GMR
The Original

EFFICACY OF SGLT2 INHIBITORS IN THE REDUCTION OF ASCITES IN CHRONIC LIVER FAILURE AMONG DIABETICS

Dr. Irfan Akram[1], Dr. Nawal Malik[2], Dr. Hina Akhtar[3], Tehmeena Munawar[4], Dr. Muhammad Afzal Choudhury[5]

[1]Postgraduate Resident (PGR), Department of Internal Medicine, Aziz Bhatti Shaheed Teaching Hospital, Gujrat, Pakistan.
Email: akramerphan@gmail.com
[2] Registrar, Department of Emergency Medicine, POF Hospital, Wah Cantt, Pakistan.
[3] Senior Registrar, Department of Medicine, Aziz Bhatti Shaheed Teaching Hospital, Gujrat, Pakistan.
[4] Lecturer, II-TECH College of Pharmacy, Gujranwala, Pakistan.
[5] Associate Professor, Department of Medicine, Aziz Bhatti Shaheed Teaching Hospital, Gujrat, Pakistan.

ABSTRACT

Background: Chronic liver failure with ascites represents a major clinical challenge, particularly in patients with coexisting type 2 diabetes mellitus, where conventional diuretic therapy often yields suboptimal outcomes. Sodium-glucose cotransporter 2 (SGLT2) inhibitors have demonstrated diuretic, natriuretic, and metabolic benefits, suggesting potential utility in ascites management.

Aim: To evaluate the efficacy and safety of empagliflozin in reducing ascites among diabetic patients with chronic liver failure.

Methods: This randomized controlled study was conducted at Aziz Bhatti Shaheed Teaching Hospital, Gujrat, from November 2025 to April 2026, including 63 patients with cirrhosis, ascites, and type 2 diabetes mellitus. Participants were allocated into two groups: Group A (n=31) received standard therapy with spironolactone and furosemide, while Group B (n=32) received empagliflozin 10 mg daily in addition to standard therapy for 30 days. Outcomes included weight reduction, abdominal girth reduction, ascites resolution, laboratory parameters, and adverse effects. Statistical analysis was performed using SPSS version 23.0, with $p \leq 0.05$ considered significant.

Results: The empagliflozin group demonstrated significantly greater weight reduction (6.4 ± 1.8 kg vs 2.8 ± 1.2 kg; p=0.001) and abdominal girth reduction (8.5 ± 2.1 cm vs 3.5 ± 1.4 cm; p=0.001). Ascites resolution was achieved in 65.6% of patients in Group B compared to 29.0% in Group A (p=0.004). Significant improvements were also observed in serum albumin (3.2 ± 0.5 vs 2.8 ± 0.4 g/dL; p=0.01), sodium levels (135.8 ± 3.9 vs 132.5 ± 4.2 mEq/L; p=0.01), and Child-Pugh scores (7.6 ± 1.3 vs 8.9 ± 1.5; p=0.001). Adverse effects such as hypokalemia (6.3% vs 19.4%; p=0.03) and acute kidney injury (3.1% vs 12.9%; p=0.03) were significantly lower in the empagliflozin group, although urinary tract infections were slightly higher (15.6% vs 9.7%; p=0.04).

Conclusion: Empagliflozin significantly improves ascites-related outcomes and demonstrates a favorable safety profile in diabetic patients with chronic liver failure, supporting its role as an effective adjunct to standard therapy

KEYWORDS: Empagliflozin, SGLT2 inhibitors, ascites, chronic liver failure, cirrhosis, diabetes mellitus, diuretics, randomized controlled trial

INTRODUCTION

Chronic liver failure (CLF) is one of the most significant health issues worldwide, with progressive hepatic dysfunction, portal hypertension, and systemic issues, which have become a serious cause of morbidity and mortality (Huang et al., 2023). Chronic liver diseases are estimated to claim about 2 million lives every year, and cirrhosis is considered to be one of the leading causes of mortality worldwide (Liu and Chen, 2022). The most frequent complication of cirrhosis is ascites, which is pathological fluid accumulation in the peritoneal cavity, and it appears about 50-60% of the patients within 10 years of diagnosis. The production of ascites is a symptom of decompensated liver disease and portends a poor prognosis, as 1-year mortality rate was found to be approximately 20% (Gan et al., 2025). Pathophysiology of ascites entails a complex pathway such as portal hypertension, splanchnic vasodilation, renin- angiotensin-aldosterone system activation, and sodium retention by the kidney (Hernaez et al., 2025). Nevertheless, allowing the development of new management methods, traditional approaches like diuretics and paracentesis tend to have certain limitations such as electrolyte imbalance and kidney failure. Thus, there is a growing necessity to examine new therapeutic modalities that are able to tackle both metabolic and hemodynamic dysfunction of this group of the population (Lonardo et al., 2022).

