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Original Article

Efficacy of SGLT-2 Inhibitors on Heart Failure in Diabetes -A Pharamacological Analysis

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ABSTRACT

Objective: We sought to investigate the pharmacological analysis of therapeutic outcome of SGLT-2 inhibitors on heart failure in diabetes patients.
Methods: In this prospective case control study, total of 56 cases (with SGLT-2) and 40 controls (without SGLT-2) of chronic heart failure with T2DM were enrolled as per inclusion-exclusion criteria. The endpoints were the effects of SGLT-2 inhibitor treatment at 3 months. The clinic-demographical parameters including New York Heart Association (NYHA) classification, were used. The effects of SGLT-2 inhibitor on those parameters were also analyzed by baseline insulin levels were measured.
Results: Demographical data showed non-significant differences between both groups, except BMI. In both groups, majority of the patients had complaints of CAD and HTN and showed a non-significant difference. The NYHA functional grading is significantly (p=0.0224*) reduced at subsequent follow-up in cases as compared to controls. The mean differences Hb, SBP, DBP, S. Cholesterol, Pro-BNP, were maximum in cases than controls.
Conclusion: In conclusion, SGLT2 inhibitors are glucose-lowering medicines that had cardiac protective roles also.

Keywords*: Type 2 diabetes, SGLT-2, NYHA class.*

INTRODUCTION

More than 592 million people are expected to have type 2 diabetes mellitus (T2DM) by 2035; this is a substantial increase from the 382 million individuals with diabetes mellitus in 2013 [2]. By 2050, the number of Indians living with diabetes is projected to rise from 32 million in 2000 to 70 million. For a HbA1c 6%, the prevalence of HF is 2.3 per 1000 person-years, while for a HbA1c >11.9%, the incidence of HF rises to 11.9 per 1000 person-years. By 2030, the estimated annual incidence of HF due to diabetes could rise from 73,600 in 2000 to 161,000 in 2030. [3]

A lower chance of heart failure has been observed in diabetics who took one of three SGLT2 inhibitors in clinical trials. [4,5] But studies examining its mechanism of action are scant. Therefore, the current research aims to investigate the impact of SGLT2 inhibitors on haemoglobin A1c, heart rate, blood pressure, and ejection fraction in diabetic patients with heart failure. Contrary to popular belief, SGLT2 inhibitors work in a way that is different from other therapies for lowering blood sugar. [6]

Dapagliflozin is a competitive regulator of sodium-glucose-linked transporter 2 in the proximal tubule of the kidney (SGLT2). When used to cause glycosuria, it is approved for use in the management of type 2 diabetes mellitus (T2DM). [8,9] Congestive heart failure is more likely in people with type 2 diabetes (CHF). [10,11] Suppressing SGLT2 in people with T2DM induces an osmotic diuresis that can increase Na+ excretion, possibly leading to a beneficial reduction in blood pressure [12,13]. Patients with type 2 diabetes, high blood pressure, or congestive heart failure who have a high blood volume may benefit more from SGLT2 antagonists.

There has been promising new research on the effectiveness of empagliflozin in reducing cardiovascular events and death in type 2 diabetics. Recent research suggests that SGLT2 inhibitors can improve heart failure outcomes for type 2 diabetes patients, setting them apart from other glucose-lowering drugs. [14]

MATERIAL AND METHODS

This prospective case-control research was carried out at King George's Medical University in Lucknow, India, in the Department of Pharmacology and Therapeutics, in collaboration with the Department of Medicine. After taking ethical clearance [Letter no- 1508/Ethics/2021] from the institutional ethical Committee of KGMU, the patients were recruited from out-patient/wards of the Department of Medicine. The consent for participation was taken from the patients, who were then enrolled in the study. All the patients were self-controlled, and baseline readings (data) were compared with follow-up readings. Total 56 patients with chronic heart failure with diabetes Type 2 with SGLT-2 inhibitors were enrolled as cases and without SGLT-2 inhibitors as controls (n=40, age-sex matched). The endpoints were the effects of SGLT-2 inhibitor treatment at 3 months. The clinic-demographical parameters, including New York Heart Association (NYHA) classification were used. The effects of SGLT-2 inhibitor on those parameters were also analyzed by baseline insulin levels were measured.

