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Research Article

SGLT2 Inhibitors and Their Role in Reducing Hospitalization in Chronic Heart Failure

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Abstract

Introduction: The condition of chronic heart failure is characterized by a high rate of morbidity and intensive hospital admission despite the increase in treatment. SGLT2 inhibitors have become a new therapeutic agent that holds potential cardiovascular advantages to glycemic control. The aim of the study was to determine their effectiveness in the reduction in hospitalization in patients with chronic heart failure.

Materials and Methods: A proposal was an observational cohort study at Khalifa Gul Nawaz Teaching Hospital, Bannu in a sample size of 320 patients with chronic heart failure. The patients were separated into two groups having SGLT2 inhibitors and normal therapy. The findings were recorded over a period of six months and the results such as the rates of hospitalization were tested by use of chi-square test, independent t-test, Kaplan-Meier test and multivariate logistic regression.

Results: In the SGLT2 group, hospitalization was seen in 21.3 percent of patients as compared to 42.5 percent in the non-SGLT2 group ($p < 0.001$). Kaplan-Meier established that time to hospitalization was much later in SGLT2 group ($p < 0.001$). The use of SGLT2 inhibitor was a predictor of a reduction in hospitalization (AOR = 0.38, $p < 0.001$). There was a tendency towards a decreased mortality, but it was not significant.

Conclusion: SGLT2 inhibitors may be considered a valuable adjunct to standard therapy in patients with chronic heart failure due to their association with reduced hospitalization rates and favorable clinical outcomes.

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Introduction

Chronic heart failure (CHF) is one of the significant health problems in the world with high morbidity, high frequency of hospitalization and high healthcare expenditure. Even with the progress in pharmacological and devices-based treatment methods, the prognosis of most patients with heart failure remains unfavorable, and frequent hospitalization has a considerable effect on the quality of life and survival [1]. Conventionally directed medical treatments, such as beta-blocker drugs, calcium ion receptor antagonists, and angiotensin receptor blockers, antihypertensive-converting inhibitors of enzymes, and, increasingly, angiotensin receptor–neprilysin inhibitors (ARNIs). have enhanced the outcomes, but still, the risk is significant [2]. As a result, there have been an increasing demands of new therapeutic modalities that will further decrease the number of hospitalization and enhance clinical outcomes among this group of people [3].

Inhibitors of sodium and glucose cotransporter 2 (SGLT2) originally were created as an oral antihyperglycemic drug used in management of type 2 diabetes mellitus. These agents, such as dapagliflozin, empagliflozin and canagliflozin, inhibit the reabsorption of glucose in the proximal renal tubules which consequently stimulates glucosuria and reduces blood glucose levels [4]. Nevertheless, SGLT2 inhibitors have cardioprotective effects other than their glycemic effects, as large cardiovascular outcome trials have indicated a heart failure hospitalization and cardiovascular mortality reduction with SGLT2 inhibitors. Such results have raised a lot of concern on their possible use as a corner stone therapy in the management of heart failure irrespective of whether diabetes is present or not [5,6].

The processes, which provide the positive results of SGLT2 inhibitors in heart failure, are multifactorial and not comprehensively explained. The suggested mechanisms involve osmotic diuresis and natriuresis that result in low preload and afterload, more favorable myocardial energetics due to a higher use of ketones, inhibition of cardiac remodeling, the decrease in inflammation and oxidative stress, and positive outcomes of renal functioning [7]. Also, these agents seem to have hemodynamic and metabolic effects that have a cumulative effect on enhancing the efficiency of the heart and minimizing the possibility of fluid overload, which is a significant cause of heart failure worsening and hospitalization [8].

Recent randomized trials and studies have continually proven that SGLT2 inhibitors can immensely decrease the chances of heart failure hospitalization in both low and normal ejection fraction patients [9]. Such effects have been found in various types of patients with or without diabetes indicating a class effect that is not limited to glucose lowering. Consequently, SGLT2 inhibitors have been progressively integrated into primary algorithms of heart failure clinical guidelines [10].