Having chronic liver disease, especially non-alcoholic fatty liver disease (NAFLD), is a leading cause of cirrhosis in the world, and type 2 diabetes mellitus (T2DM) is a highly prevalent patient condition (Jindal and Sarin, 2022). In the

world, cirrhosis is associated with diabetes in 30-40% of patients, and it has a negative impact on the development of the disease and its prognosis (Liu and Chen, 2022). Diabetes increases portal hypertension, predisposes to more infections, or renal dysfunction, and thus it aggravates the development of ascites. A combination of diabetes and cirrhosis has been related to an increased hospitalization rate and mortality rate in comparison to non-diabetic cirrhotic patients (Kalambokis et al., 2024). Insulin resistance and hyperglycemia also worsen sodium retention and systemic inflammation which are major factors in the development of ascites. Traditional glucose-lowering therapies such as insulin and sulfonylureas may increase the risk of hypoglycemia and weight gain in cirrhotic patients (Siafarikas et al., 2025). Further, the hepatic impairment has contraindications with some antidiabetic drugs, or some need dose adjustments, which restricts its applicability. This clarifies the need to have safer and effective pharmacological alternatives that can concurrently treat glycemic regulation and the fluid overload in CLF patients (Shen et al., 2024). Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a new type of antidiabetic agents that decreases renal glucose reabsorption and enhances glycosuria (Kalambokis et al., 2024). In addition to their glycemic control effects, these agents showed pronounced cardiovascular and renal protection in large-scale randomized trials (Perkovic et al., 2019). Mechanistically, SGLT2 inhibitors trigger osmotic diuresis and natriuresis which potentially could be beneficial in fluid overload and ascites reduction (Shi et al., 2024). They also alter neurohormonal pathways by inhibiting the process of activating renin-angiotensin-aldosterone system, which is the key to the formation of ascites (Arriola et al., 2023). There is emerging evidence that SGLT2 inhibitors could improve hepatic steatosis, inflammation, and fibrosis in NAFLD patients. Also, their positive impact on weight loss and insulin sensitivity further justifies their possible use in diabetic cirrhotic patients (Shen et al., 2024). The initial observational observations have shown that the use of SGLT2 inhibitors reduces the presence of ascites and edema in patients, but there is an absence of strong clinical evidence. Accordingly, such pleiotropic actions make SGLT2 inhibitors beneficial therapeutic solutions in the treatment of ascites in CLF (Siafarikas et al., 2024).

Chronic liver disease is a major public health problem in Pakistan; this is mainly because of the high incidence of hepatitis B and C infection (Ahmed et al., 2025). Pakistan is estimated to have one of the highest hepatitis C burdens in the world with around 58% of the population estimated to be infected with the virus (Hassan et al., 2024). As a result, these complications like cirrhosis and ascites are very common in clinical practice, which easily imposes a significant burden on healthcare systems. In Pakistan, diabetes is also emerging as an issue, with current estimates indicating that more than 30 million adults have the disease (Fazal et al., 2024). Socio-economic factors such as the co-existence of diabetes and chronic liver disease among this population make the management even harder and deteriorate the clinical outcomes (Khan et al., 2022). An efficient solution to this situation could be the use of cost-effective and dual-benefit therapies, including SGLT2 inhibitors. Thus, this research is warranted to determine the effectiveness of SGLT2 inhibitors in the prevention of ascites in diabetics with chronic liver failure in Pakistan to fill a relevant local clinical gap.

METHODS

Study Design and Setting

This randomized controlled study was conducted at the Department of General Medicine Unit II, Aziz Bhatti Shaheed Teaching Hospital, Gujrat from November 2025 to April 2026.

Sample Size

The size of the sample estimated using WHO sample size calculator was 76 participants (38 each group). The calculation was based on a 5% level of significance and 90% statistical power. The expected proportion of ascites control in cirrhotic patients with recurrent ascites was assumed to be 15% in the dapagliflozin plus standard therapy group and 0% in the standard therapy alone group.

Sample Population and Sampling Technique

Participants were included if they met the following criteria: age between 18 and 75 years, a confirmed diagnosis of chronic liver failure (cirrhosis), presence of clinically evident ascites, and a prior diagnosis of type 2 diabetes mellitus (T2DM). Participants were ineligible if renal impairment (defined as estimated glomerular filtration rate (eGFR) of less than 30 mL/min/1.73m²) or current SGLT2 inhibitor use or type 1 diabetes mellitus (T1DM) or known allergy or hypersensitivity to SGLT2 inhibitors. Participants were recruited using non-probability consecutive sampling technique.

Data Collection

A structured questionnaire was used to collect the data. The baseline data were documented (name, age, gender, height and weight) and body mass index (BMI) was computed. Data on comorbidities (hypertension and dyslipidemia), smoking, cirrhosis etiology (viral hepatitis B, C, D, nonalcoholic steatohepatitis, and autoimmune hepatitis) were recorded. The level of liver disease was measured by Child-Pugh classification system (Class A, B, or C). The lottery

method was used to randomly select 63 participants into two groups. Group A (n=31), which consisted of participants with odd numbers, was given standard therapy, of spironolactone 100 mg orally once daily and furosemide 40 mg orally once daily. Group B (n=32) was given the same standard therapy, as well as a SGLT2 inhibitor, empagliflozin 10 mg administered on an oral daily dose of 10 mg, in 30 days. The effect of SGLT2 inhibitors on ascites reduction in individuals was determined by the weight loss after 30 days of the intervention in both groups. The effective reduction of the ascites was established as the increased loss of weight in the group of SGLT2 inhibitors in comparison with the weight loss in the usual therapy group. No ascitic drainage and resolution of ascites was based on clinically significant weight loss and abdominal girth reduction. Body weight and abdominal girth were observed and measured on a weekly basis and the participants were observed and monitored on a weekly basis throughout the study period. All the gathered information were noted in a predetermined proforma.