Statistical Analysis:

A organised proforma was used for data collection. SPSS version 26.0 was used to evaluate data entered into a Microsoft Excel spreadsheet. Quantitative information was presented as a percentage. Mean and standard deviation were used to represent quantitative statistics. The Chi-square test revealed an association between two qualitative factors. An unpaired t-test was used to compare the means of the two groups and determine if there was a statistically significant variation between them. Statistical significance was defined as a p-value of 0.05, with a p-value of 0.0001 being regarded as extremely significant.

RESULTS

Patient's demographical data showed in Table-1 and mostly showed non-significant differences except for weight (**p= 0.043*)** and BMI (**p<0.0001***). In Cases Group majority of patients have positive family history in both groups[p=0.0951]. The mean duration of Diabetes mellitus was higher in cases (23.86±5.38 years) than in controls (22.58±5.29 years) [Figure-1]. Along with statistically, an insignificant difference among them [p=0.2501]. In both groups, majority of the patients had complaints of CAD and HTN and showed a non-significant difference [Table-2]. CKD and MI were significantly lower in cases as compared to controls [Figure-2].

In both cases & controls, maximum patients (57.14% & 40%) were performing no exercise at all, respectively, followed by patients performing moderate exercise only and so on. Along with statistically, an insignificant difference among them [p=0.2426]. In both the group of cases & controls maximum number of patients (28.57% & 21.43%) were consuming tobacco only, followed by 19.64% smoking cases & 14.29% in controls consuming alcohol. Statistically, an insignificant difference was found [p=0.9788] [Table-3].

When describing the severity of heart failure, doctors frequently refer to the extent to which patients are unable to engage in normal daily activities. The NYHA Functional Classification is widely used as a system for categorising heart failure by medical professionals. In cases gradual increase in number of patients from baseline to 3rd month was observed for II stage. However, a decrease in the number for III stages was observed along with significant differences among them (p=0.0224*). Similarly, in controls, gradual increase in the number of patients from baseline to 3rd month was observed for II stage. However, a decrease in number for III stages was observed along with insignificant difference among them (p=0.1939) [Figure-3].

In cases, while observing the Chest-examination for both (bilateral clarity in the chest cavity & Left side crepitus), gradual improvement was shown at follow-up. While observing the follow-up of Jugular Venous Pressure till 3rd month, a significant gradual improvement was observed in cases as compared to controls (p=0.0157*). While comparing the vitals, biochemical parameters, including lipid profile, BNP, etc. both groups showed almost significant improvement from baseline. However, cases had additional benefits in improvement in heart rate and serum creatinine also. Moreover, cases also had significantly higher mean differences as compared to controls [Table-4].

While analysing the mean differences of vitals, considering heart rate was comparable. In contrast, in Hb, SBP, DBP, S. Cholesterol, Pro-BNP, maximum mean differences were observed in cases then controls, with a significant difference among them (p<0.0001*) for both. Further, considering other associated parameters of heart health maximum mean difference was observed in cases than controls. Also, the above tables implies that cases had the significant beneficial effect it term of heart health, lipid profile, blood sugar, etc. [Figure-4].

TABLES AND FIGURES

TABLE-1: Clinico-demographical characteristics of enrolled patients.