Although the existing amount of evidence is increasing, a number of gaps are present in the knowledge and use of SGLT2s inhibitors in the treatment of long-term heart failure. Their long-term impact on certain subgroups is not very clear, the optimum time to start therapy, their relative efficacy compared to other agents, and how they can be used alongside current therapies in mixed clinical practices are not well understood. In addition, the information on different populations, especially the low- and middle-income ones, is inadequate. Considering these shortcomings, the current study will close the current knowledge gap by assessing the importance of SGLT2 inhibitors in the avoidance of hospitalization in patients with chronic heart failure in a specific clinical environment. This study aims to evaluate their effectiveness, safety, and clinical outcome implications, hence making contributions to the optimization of heart failure management strategies

Materials and Methods

Study Design

This research was done in the form of a prospective observational cohort study to determine the effect of SGLT2 inhibitors on hospitalizations in patients with chronic heart failure. This design was able to measure effectiveness and safety of these agents in routine clinical practice during a specific follow up period.

Study Setting

The research was conducted in Khalifa Gul Nawaz Teaching Hospital, which is a tertiary care teaching hospital, and serves a large population in Bannu and surrounding areas. Recruitment and follow-up of patients were done in the cardiology department and outpatient clinics.

Study Duration

The research was carried out in the 18 months of the study, July 2024 to December 2025. Recruitment of the patients was done within the initial six months and the minimum time required to follow up with the participants was six months.

Study Population

The adult patients in the study group had been

identified as chronic heart failure, irrespective of ejection fraction status. Patients were enrolled from both inpatient and outpatient departments of the hospital. Before being included in the study, each subject gave their informed consent.

Inclusion Criteria

Patients aged ≥18 years with confirmed chronic heart failure were included based on clinical and echocardiographic diagnosis. The inclusion criteria were that the patients either started using SGLT2 inhibitors as a part of their treatment plan or had them, already existing in the patients.

Exclusion Criteria

Patients who had acute decompensated heart failure and who needed to receive urgent intensive care, patients with severe renal impairment (eGFR <30 mL/min/1.73 m2), patients with type 1 diabetes mellitus, and patients with a history of hypersensitivity to SGLT2 inhibitors were excluded. The pregnant and lactating women were also not to participate in the study.

Sample Size Calculation

Sample size was calculated using a population proportion formula on the basis of the past studies that have yielded values of a decline in hospitalization rates among heart failure patients who are under SGLT2 inhibitors treatment by about 25 percent. Given a confidence level of 95% (Z = 1.96), margin of error of 5% and expected proportion (p) of 0.25, the sample size was determined applying the following formula:

$$n = Z^2 \times p \times (1 - p) / d^2$$

Substituting the values:

$$n=(1.96)^2\times0.25\times(0.75)/(0.05)^2$$
$$n \approx 288$$

After adding 10% to account for potential loss to follow-up, the final sample size was increased to 320 patients.

Sampling Technique

The sampling method was a consecutive sampling in which all eligible patients presenting during the study period and meeting the inclusion criteria were enrolled until the required sample size was achieved. However, as this was a non-random sampling technique, it may have introduced selection bias.

Data Collection Procedure

Structured pro forma was employed to collect data. At the time of enrollment, baseline clinical features, demographic information, comorbidities, medication history, and laboratory findings were taken. Two categories for patients were established, and including the patients receiving SGLT2 inhibitors and the patients receiving standard heart failure therapy in the absence of SGLT2 inhibitors.

Follow-up measures were done regularly, either by outpatient or telephonic interview. The first outcome of interest was the number of patients who were hospitalized as a result of exacerbation of heart failure during the follow up. The all-cause mortality and adverse drug events were used as secondary outcomes.

Variables

SGLT2 inhibitors were the main independent variable. The main dependent variable was hospitalization of chronic heart failure rate. This was adjusted by other covariates like age, gender, comorbidity, like hypertension and diabetes mellitus, baseline renal functioning, and ejection fraction.

Statistical Analysis

The data was entered and examined using the Statistical Software of the Social Sciences (SPSS) version 26. The data were expressed as mean ± standard deviation, whereas percentages and frequencies were used to quote categorical variables.