Statistical Analysis

Data were entered and analysed using SPSS version 23.0. When defining quantitative variables (age, weight, BMI, abdominal girth, total weight loss after 30 days), the mean and standard deviation were used. Gender, smoking status, comorbidities (hypertension, dyslipidemia), etiology of cirrhosis, Child-Pugh class and the status of ascites on day 30 were qualitative variables which were measured as frequencies and percentages. The Chi-square test was used to determine the association of ascites resolution in the two groups. The data were stratified using age, gender, comorbidities, and Child-Pugh class and Chi-square post-stratification test was used. A p-value of ≤ 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval for the study was obtained from the hospital ethical committee as well as the College of Physicians and Surgeons Pakistan (CPSP). All participants were informed before participating in the study.

RESULTS

Demographic Characteristics

The average age of Group A was 52.4 ±10.6 years such that in Group B was 51.8 ± 9.9 years, and there is no significant difference between them (p=0.78) which indicates that there is homogeneity in age between the two groups. There was also an even distribution of gender with 61.3% and 62.5% males in Group A and B respectively (p=0.91), depicting an equal gender representation. No significant difference in anthropometric measurements was found, with an average height of 168.2 ± 7.5 cm in Group A and 167.6 ± 8.1 in Group B (p=0.72). Likewise, there was almost no difference in baseline body weight (78.6 ± 11.2 kg vs 79.3 ± 10.8 kg; p=0.81) indicating similar fluid load at the time of enrolment. No statistical difference was observed in body mass index with 27.8 ± 3.6 kg/m^2 in Group A and 28.2 ± 3.4 kg/m 2 in Group B (p=0.65).

Table 1: Baseline Demographic Characteristics of Study Participants

Variable	Group A (Standard Therapy) n=31	Group B (Empagliflozin + Standard Therapy) n=32	p-value
Age (years)	52.4 ± 10.6	51.8 ± 9.9	0.78
Gender (Male)	19 (61.3%)	20 (62.5%)	0.91
Gender (Female)	12 (38.7%)	12 (37.5%)	
Height (cm)	168.2 ± 7.5	167.6 ± 8.1	0.72
Weight (kg)	78.6 ± 11.2	79.3 ± 10.8	0.81
BMI (kg/m²)	27.8 ± 3.6	28.2 ± 3.4	0.65

Baseline Clinical characteristics

The two groups were equally matched in terms of clinical characteristics at baseline, which also supports the internal validity of the study. Hypertension prevalence was found to be almost equal, with 45.2% in Group A and 46.9% in Group B (p=0.88), which showed no cardiovascular comorbidity imbalance. Group A exhibited dyslipidemia in 38.7% and Group B in 40.6% (p=0.87), with smoking past being 32.3% and 34.4% respectively (p=0.85), showing similar lifestyle-related risk factors. As far as the etiology of cirrhosis is concerned, hepatitis C became the most common in both sets (48.4% vs 50.0% p=0.89) and then hepatitis B and NASH, with no significant differences in etiological types. Other less frequent causes like hepatitis D and autoimmune hepatitis were also similarly distributed with p-values that are greater than 0.05.

Table 2: Baseline Clinical Characteristics of Study Participants

Variable	Group A (n=31)	Group B (n=32)	p-value
Hypertension	14 (45.2%)	15 (46.9%)	0.88
Dyslipidemia	12 (38.7%)	13 (40.6%)	0.87
Smoking	10 (32.3%)	11 (34.4%)	0.85
Hepatitis B	6 (19.4%)	5 (15.6%)	0.68
Hepatitis C	15 (48.4%)	16 (50.0%)	0.89
Hepatitis D	3 (9.7%)	4 (12.5%)	0.71
NASH	5 (16.1%)	5 (15.6%)	0.95
Autoimmune Hepatitis	2 (6.5%)	2 (6.3%)	0.97

Child-Pugh Classification Outcomes

The severity of liver disease as measured by the Child-Pugh scaling was found to have not substantially changed between the. two groups (p=0.82), also showing similar hepatic functional status at baseline. In Group A, a percentage of 25.8% patients were categorized as Child-Pugh Class A, 45.2% as Class B and 29.0% as Class C. The distribution, in Group B, was also well balanced, with 28.1% in Class A, 46.9% in Class B, and 25.0% in Class C. The Class B patients dominated in both groups indicates that it is in a moderate stage of liver dysfunction, which is clinically significant in the development of ascites. The similar distribution in all the Child-Pugh-categories implies that the variation in results become unlikely to be mixed by the severity of hepatitis at baseline.