AGE DISTRIBUTION (YEARS)		CASES		CONTROLS		P-VALUE
		N	%	N	%	
45-54		16	28.57%	10	25.00%	X=0.1507
55-65		40	71.42%	30	75.00%	p=0.6979
SEX	Female	27	48.21%	23	57.50%	X=0.8062
	Male	29	51.79%	17	42.50%	p=0.3693
ANTHROPOMETRICS	Weight (kg)	65.57	8.92	69.28	9.32	t=2.045 **p= 0.043***
	Height (meter)	1.65	0.05	1.66	0.05	t=1.005 p=0.317
	BMI (kg/m^2)	24.83	4.83	28.64	3.96	t=4.293. **p<0.0001***
SOCIOECONOMIC STATUS	Upper Class	2	5.00%	1	2.50%	
	Upper Middle	5	12.50%	3	7.50%	
	Lower Middle	24	60.00%	19	47.50%	
	Upper Lower	17	42.50%	13	32.50%	X=0.6323
	Lower	8	20.00%	4	10.00%	p=0.9594

TABLE-2: Co-morbidities status for total enrolled patients within the study.

CO-MORBIDITIES	CASES		CONTROLS		P-VALUE
	N	%	N	%	
CAD	44	78.57%	34	85.00%	X=0.6330 p=0.4263
Arthritis	4	7.14%	3	7.50%	X=0.004403 p=0.9471
HTN	20	35.71%	18	45.00%	X=0.8413 p=0.3590
DCMP	4	7.14%	3	7.50%	X=0.004403 p=0.9471
LBBB	4	7.14%	4	10.00%	X=0.2494 p=0.6175
Hypothyroidism	4	7.14%	15	37.50%	X=3.584 p=0.0596

TABLE-3: Exercise status for total enrolled patients within the study.

EXERCISE	CASES		CONTROLS		P-VALUE
	N	%	N	%	
EXERCISE					
Mild	10	17.86%	9	22.50%	
Moderate	14	25.00%	15	37.50%	
None	32	57.14%	16	40.00%	X=2.832 p=0.2426
ADDICTION					
Tobacco Consumption	16	28.57%	12	21.43%	
Alcohol Consumption	9	16.07%	8	14.29%	
Smoking	11	19.64%	6	10.71%	
Alcohol + Tobacco	6	10.71%	3	5.36%	
Alcohol + Tobacco + Smoking	3	5.36%	2	3.57%	
NO Alcohol + Tobacco + Smoking	11	19.64%	7	12.50%	X=0.7712 p=0.9788

TABLE-4: General parameters follow-up status for total enrolled patients within the study.

		BASELINE Mean±SD	1ST MONTH Mean±SD	3RD MONTHS Mean±SD	P-VALUE
CASES	HR	93.71±9.00	91.93±9.48	85.13±10.46	F=10.97 **p<0.0001***

	HbA1c (%)	8.53±1.09	7.96±0.70	6.08±0.38	F=135.3 **p<0.0001***
	FPG (mg/dl)	263.06±33.43	147.45±22.97	132.95±23.28	F=348.7 **p<0.0001***
	SBP	134.70±14.55	129.96±13.85	115.63±14.27	F=24.35 **p<0.0001***
	DBP	88.89±9.65	78.54±9.63	77.04±7.26	F=26.18 **p<0.0001***
	Ejection Fraction	56.93±3.01	57.84±3.14	60.42±4.23	F=13.35 **p<0.0001***
	Hb	12.26±1.26	12.40±1.25	12.52±1.22	F=0.5476 p=0.5795
	Hct	36.23±3.91	37.05±3.50	39.57±2.80	F=12.85 **p<0.0001***
	S. Cholesterol	259.52±50.06	211.94±46.77	186.11±43.03	F=35.59 **p<0.0001***
	Triglyceride	147.21±21.09	135.43±24.26	132.09±25.64	F=6.269 **p=0.0024***
	HDL	57.87±15.94	58.69±13.43	59.92±13.30	F=0.2612 p=0.7705
	S. Creatinine	1.48±0.14	0.80±0.19	0.82±0.21	F=225.1 **p<0.0001***
	Pro. BNP	168.21±26.41	121.21±15.43	79.21±11.52	F=278.3 **p<0.0001***
CONTROLS	**HR**	94.15±15.03	92.15±15.17	88.50±11.57	F=1.920 p=0.1506
	HbA1c (%)	8.57±1.45	8.05±1.02	7.20±1.11	F=15.09 **p<0.0001***
	FPG (mg/dl)	265.01±17.57	222.61±20.67	167.30±28.14	F=216.8 **p<0.0001***
	SBP	132.03±8.07	124.03±8.07	124.03±8.07	F=15.07 **p<0.0001***
	DBP	87.00±9.35	85.00±9.02	81.68±7.67	F=4.378 **p=0.0144***
	Ejection Fraction	55.08±3.29	56.08±3.24	58.26±4.22	F=9.325 **p=0.0002***
	Hb	12.48±2.23	12.63±2.21	12.83±2.19	F=0.2704 p=0.7484
	Hct	36.71±6.85	36.94±5.73	38.12±6.63	F=0.6383 p=0.5298
	S. Cholesterol	256.25±61.20	231.07±56.46	204.96±45.05	F=12.33 **P<0.0001***
	Triglyceride	134.81±29.46	126.43±26.57	122.13±20.84	F=3.479 **p=0.0331***
	HDL	36.24±7.92	36.93±8.63	37.24±6.67	F=0.1990 p=0.8198
	S. Creatinine	1.46±1.38	1.39±1.12	1.03±0.56	F=2.116 p=0.1245
	Pro. BNP	165.57±28.78	136.63±21.98	104.72±19.65	F=75.31 **p<0.0001***

