.435. Terlipressin and albumin treatment resulted in a complete response in 60% of patients while having no effect in the other 40%. 85% of patients did not get better on albumin alone, and only 15% of them totally recovered. Having a  $p$  value of 0.000032, statistically significant. More patients in the group that got both terlipressin and albumin had complete responses to therapy. When given together, terlipressin and albumin may be more effective at treating hepatorenal syndrome.

**KEYWORDS:** Model for End Stage Liver Disease, Terlipressin, Albumin.

## INTRODUCTION

The tenth largest cause of death in India, cirrhosis of the liver is also a substantial contributor to the illness burden that is experienced by the community. The cost of treatment not only depletes the nation's financial resources but is also a primary factor in employee absenteeism due to illness, which results in a reduction in the number of working days.<sup>1,2</sup> According to the most recent WHO data, which was published in May 2014, "Deaths due Liver Disease" and its complications in India are responsible for the deaths of nearly 216,865 people. This accounts for nearly 2.44% of all deaths, and India ranks 61 among the other nations of the world in mortality due to cirrhosis.

One of the many things that could go wrong is the development of hepatorenal syndrome, which is very bad for people with cirrhosis. Since HRS is usually a broader form of prerenal azotemia, it can usually be treated and is sometimes even reversible. However, if the disease has progressed, the median amount of time a patient can

expect to live without a liver transplant or treatment with vasoconstrictors is only two weeks.<sup>3</sup> The development of HRS is one of the many processes that might take place in the context of cirrhosis and acute liver injury. People think that splanchnic arterial vasodilation and renal arterial vasoconstriction are two major causes of HRS. Even though the kidneys look normal under a microscope, this causes renal failure to happen over time.<sup>4</sup> This pathogenic idea has changed how HRS is treated, and a number of studies have been done to look at how well vasoconstrictors, especially vasopressin analogues, work to increase the effective arterial blood volume.<sup>5</sup> According to this research, people diagnosed with HRS who take vasopressin analogues have an improvement in their renal function. The information that is accessible is restricted, however, because the studies that were conducted were either retrospective, had a low number of patients, or were not randomized.

For this reason, the current study was designed to investigate the impact of terlipressin treatment on the renal function and overall survival of patients diagnosed with cirrhosis and HRS.

## **AIM:**

The goal of this study was to compare how well Terlipressin's works with albumin to how well albumin works alone in people with hepatorenal syndrome.

## **SOURCE OF SAMPLE:**

This was a study that was conducted inside of a medical facility, namely at a specific site, with participants consisting of patients who were currently being treated in an intensive care unit (ICU).

## **INCLUSION CRITERIA**

### **MAJOR CRITERIA**

- i. "Chronic or acute liver disease with advanced hepatic failure and portal hypertension.
- ii. Low GFR as indicated by serum creatinine  $> 1.5$  mg/dL or 24 hr. creatinine clearance  $< 40$  mL/min.
- iii. Absence of shock, on-going bacterial infection, and current or recent treatment with nephrotoxic drugs and absence of gastrointestinal fluid losses (repeated vomiting or intense diarrhea).
- iv. No sustained improvement in renal function (decrease in serum creatinine  $\leq 1.5$  mg/dL or increase in creatinine clearance to  $\geq 40$  mL/min) following diuretic withdrawal for 48 hrs. and expansion of plasma volume with 1.5 L of isotonic saline.
- v. No sonographic evidence of obstructiveuropathy or parenchymal renal disease".

### **ADDITIONAL CRITERIA**

1. Serum sodium  $< 130$  mEq/L
2. Cirrhosis with ascites
3. Serum creatinine  $> 133$   $\mu$ mol/L (1.5 mg/dL)
4. No current or recent treatment with nephrotoxic drugs

## EXCLUSION CRITERIA

The exclusion criteria were as follows:

“Presence of severe extrahepatic condition, including cardiovascular (coronary and/or peripheral arterial disease) and neurological diseases, septic shock, and hepato cellular carcinoma”.

## STUDY DESIGN:

This was an observational, cross-sectional study with descriptive aspects.

## STUDY PERIOD:

The current research was conducted from October 2019 to March 2021, a span of 18 months.