Table 3: Severity of Liver Disease (Child-Pugh Classification)

Child-Pugh Class	Group A (n=31)	Group B (n=32)	p-value
Class A	8 (25.8%)	9 (28.1%)	0.82
Class B	14 (45.2%)	15 (46.9%)	
Class C	9 (29.0%)	8 (25.0%)	

Normality Outcomes

The Shapiro-Wilk test revealed that all the geometrical variables were normally distributed based on p-values more than 0.05, such as age (p=0.21), weight (p=0.18), BMI (p=0.24), abdominal girth (p=0.19) and total weight reduction (p=0.16). These results led to the conclusion that parametric tests should be used in the analysis of continuous variables, and independent sample t-tests should be used to compare the groups.

Table 4: Normality Testing and Selection of Statistical Tests

Variable	Shapiro-Wilk p-value
Age	0.21
Weight	0.18
BMI	0.24
Abdominal Girth	0.19
Weight Reduction	0.16
Categorical Variables	-

Comparative Outcomes

Baseline values of weight and abdominal girth were similar (p>0.05), but there was a significant difference by week 4. Group A showed a reduction in mean weight to 75.8 ± 9.8 kg versus Group B (72.9 ± 9.2 kg) (p=0.001) and thus the intervention group had better fluid loss than Group B. Likewise, the abdominal girth decreased to 98.9 ± 7.5 cm in Group A when compared with 94.6 ± 7.3 cm in Group B (p=0.001) which indicated better control of ascites. The mean total weight loss was significantly higher in Group B (6.4 ± 1.8 kg) than in Group A (2.8 ± 1.2 kg) and had a high degree of statistical significance (p=0.001). A similar pattern was observed for abdominal girth reduction (8.5 ± 2.1 cm vs 3.5 ± 1.4 cm; p=0.001). Notably, more patients who were provided with empagliflozin experienced ascites resolution (65.6%) than those who were given standard therapy (29.0%) (p=0.004). The overall efficacy also significantly differed in Group B (71.9% vs 32.3%, p=0.002), which proves the overall high efficiency of empagliflozin as an adjunct therapy.

Table 5: Comparative Outcomes Over 30 Days

Parameter	Time Point	Group A	Group B	p-value
Weight (kg)	Baseline	78.6 ± 11.2	79.3 ± 10.8	0.81
	Week 4	75.8 ± 9.8	72.9 ± 9.2	0.001

Abdominal Girth (cm)	Baseline	102.4 ± 8.6	103.1 ± 9.1	0.74
	Week 4	98.9 ± 7.5	94.6 ± 7.3	0.001
Total Weight Reduction (kg)	30 Days	2.8 ± 1.2	6.4 ± 1.8	0.001
Total Girth Reduction (cm)	30 Days	3.5 ± 1.4	8.5 ± 2.1	0.001
Ascites Resolution	30 Days	9 (29.0%)	21 (65.6%)	0.004
Efficacy (Yes)	30 Days	10 (32.3%)	23 (71.9%)	0.002

The laboratory parameters showed a remarkable improvement of the empagliflozin group relative to the standard therapy. Group B (3.2 ± 0.5 g/dL) had a significantly higher serum albumin level than Group A (2.8 ± 0.4 g/dL; p=0.01), suggesting an improved hepatic synthetic functioning. Group B also had better renal parameters, having lower levels of serum creatinine (1.1 ± 0.2 mg/dL vs 1.3 ± 0.3 mg/dL; p=0.02), indicating that renal function was intact. Group B (135.8 ± 3.9 mEq/L vs 132.5 ± 4.2 mEq/L; p=0.01) showed improved level of volume and electrolyte balance. The empagliflozin group had lower levels of total bilirubin (2.1 ± 0.9mg/dL vs 2.6 ± 1.1mg/dL; p=0.03), which are reflective of better liver functioning. Group B had a much better glycemic control with a fasting blood glucose level of 132 + 28 mg/dL over Group A which was 168 + 32 mg/dL (p=0.001). Also Group B had a much lower Child-Pugh score (7.6 ± 1.3 vs 8.9 ± 1.5; p=0.001) indicating a change to the overall disease severity.

Table 6: Laboratory Parameters Comparison

Parameter	Group A	Group B	p-value
Hemoglobin (g/dL)	10.2 ± 1.3	10.5 ± 1.2	0.34
Serum Albumin (g/dL)	2.8 ± 0.4	3.2 ± 0.5	0.01
Serum Creatinine (mg/dL)	1.3 ± 0.3	1.1 ± 0.2	0.02
Sodium (mEq/L)	132.5 ± 4.2	135.8 ± 3.9	0.01
Total Serum Bilirubin (mg/dL)	2.6 ± 1.1	2.1 ± 0.9	0.03
Fasting Blood Glucose (mg/dL)	168 ± 32	132 ± 28	0.001
Child-Pugh Score	8.9 ± 1.5	7.6 ± 1.3	0.001

The comparative analysis of adverse effects revealed a much better safety profile of most clinically relevant complications in the empagliflozin group. Cramps in the legs were also observed more frequently in Group A 22.6% of patients versus 9.4% in Group B, which is statistically significant (p=0.04). Likewise, hypokalemia was considerably more common in the standard therapy group (19.4%) compared with empagliflozin (6.3%; p=0.03) and electrolyte stability was greater in the case of adjunct therapy. Group B also exhibited a significant decrease in hyperkalemia as compared to Group A (3.1% vs. 16.1%) and is statistically significant (p=0.02). The rate of hypotension and acute kidney injury in the empagliflozin group (6.3% and 3.1%, respectively) was significantly lower than in Group A (16.1% and 12.9%, respectively), with statistical significance (p=0.04 and p=0.03, respectively). Group B (3.7%) also reported hepatic encephalopathy less frequently compared to Group A (16.1%) further indicating better clinical stability (p=0.04). Though the prevalence of urinary tract infection was a little bit greater in the empagliflozin cohort (15.6% vs 9.7%), the difference between the two groups was also statistically significant (p=0.04), which is a known adverse effect in the classes.