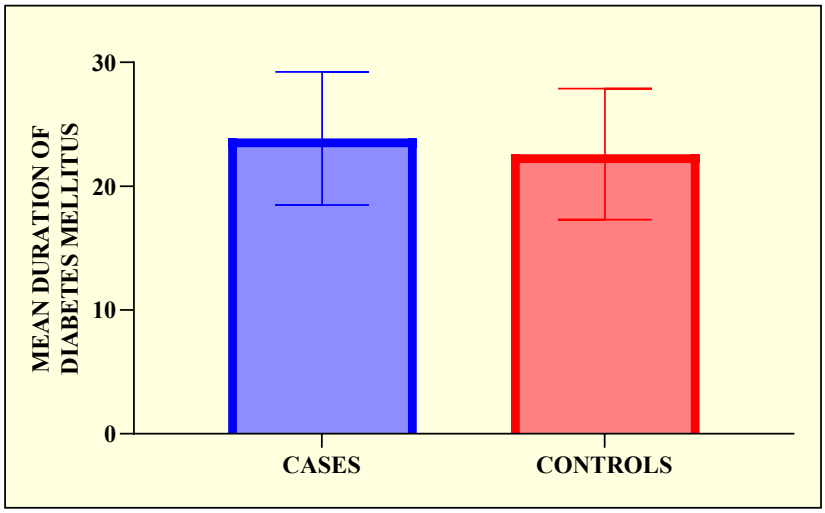

FIGURE-1: Graphical presentation for duration of Diabetes Mellitus for total enrolled patients within the study.