Two continuous variables were compared using the independent sample t-test between the two groups. Chi-square test was used to determine relationships among categorical dependent variables such as the hospitalization rates. Kaplan-Meier analysis of survival was done to estimate the time to first hospitalization and the difference between them were analyzed using log-rank test.

To identify the factors that were independent, a multivariate logistic regression investigation was conducted. The p-value of below 0.05 was taken as statistically significant.

Ethical Considerations

The ethical review committee of the Khalifa Gul Nawaz Teaching Hospital was the institutional ethical review committee of this study. Everyone gave their informed consent the participants in written form. The privacy of patient data was ensured during the study and all the procedures were performed according to the ethical standards.

Results

The study enrolled a total of 320 patients with chronic heart failure to complete the follow up. Of them, 160 patients were using SGLT2 inhibitors and 160 patients were treated using regular heart failure therapy but not using SGLT2 inhibitors. The average age of the

whole study population was 58.4 ± 11.2 years. The SGLT2 inhibitor group patients were aged 57.9 ± 10.8 years and the non-SGLT2 group patients were aged 58.9 ± 11.6 years. The difference in mean age between the two groups was not statistically significant (independent sample t-test, p = 0.48).

Male patients constituted 62.5% of the total population, with a similar distribution in both groups (64.4% in the SGLT2 group vs. 60.6% in the non-SGLT2 group). The difference in gender distribution was not statistically significant (chi-square test, p = 0.49).

Comorbid conditions were comparable between the two groups. Hypertension was present in 68.1% of patients in the SGLT2 group and 70.0% in the non-SGLT2 group (p = 0.71), while diabetes mellitus was observed in 55.6% and 53.8% of patients, respectively (p = 0.76). The mean left ventricular ejection fraction was 38.2 ± 9.5% in the SGLT2 group and 37.6 ± 10.1% in the non-SGLT2 group, with no statistically significant difference (p = 0.62, Table 1).

Table 1: Baseline Demographic and Clinical Characteristics

Variable	SGLT2 Group (n=160)	Non-SGLT2 Group (n=160)	p-value
Age (years, mean ± SD)	57.9 ± 10.8	58.9 ± 11.6	0.48
Male Gender, n (%)	103 (64.4%)	97 (60.6%)	0.49
Hypertension, n (%)	109 (68.1%)	112 (70.0%)	0.71
Diabetes Mellitus, n (%)	89 (55.6%)	86 (53.8%)	0.76
Ejection Fraction (% mean ± SD)	38.2 ± 9.5	37.6 ± 10.1	0.62

During the 6-month follow-up period, a total of 102 patients (31.9%) experienced at least one hospitalization due to heart failure exacerbation. The incidence of hospitalization was significantly lower in the SGLT2 inhibitor group compared to the non-SGLT2 group. In the SGLT2 group, 34 patients (21.3%) were hospitalized, whereas 68 patients (42.5%) in the non-SGLT2 group required hospitalization (Figure 1). The association between SGLT2 inhibitor use and hospitalization was statistically significant (chi-square test, $\chi^2 = 15.84$, $p < 0.001$), indicating a substantial reduction in hospitalization rates among patients receiving SGLT2 inhibitors.