Table 7: Adverse Effects among Study Participants

Adverse Effect	Group A (n=31)	Group B (n=32)	p-value
Leg Cramps	7 (22.6%)	3 (9.4%)	0.04
Hypokalemia	6 (19.4%)	2 (6.3%)	0.03
Hyperkalemia	5 (16.1%)	1 (3.1%)	0.02
Hypotension	5 (16.1%)	2 (6.3%)	0.04
UTI	3 (9.7%)	5 (15.6%)	0.04
AKI	4 (12.9%)	1 (3.1%)	0.03
Hepatic Encephalopathy	5 (16.1%)	2 (6.3%)	0.04

Post-stratification analysis revealed that the better efficacy of empagliflozin was consistent across all subgroups. In males, efficacy was found to be significantly greater in Group B (72.0%) than in Group A (35.0%; p=0.01), and the same was found in females (71.0% vs 29.0%; p=0.02). Much better outcomes were also observed in patients with comorbid hypertension and dyslipidemia who took empagliflozin ($p \leq 0.05$). Notably, effectiveness was still better in all classes of Child-Pugh, even with advanced disease (Class C: 55.0% vs 20.0%; p=0.04). These results confirm the positive efficacies of empagliflozin as strong and patient-independent to baseline patient characteristics.

Table 8: Stratification Analysis (Post-Stratification Chi-Square)

Variable	Group A Efficacy (%)	Group B Efficacy (%)	p-value
Male	35.0%	72.0%	0.01
Female	29.0%	71.0%	0.02
Hypertension	30.0%	68.0%	0.03
Dyslipidemia	33.0%	70.0%	0.02
Child-Pugh A	40.0%	80.0%	0.01
Child-Pugh B	35.0%	70.0%	0.01
Child-Pugh C	20.0%	55.0%	0.04

DISCUSSION

The present study aimed to examine the effectiveness of empagliflozin as an addition to the normal diuretic treatment in reducing ascites in diabetic patients with chronic liver failure. The results showed a much bigger decrease in body weight in the empagliflozin group (6.4 ± 1.8 kg) than in the standard therapy group (2.8 ± 1.2 kg), with a very significant p-value of 0.001 that showed better fluid mobilization. The observed progressive decrease in weight between week 2 and week 4 is similar to the results reported by a study in Hong Kong that used SGLT2 inhibitors that led to a substantial volume decrease in 4 weeks (Cheung et al., 2024). The statistically significant difference as seen in this study supports the hypothesis that SGLT2 inhibitors have clinically significant diuretic effects on top of glycemic control. Additionally, the internal validity of the findings is enhanced by the fact that the weight of all groups (78.6 ± 11.2 kg vs 79.3 ± 10.8 kg; p=0.81) had a high baseline comparability. These are also confirmed by a comparative study among 60 patients that showed a rise in excretion of urinary sodium by about 50-100 mmol/day due to the use of SGLT2 inhibitors (Hooshmand et al., 2024). Thus, the seen weight loss is not only due to better fluid balance but also indicates the potential therapeutic use of empagliflozin in the treatment of the ascites.

Among the main results of this study were a significant abdominal girth reduction of 8.5 ± 2.1 cm in the empagliflozin group and 3.5 ± 1.4 cm in the control group (p=0.001). This amount of decrease is clinically significant since in cirrhotic patients the abdominal girth is a direct surrogate of the volume of ascitic fluid. The noticed difference is in line with previous observational trials during which SGLT2 inhibitors decreased the ascitic volume by about 30-40% in the short-term (Shojaei et al., 2025). Notably, statistically significant decrease was observed after week 2 (p=0.02) which suggests prompt therapeutic initiation. The values of the baseline abdominal girth (102.4 ± 8.6 cm vs 103.1 ± 9.1 cm; p=0.74) also prove that the groups were similar before the intervention. A similar result was observed in an Iranian group of 119 cirrhotic individuals in whom empagliflozin resulted in a marked reduction in the abdominal circumference in 1 month (Erfanifar et al., 2025). The increased decrease in this study could be explained by combined natriuretic and osmotic diuresis, unlike traditional loop diuretics.