## MATERIAL & METHOD

The 80 patients were randomly divided into two groups of 40. Albumin was given to Group 1, while Terlipressin and albumin were given to Group 2.

## SAMPLE SIZE:

About 80 people with Hepatorenal Syndrome took part in the study.

## STASTICAL ANALYSIS

IBM SPSS version 20, a statistical application tailored to the social sciences, was used at every stage of the analysis process. The tables were made using a frequency distribution and a cross-tabulation. The data's mean, standard deviation (SD), and median are displayed in that order (minimum–maximum). The data was analysed and comparisons between continuous variables were made using both the student's t test and the Mann-Whitney U test. To examine the categorical variables, we employed both the Pearson Chi-square and Fisher's exact tests. The cutoff for statistical significance was chosen at a p-value of less than 0.05.

## RESULT

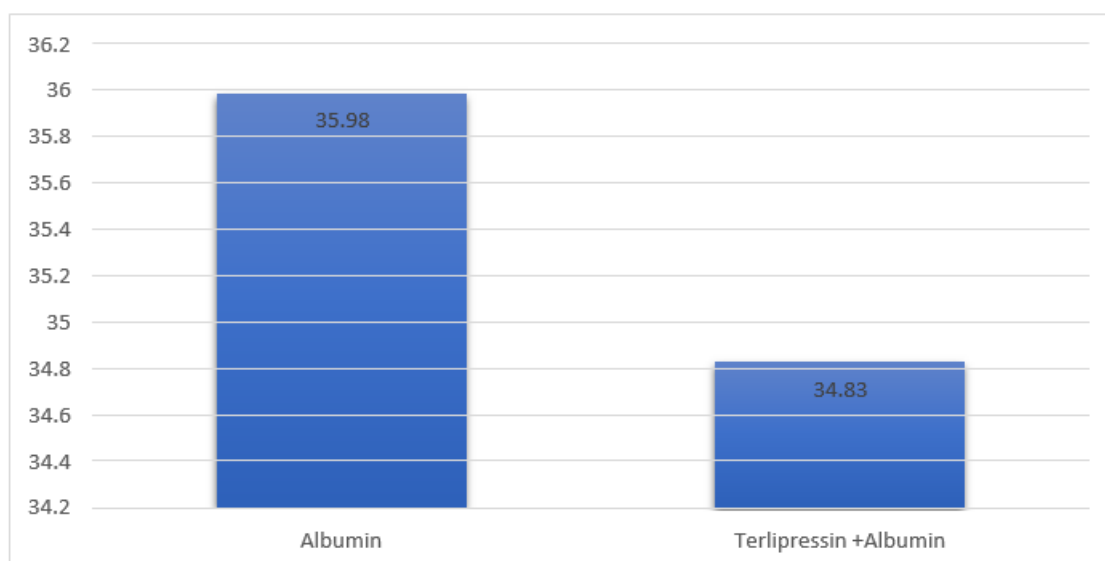
### STUDY OF COMPARING MELD SCORE IN BOTH THE GROUPS

Analyzing the similarity between MELD scores is the current study's (Model for end stage liver disease). There was no significant difference in MELD scores between the two groups, as indicated by the insignificant p value of 0.435.

Table 1: Study of Comparing MELD score in both the groups.

MELD	Treatment		Total	P value
	Albumin	Terlipressin +Albumin		
Mean	35.98	34.83	35.48	0.435
SD	2.85	3.98	3.42	