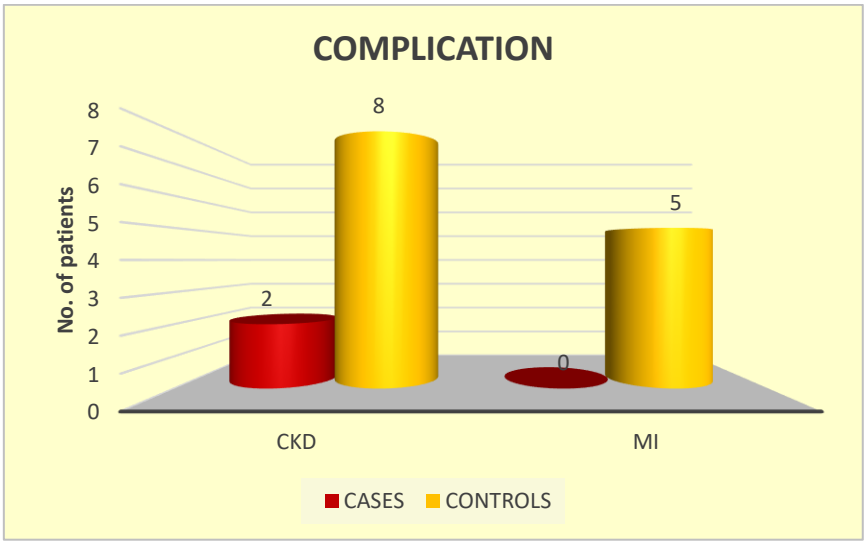

FIGURE-2: Graphical presentation of complication status for total enrolled patients within the study.

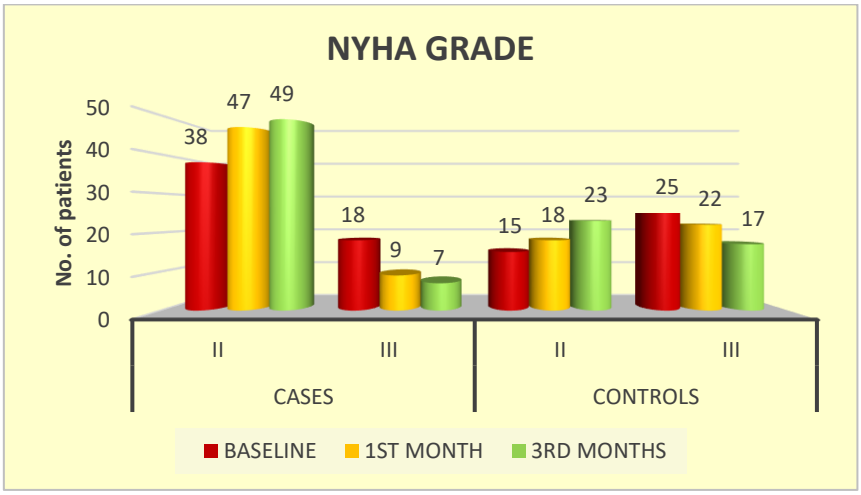

FIGURE-3: Graphical presentation for NYHA Grade status for total enrolled patients within the study.

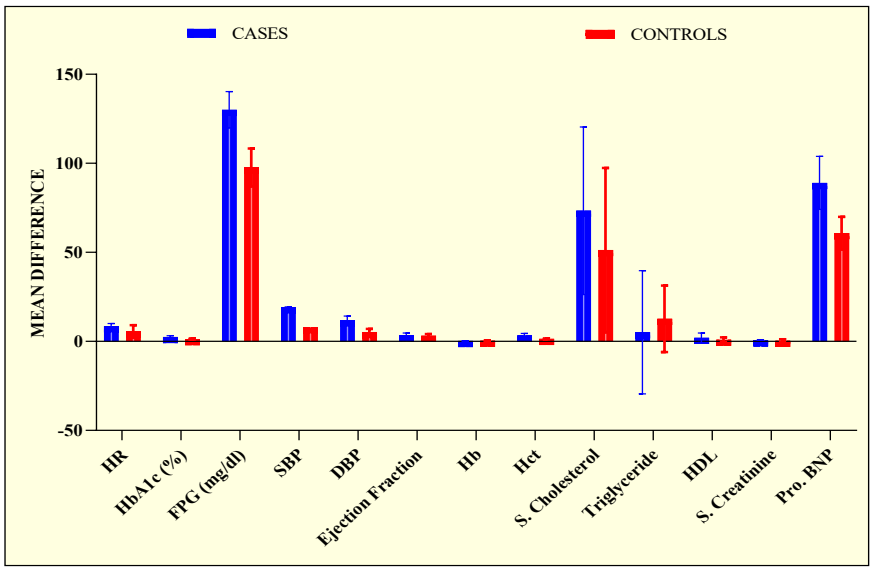

FIGURE-4: Graphical presentation of mean difference of Vitals for total enrolled patients within the study.