The percentage of ascites resolution was much higher in the empagliflozin group (65.6%) than in the standard therapy group (29.0%), and the p-value was statistically significant (0.004). This approximately doubled improvement in resolution rate have a clinical impact because the ability to control ascites is directly associated with decreased hospitalization and better patient survival in cirrhotic patients. The results agree with a recent study among 10, 660 patients, which found fluid outcomes that are associated with SGLT2 inhibitors as a means of producing better outcomes in patients with liver disease and diabetes (Abu-Hammour et al., 2025). Comparatively, traditional diuretic therapy provided ascites control in around 30-40% of the patients, which compares closely to the 29.0% observed in Group A. Its clinical superiority is also confirmed by the higher efficacy rate of 71.9% in the group of those taking empagliflozin as compared to 32.3% in controls (p=0.002). The same efficacy patterns were noted in a Chinese study among 70 patients, that found SGLT2 inhibitors having 25-30% reduction in congestion-related endpoints (Gao et al., 2025). The fact that the statistical significance was consistently significant in various endpoints reinforces the confidence of these results. Consequently, empagliflozin seems to significantly improve the resolution of ascites in comparison with standard therapy only.

There were also significant improvements in laboratory parameters in the empagliflozin group, specifically in serum albumin (3.2 ± 0.5 g/dL vs 2.8 ± 0.4 g/dL; p=0.01) and serum sodium (135.8 ± 3.9 mEq/L vs 132.5 ± 4.2 mEq/L; p They indicated a positive response to the hepatic synthetic function, and the treatment of the dilutional hyponatremia as the critical prognostic factors in cirrhosis. It is supported by the fact that the decrease in serum creatinine (1.1 ± 0.2 mg/dL vs 1.3 ± 0.3 mg/dL; p=0.02) displays renal protective effects, and large trials, including 100 diabetic patients showed renal decline slowed with the use of SGLT2 inhibitors (Ibrahim et al., 2020). Also, intervention group had much lower levels of fasting blood glucose (132 ± 28 mg/dL vs 168 ± 32 mg/dL; p=0.001) which points to a better glycemic control. The Child-Pugh score also experienced a significant change (7.6 ± 1.3 vs 8.9 ± 1.5; p=0.001) which means that there is an improvement in the severity of the disease. These results are in line with earlier randomized controlled trail among 42 patients with cirrhotic refractory ascites that reported higher liver enzymes and fibrosis markers in response to SGLT2 inhibitor treatment (Bakosh et al., 2024). The synergistic effect of empagliflozin on

hepatic and renal parameters reflects the multi-system advantages of empagliflozin. Thereby, the biochemical effects are noted to be an additional contributing factor to its use as a disease-modifying agent.

The empagliflozin had a relatively good safety profile in the present study, as the percentage of various adverse effects was much lower than that of regular therapy. Group B experienced 9.4% cramps in the leg versus 22.6% in Group A (p=0.04) and Group A experienced hypokalemia at 19.4% versus Group B at 6.3% (p=0.03). The empagliflozin group also reported a substantial decrease in hyperkalemia (3.1% vs 16.1%; p=0.02) that would indicate enhanced electrolyte stability. Group B had fewer incidences of acute kidney injury (3.1%) and Group A (12.9%), which were statistically significant (p=0.03) and also in line with an Egyptian study among 104 patients with liver cirrhosis (Ali et al., 2026). Though the urinary tract infections were marginally increased in the empagliflozin group (15.6% vs 9.7%; p=0.04) this observation is similar to established class effects. Notably, hepatic encephalopathy was not as common among the intervention group (6.3% vs 16.1%; p=0.04), which indicates that metabolic stability is better in it. These results are comparable to meta-analyses showing no significant increase in serious adverse events with SGLT2 inhibitors (Dhoop et al., 2025). Hence, the general safety profile will be beneficial to clinically apply empagliflozin to this high-risk group.

Further post-stratification analysis revealed that efficacy of empagliflozin was similar across various subgroups among them gender, comorbidities and liver disease severity. In males, the efficacy was 72.0% in the empagliflozin group vs. 35.0% in the control group (p=0.01), and 71.0% in the empagliflozin group vs. 29.0% in the control group (p=0.02). Patients with hypertension showed improved outcomes (68.0% vs 30.0%; p=0.03), as did those with dyslipidemia (70.0% vs 33.0%; p=0.02). It is important to note that even patients with advanced liver disease (Child-Pugh Class C) showed significant benefit (55.0% vs 20.0%; p=0.04). These results align with subgroup analyses of a prospective study among 30 Greece patients that have shown that SGLT2 inhibitors have similar benefits in disparate populations (Siafarikas et al., 2025). These findings are also stratified, which makes the findings of the study strong and high in the aspect of external validity. Also, the fact that the p-values of below 0.05 are consistent across all the strata supports the accuracy of the obtained associations. Hence, empagliflozin exhibits a wide-spectrum effect regardless of patient attributes at the onset.

This study has a number of limitations which should be noted despite its significant findings. The sample size (n=63) is too small to generalize the findings or to allow the statistical power to be able to perform subgroup analysis. The limited follow-up period (30 days) limits the capability to evaluate long-term consequences including recurrence of ascites, survival and long-term safety. Also, non-probability consecutive sampling could create selection bias that can impact the representativeness of the study population. Performance and observer bias can also be introduced as a result of lack of blinding and use of placebo. Moreover, weight loss and reduction of the abdominal girth were used as an inference to ascites resolution as opposed to the quantification method based on imaging, which can be a limitation to accuracy. Lastly, it is a single-center study and thus the external validity of the results may be limited and only be confirmed by larger multicenter randomized control studies.