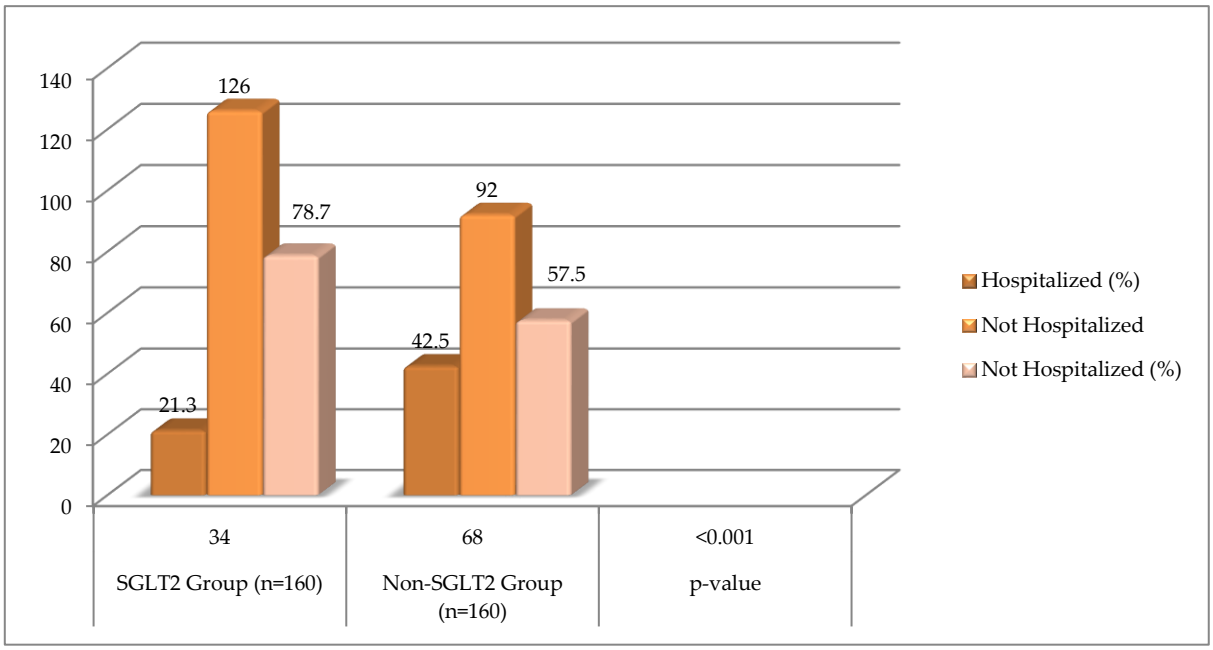

Figure 1: Comparison of Hospitalization Rates

The Kaplan-Meier survival analysis (Table 2) showed that patients who received SGLT2 inhibitors took a much longer time before first hospitalization than the patients who received a standard therapy. The survival curves showed early divergence during the first two months of follow-up and stayed steadfastly apart during the remainder of the study period.

The result of the log-rank test was statistically significant between the two groups ($p < 0.001$), which proves that hospitalization was less likely and delayed in patients under SGLT2 inhibitors. The median time to hospitalization was not achieved in the SGLT2 group and it was approximated about 4.2 months in the non-SGLT2 group.

Table 2: Kaplan–Meier Analysis Summary

Parameter	SGLT2 Group	Non-SGLT2 Group	p-value
Median Time to Hospitalization	Not reached	4.2 months	<0.001
Log-rank Test			<0.001

Note: Log-rank test p-value <0.001.

The deaths due to all causes were also noted in 28 patients (8.8%). The mortality rate in the SGLT2 group (9 patients, 5.6%), as opposed to non-SGLT2 group (19 patients, 11.9%), was lower. This difference was however, not significant (chi-square test, p = 0.06) though a tendency was observed to have a lower mortality.

SGLT2 inhibitor adverse drug events were also identified among 18 patients (11.3%), most of which were mild urinary tract infections and transient hypotension. No severe cases of ketoacidosis or life threatening complications were present (Table 3).

Table 3: Secondary Outcomes

Outcome	SGLT2 Group (n=160)	Non-SGLT2 Group (n=160)	p-value
Mortality, n (%)	9 (5.6%)	19 (11.9%)	0.06
Adverse Events, n (%)	18 (11.3%)	—	—

Note: p = 0.02 Adjustment predictors Adverse events related to SGLT2 inhibitor therapy were only monitored in the SGLT2 group; therefore, comparable adverse-event data were not collected for the non-SGLT2 group.

It was done through multivariate logistic regression analysis to conclude on independent predictors of hospitalization whilst controlling environmental conditions such as age, gender, hypertension, diabetes mellitus, ejection fraction, and renal function.

The application of SGLT2 inhibitors turned out to be an important independent protective variable against hospitalization (adjusted odds ratio [AOR] = 0.38, 95% confidence interval [CI]: 0.23-0.62, p < 0.001). Other significant predictors of increased hospitalization risk included reduced ejection fraction (AOR = 1.45 per 5% decrease, p = 0.01) and the presence of chronic kidney disease (AOR = 1.72, p = 0.02 Age, gender, and diabetes mellitus were not statistically significant predictors (Table 4).