DISCUSSION

In the present study, in both cases & controls, the maximum number of patients was 78.57% & 85% reported the complaint of CAD, followed by 35.71% of cases & 45% of controls reported the complaint of HTN. Similarly, according to Drexel et al., 2019 [19], most of cases had CAD at baseline or the occurrence of cardiovascular events, followed by hypertension. In the present study, as compared to controls (20%), only 3.57% cases had Chronic kidney disease (CKD). Similarly, myocardial infarction (MI) is reported only in controls. Thus, we found a significant reduction in CKD and MI were found in cases (with SGLT2). Similarly, Neuen et al., 2019 [20], suggested in their study that SGLT2 inhibitors also reduced end-stage kidney disease (0.65, $p<0.0001$*) and acute kidney damage (0.75, $p<0.0001$*).

In our study, the mean differences of vitals, considering heart rate maximum mean difference, were observed among cases (8.58±-1.46) and then controlled with a significant difference among them ($p<0.0001$*). Similarly, in SBP and DBP, maximum mean differences were observed in cases (19.07±0.28 & 8.0±0.0) than in controls (11.85±2.39 & 5.32±1.68). Considering other associated parameters of heart health, the maximum mean difference was observed in cases then controls. The positive difference was noted in cases for HbA1c, FPG, S. Cholesterol, Triglyceride, S. Creatinine and Pro. BNP. However, a negative was observed for Ejection Fraction, Hb, Hct, HDL and so on. Similarly, Li et al., 2020 [21], reported that SGLT2 inhibitors significantly decreased heart failure events (RR: 0.73; $p<0.0001$), HbA1c (WMD: 0.62 per cent; $p<0.0001$). Also, while considering the stability of vitals was important for admission. The mean differences in HR and SBP were maximum in cases than controls. However, DBP was maximum in controls than cases.

In our research, in cases, while observing the chest examination in both cases and controls, left-side crepitus was found in 3.57% and 10.87% at 3 months of treatment. Although no significant differences were observed. Guidelines suggest electrocardiography, chest x-ray, and blood work, as well as an evaluation of LV function, when clinical concern persists, as was the case in the study by Woo V et al., 2019 [26]. Systolic and diastolic function must be evaluated via echocardiography at the time of diagnosis and whenever there is a change in the patient's condition. As the duration extends bilateral clarity in the chest cavity & left side crepitus was observed in the maximum number of patients.

Further, while observing the follow-up of Jugular Venous Pressure in our research, till the 3rd month, a significant gradual increase in the number of patients with normal readings and a gradual decrease with a rise in the measurement was observed in cases as compared to controls. Similarly, Tromp J et al., 2021 [27] stated that in elevated jugular venous pressure was observed at follow-up. Patients are enrolled during hospitalization (following stabilization between 24 h and five days after admission).

In the present study, while observing the follow-up for mean readings of the co-morbidities till 3rd month in both cases & controls, the gradual decrease in the mean findings from baseline to 3rd month was observed in cases for most of the complaints, except for transverse increase was observed in Hb, Hct, and HDL (parameters observed with a negative mean difference). The gradual decrease in the other parameters with significant differences, as well as the increase in Hb, Hct & HDL with insignificant differences, indicates the good prognosis. Similarly, according to Chambergo-Michilot et al., 2021 [23], sodium-glucose transporter 2 inhibitors (SGLT2i) in patients with heart failure. In addition, the score on the

Kansas City Cardiomyopathy Questionnaire (KCCQ, MD: 1.70, 95% CI 1.67–1.73, I2 = 54%) improved significantly. SGLT2i decreased adverse events, blood pressure, and body mass index. However, hematocrit and creatinine levels increased. The meta-analysis of RCTs with > 12 weeks of follow-up revealed that SGTL2i lowered NT-proBNP substantially. SGLT2i has been shown to enhance crucial outcomes in patients with HF, and it appears to be safe. Doenst T, et al., 2013 [16], despite enhanced rates of FA oxidation, the diabetic heart accumulates triglycerides and other lipid metabolites such as ceramides.