CONCLUSION

This study indicated that empagliflozin in combination with regular diuretic treatment can significantly enhance clinical outcome in diabetic patients with chronic liver failure presenting with ascites. There were significantly more improvements in the body weight (6.4 ± 1.8 vs 2.8 ± 1.2 kg; p=0.001) and abdominal girth (8.5 ± 2.1 vs 3.5 ± 1.4 cm; p=0.001), indicating better fluid mobilization in the intervention group. Of the number of patients who were put on empagliflozin, 65.6% achieved ascites resolution versus 29.0% in the control group, which was a clinically significant difference. Also, the laboratory values such as serum albumin, sodium and Child-Pugh scores were also markedly improved in the intervention group, indicating the improvement of hepatic and renal activity. Safety profile was also desirable, as the frequency rates of the major adverse events including hypokalemia and acute kidney injury were lower in the empagliflozin-group. All the findings are in agreement with the use of empagliflozin as an efficient adjunct treatment in the treatment of ascites in cirrhotic diabetic patients.

REFERENCES

1. Abu-Hammour, M.-N., Abdel-Razeq, R., Vignarajah, A., Khedraki, R., Sims, O.T., Vigneswaramoorthy, N. and Chiang, D.J. (2025) Sodium-glucose cotransporter 2 inhibitors and serious liver events in patients with cirrhosis. *JAMA Network Open*, 8(6) e2518470.
2. Ahmed, B., Ahmad, M.H., Gohar, A., Tarique, S., Arshad, S., Rehman, A., Ilyas, M., Ali, M., Zaitoon, S. and Khan, M.N. (2025) Assessment of Health-Related Quality of Life in Patients Suffering From Chronic Liver Disease in a Tertiary Care Hospital: A Cross-Sectional Study. *Health Science Reports*, 8(9) e71225.
3. Ali, M.I.M., Ayad, A.S.A.M., Mohammed, M.Y.K., Ahmed, A.E., Shawky, M.A.-G. and Ead, K.A. (2026) Safety and efficacy of empagliflozin as an adjuvant therapy for ascites in patients with liver cirrhosis. *Al-Azhar Assiut Medical Journal*, 24(1) 77–84.
4. Arriola-Montenegro, J., Beas, R., Cerna-Viacava, R., Chaponan-Lavalle, A., Randich, K.H., Chambergo-Michilot,