Figure 1: Comparing MELD



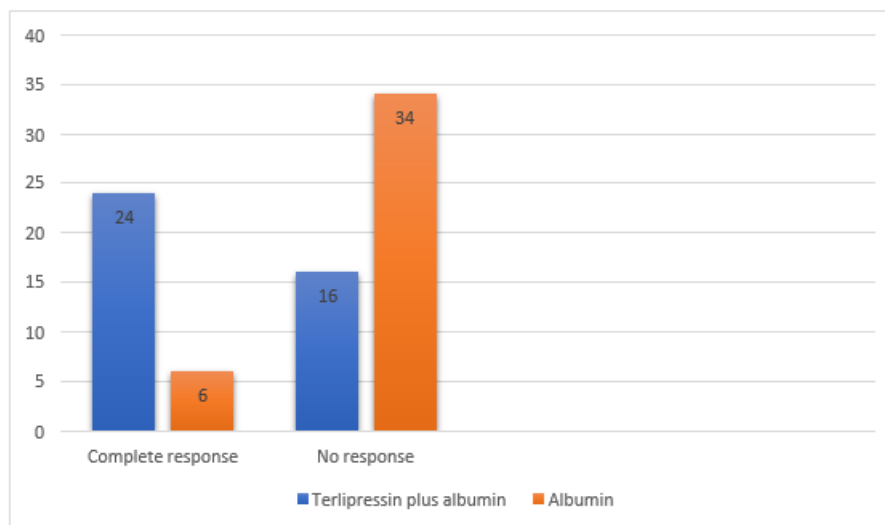
### STUDY OF COMPARING TREATMENT RESPONSE IN BOTH GROUPS

In the current study, “60% of the patients who were given a combination of terlipressin and albumin had a complete response, while only 40% of the patients had no reaction. The majority of those who were given albumin alone did not show any signs of improvement (85%), and only 15% showed a full response to the medication. With a p value of 0.000032, the comparison was determined to be statistically significant”.

Table 2: Comparing Treatment Response

Treatment	Complete response (%)	No response (%)	total	'P' value
<b>Terlipressin plus albumin</b>	24(60)	16(40)	40	0.000032
<b>Albumin</b>	6(15)	34(85)	40	
	30(37.5)	50(62.5)	80	

Figure 2: Comparing Treatment Response



## DISCUSSION

“Acute kidney injury, especially hepatorenal syndrome type 1 (HRS-1), is a strong predictor of death risk in patients with advanced liver disease and hepatorenal syndrome (HRS), one of the worst effects of advanced liver disease.<sup>6,7</sup> It is possible that reversing HRS-1 before a transplant will improve short-term patient survival before the transplant and reduce the need for renal replacement therapy after the transplant.<sup>8</sup> Terlipressin is a synthetic vasopressin analogue that works as a vasoconstrictor in both the systemic and splanchnic blood vessels.<sup>9</sup> Because of this activity, the amount of blood that flows through the portal veins is reduced, which in turn reduces the amount of hypertension that occurs in the portal system. This is the primary source of the hemodynamic abnormalities that are associated with advanced cirrhosis. Systemic hemodynamics are improved as a result of the ensuing shift of circulatory volume from the splanchnic circulation to the systemic circulation, which also results in an increase in renal perfusion pressure”.<sup>10,11</sup>

As a result of the, “increased effective arterial volume, the compensatory renal and systemic vasoconstrictor activities are reduced, which leads to an even greater improvement in renal hemodynamics in these individuals. Previous randomized, multicenter, placebo-controlled trials of varied sizes have been conducted in order to examine the efficacy and safety of terlipressin in patients who have been diagnosed with HRS-1”.<sup>12,13,14</sup>

Current study looked at how patients with Hepatorenal Syndrome responded to treatment with either albumin alone or albumin plus terlipressin. This was a hospital-based, cross-sectional, descriptive observational study that was done on patients admitted to our institute's Intensive Care Unit (ICU) over the course of 18 months,

from October 2019 to March 2021.

During the course of the trial, “we compared the MELD scores of both groups. The negligible p value of 0.435 reveals that there was not a meaningful difference obtained in terms of MELD in either of the treatment groups. The findings of the current study were found to be comparable to those of a study that was conducted by Martín-Llahí M et al, which stated that there were no significant differences between the 2 groups with respect to the number of patients who were alive at 3 months, which was 6 in the group that received terlipressin and albumin (27%) and 4 in the group that received albumin (19%) (P =0.7).<sup>3</sup> In a study that was conducted in a similar manner, Wong F. and colleagues found that the percentage of patients who received a liver transplant within 90 days after the first dose was lower in the terlipressin group than it was in the placebo group. This was the case despite the fact that there was no difference in MELD score between the two groups while the treatment was being administered”.<sup>15</sup>

## CONCLUSION

The number of people who responded completely to treatment was much higher in the group that got both terlipressin and albumin than in the group that got only albumin. Because of this, we have come to realize that terlipressin and albumin may be a better way to treat hepatorenal syndrome when used together.

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