Table 4: Multivariate Logistic Regression Analysis

Variable	AOR	95% CI	p-value
SGLT2 Inhibitor Use	0.38	0.23–0.62	<0.001
Reduced Ejection Fraction	1.45	1.09–1.92	0.01
Chronic Kidney Disease	1.72	1.08–2.74	0.02
Age	1.02	0.98–1.05	0.21
Male Gender	1.11	0.68–1.80	0.66
Diabetes Mellitus	1.08	0.66–1.75	0.75

AOR: Adjusted Odds Ratio

Discussion

The study's findings demonstrated that the use of SGLT2 inhibitors to patients with chronic heart failure was linked to a vast decrease in the hospitalization rates. Patients who were treated with SGLT2 inhibitors had a lower number of hospitalizations, postponed hospitalization, and an overall projection of lower mortality than those who got standard treatment alone. The findings indicate that SGLT2 inhibitors can be useful in clinical practice in addition to traditional heart failure treatment and can be used to enhance patient outcomes.

The decrease in the rates of hospitalization is in line with the known mechanisms of SGLT2 inhibitors such as their diuretic and natriuretic actions, enhanced cardiac metabolism, and renal protection [11]. The substantial correlation in univariate and multivariate analyses supports the fact that SGLT2 inhibitors have an independent effect of risk of heart failure exacerbations with hospitalization [12]. Moreover, their contribution to the stabilization of the disease progression is indicated by the Kaplan-Meier analysis that shows the increased time to hospitalization.

The findings of this study are in tandem with other large randomized controlled studies and literature that have been carried out consistently, and indicated a decrease in heart failure hospitalizations with SGLT2 inhibitor therapy [13, 14]. Other studies have indicated relative hospitalization risk reduction of about 25 to 35 which is similar to that in this paper [15]. Moreover, similarly to the previous results, the advantages were detected regardless of the diabetic status, which supports the idea that these agents have cardioprotective actions beyond the control of glucose [16].

The tendency towards the decrease in all-cause

mortality that was not statistically significant in this study is consistent with the data provided in previous clinical trials which reported small mortality advantages [17]. It is possible that the cause of the non-statical significant mortality results in this study is because there was a relatively shorter follow up period and there was a small sample size versus the large multicenter trials. Also, the safety profile presented in the current study and mostly mild adverse effects are in line with prior findings, which is why the tolerability of SGLT2 inhibitors in heart failure patients can be supported.

Limitations and Future Suggestions

This study had several limitations that should be considered consideration when viewing the results. The study is a single center study, which is performed in a tertiary care hospital, and thus cannot have generalizability to a wider population. With the observational design, there is the risk of selection bias and the presence of the residual confounding even with multivariate adjustment. The six-month follow-up might not have been enough time to estimate the long-term outcomes like mortality and disease progression. Also, the differences in medication adherence and differences in background treatment of heart failure might have impacted the outcomes.

Future studies must be centered on multicenter research that involves a larger and more diverse population to make the research more generalizable. The optimal way to assess long-term results, such as mortality and quality of life, should be longer follow-up periods. The similarity or dissimilarity between the different types of SGLT2 inhibitors could be determined through the comparative analysis of the drugs to determine whether the classes of these drugs differ in their efficacy. Additional studies should also be done to know what these agents can in some sub-population such as normal ejection fraction patients, chronic renal failure patients and various socioeconomic status patients.

Conclusion

Additionally, SGLT2 inhibitors were linked to a notable decrease in of hospitalization of patients with chronic heart failure, and, the time to the first hospitalization, and favorable safety profile. These findings support why they can be used as an addition to standard heart failure medication.

Author Contributions

SAAS contributed to the study conception, design, and manuscript drafting. AM and YN assisted in data collection and literature review. AU contributed to data analysis and interpretation. MIU supported statistical evaluation and critical revision of the manuscript. AUK supervised the overall research work and provided final approval of the manuscript.

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