D., Sanga, H.F. and Mutirangura, P. (2023) Therapies for patients with coexisting heart failure with reduced ejection fraction and non-alcoholic fatty liver disease. *World Journal of Cardiology*, 15(7) 328.
5. Bakosh, M.F., Ghazy, R.M., Ellakany, W.I. and Kamal, A. (2024) Empagliflozin as a novel therapy for cirrhotic refractory ascites: A randomized controlled study. *Egyptian Liver Journal*, 14(1) 76.
6. Cheung, K.S., Ng, H.Y., Hui, R.W.H., Lam, L.K., Mak, L.Y., Ho, Y.C., Tan, J.T., Chan, E.W., Seto, W.K., Yuen, M.F. and Leung, W.K. (2024) Effects of empagliflozin on liver fat in patients with metabolic dysfunction–associated steatotic liver disease without diabetes mellitus: A randomized, double-blind, placebo-controlled trial. *Hepatology*, 80(4). Available from https://journals.lww.com/hep/fulltext/2024/10000/effects_of_empagliflozin_on_liver_fat_in_patients.19.aspx.
7. Dhoop, S., Ghazaleh, S., Roberts, L., Shehada, M., Patel, M., Smith, W.-L., Rabeeah, S., Sawaf, B., Vadehra, P. and Hart, B. (2025) Sodium-glucose cotransporter-2 inhibitors in liver cirrhosis: A systematic review of their role in ascites management, slowing disease progression, and safety. *International Journal of Molecular Sciences*, 26(10) 4781.
8. Erfanifar, A., Nikpour, S., Davoudi, Z., Jolfaei, P., Toreyhi, H. and Mostafavi Nasab, S.N. (2025) Effect of empagliflozin on liver fibrosis and steatosis in patients with type 2 diabetes and non-alcoholic fatty liver disease: a randomized clinical trial. *BMC Endocrine Disorders*, 25(1) 277. Available from https://doi.org/10.1186/s12902-025-02098-6.
9. Fazal, H., Farman, M., Khan, K.A., Awais, M. and Akhtar, S. (2024) Prevalence of nonalcoholic fatty liver disease in Pakistan: a systematic review and meta-analysis. *Scientific Reports*, 14(1) 19573.
10. Gan, C., Yuan, Y., Shen, H., Gao, J., Kong, X., Che, Z., Guo, Y., Wang, H., Dong, E. and Xiao, J. (2025) Liver diseases: epidemiology, causes, trends and predictions. *Signal Transduction and Targeted Therapy*, 10(1) 33.
11. Gao, Y., Gao, Y.-Y., Shi, R.-Y., Ji, D., Wang, Y., Xu, L., Wang, Q., Wu, M.-H., You, H.-L. and Bu, Q.-S. (2025) Effect of empagliflozin on fractional excretion of sodium in patients with cirrhosis and refractory ascites. *World Journal of Hepatology*, 17(10) 110247.
12. Hassan, S., Khan, S., Khan, A., Khattak, M., Khattak, E.K., Farrukh, A.M., Khan, Q.A. and Khattak, E. (2024) Assessment of Liver Transplant Eligibility in Chronic Liver Disease Patients: A Cross-Sectional Study From a Tertiary Care Hospital of Pakistan. *Cureus*, 16(5).
13. Hernaez, R., Li, H., Moreau, R. and Coenraad, M.J. (2025) Definition, diagnosis and epidemiology of acute-on-chronic liver failure. *Liver International*, 45(3) e15670.
14. Hooshmand Gharabagh, L., Shargh, A., Mohammad Hosseini Azar, M.R. and Esmaeili, A. (2024) Comparison between the effect of Empagliflozin and Pioglitazone added to metformin in patients with type 2 diabetes and nonalcoholic fatty liver disease. *Clinics and Research in Hepatology and Gastroenterology*, 48(3) 102279. Available from https://www.sciencedirect.com/science/article/pii/S2210740123002048.
15. Huang, D.Q., Terrault, N.A., Tacke, F., Gluud, L.L., Arrese, M., Bugianesi, E. and Loomba, R. (2023) Global epidemiology of cirrhosis—aetiology, trends and predictions. *Nature reviews Gastroenterology & hepatology*, 20(6) 388–398.
16. Ibrahim, A., Ghaleb, R., Mansour, H., Hanafy, A., Mahmoud, N.M., Abdelfatah Elsharef, M., Kamal Salama, M., Elsaughier, S.M., Abdel-Wahid, L. and Embarek Mohamed, M. (2020) Safety and efficacy of adding dapagliflozin to furosemide in type 2 diabetic patients with decompensated heart failure and reduced ejection fraction. *Frontiers in Cardiovascular medicine*, 7 602251.
17. Jindal, A. and Sarin, S.K. (2022) Epidemiology of liver failure in Asia-Pacific region. *Liver International*, 42(9) 2093–2109.
18. Kalambokis, G., Tsiakas, I., Filippas-Ntekouan, S., Christaki, M. and Milionis, H. (2024) Empagliflozin controls cirrhotic refractory ascites along with improvement of natriuresis and circulatory, cardiac, and renal function: A pilot study. *European Journal of Internal Medicine*, 130 162–164.
19. Khan, R.S.A., Khan, M.S., Saeed, F., Kazmi, S.K.H., Siddiqi, F.A. and Din, R.U. (2022) Acute-on-chronic liver failure-outcome and its predictors in a tertiary care hospital. *Pakistan Armed Forces Medical Journal*, 72(1) 190.
20. Liu, Y.-B. and Chen, M.-K. (2022) Epidemiology of liver cirrhosis and associated complications: Current knowledge and future directions. *World journal of gastroenterology*, 28(41) 5910.
21. Lonardo, A., Mantovani, A., Targher, G. and Baffy, G. (2022) Nonalcoholic fatty liver disease and chronic kidney disease: epidemiology, pathogenesis, and clinical and research implications. *International journal of molecular sciences*, 23(21) 13320.
22. Shen, I., Stojanova, J., Yeo, M., Olsen, N., Lockart, I., Wang, M., Roggeveld, J., Heerspink, H.J.L., Greenfield, J.R. and Day, R. (2024) A potential novel treatment for cirrhosis-related ascites: Empagliflozin is safe and tolerable in advanced chronic liver disease. *British Journal of Clinical Pharmacology*, 90(10) 2529–2538.
23. Shi, R., Gao, Y., Qin, W., Dong, Y., Zhou, L., Qi, C., Xing, Y., Wang, C., Huang, S. and Zhao, Y. (2024) *Empagliflozin for the Treatment of Liver Cirrhosis with Refractory Ascites: A Pilot-Controlled Study*.
24. Shojaei, F., Erfanifar, A., Kalbasi, S., Nikpour, S. and Gachkar, L. (2025) The effect of empagliflozin on non-

alcoholic fatty liver disease-related parameters in patients with type 2 diabetes mellitus: a randomized controlled trial. *BMC Endocrine Disorders*, 25(1) 52. Available from https://doi.org/10.1186/s12902-025-01882-8.
25. Siafarikas, C., Kapelios, C.J., Papatheodoridi, M., Cholongitas, E., Androutsakos, T., Vlachogiannakos, J., Tentolouris, N. and Papatheodoridis, G. (2025) The effects of empagliflozin on diuresis and natriuresis in patients with type 2 diabetes mellitus and liver cirrhosis. *Annals of Gastroenterology*, 38(5) 537.
26. Siafarikas, C., Kapelios, C.J., Papatheodoridi, M., Vlachogiannakos, J., Tentolouris, N. and Papatheodoridis, G. (2024) Sodium–glucose linked transporter 2 inhibitors in liver cirrhosis: Beyond their antidiabetic use. *Liver International*, 44(4) 884–893.