When describing the severity of heart failure, doctors frequently refer to the extent to which patients are unable to engage in normal daily activities. The New York Heart Association (NYHA) Functional Classification is widely used as a system for categorising heart failure by medical professionals. In the present study, in cases, a gradual increase in the number of patients from baseline to 3rd month was observed for the II stage. However, a decrease in the number for III stages was observed similarly; in controls, a gradual increase in the number of patients from baseline to 3rd month was observed for the II stage. However, a decrease in the number of III stages was observed. Similarly, in the study by Cardoso et al., 2021[22] SGLT2 inhibitors significantly reduced cardiovascular mortality, HF hospitalizations, and urgent visits for HF across all subgroups with preserved ejection fraction.

Kato ET et al. 2019 [25] reported that 671 (3.9%) of the overall trial cohort of 17160 patients were diagnosed with HFrEF because their EF was less than 45%. A total of 1316 patients (7.7% of the trial cohort) were diagnosed with HF without documented reduced EF and had a history of CAD. Around 28% patients reported the history of hypertension too. Similarly, in the present study, 64.29% reported a positive history of Coronary Artery Disease (CAD), followed by 28.57% cases reporting a history of Anterior wall myocardial infarction (AWMI) & Percutaneous Coronary Intervention of Left anterior descending artery (PCI-LAD). Similarly, in the Control Group majority of patients, i.e. 67.50%, reported a positive history of Coronary Artery Disease (CAD), followed by 35% of control reporting a history of Hypertension (HTN).

In the present study, we observed that majority of patients have a positive family history. Further, according to Karwi QG et al., 2018 [17], GDM risk factors include advanced age, obesity, high prenatal weight gain, a history of congenital abnormalities in prior infants or stillbirth, or a family history of Diabetes. Out of total enrolled patients majority of them reported the positive history of associative disorders, diabetes, hypertension and so on, along with significant difference among them.

Patients with HFrEF were more likely to be masculine and to have a history of ASCVD, especially coronary artery disease, as reported in 2015 by Zelniker TA et al. [18]. Glovaci D et al., 2019 [15], also observed that males have a somewhat higher prevalence of T2DM than women. Similar to their results, we also observed that in the cases group, male dominance was observed with 51.79% males and only 48.21% females. In the present study, majority of patients belonged to the lower middle class. Similar to our study, Falkentoft AC et al., 2022 [24], also found majority of patients of middle class.

CONCLUSION

In summation, SGLT2 inhibitors are medicines that help reduce blood sugar by increasing the amount of glucose that is urinated out. Through their one-of-a-kind mode of action, SGLT2 inhibitors safeguard pancreatic beta-cell function and alleviate excess insulin overload by lowering glucose toxicity independently of insulin secretion. Multiple clinical and laboratory investigations have shown that blocking SGLT2 reduces insulin resistance.

These findings indicate that glycemic control is not a necessary condition for the therapeutic benefits of SGLT2 inhibitors on HF-related outcomes. Curiously, it has been postulated that lowering SGLT2 levels, which causes a slight rise in ketone body levels, benefits cardiac energy shifts and insulin resistance. Therefore, it is probable that the improvement in insulin resistance that accompanies SGLT2 inhibitor therapy contributes to the decrease in the risk of HF-related events.

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Conflict of interest

None.

REFERENCES

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of Diabetes prevalence for 2013 and projections for 2035. Diabetes Res ClinPract. 2014; 103:137–149. https://doi.org/10.1016/j.diabres.2013.11.002

2. Zimmet P, Alberti KG, Magliano DJ, Bennett PH. Diabetes mellitus statistics on prevalence and mortality: facts and fallacies. Nat Rev Endocrinol. 2016;12:616–622. doi: 10.1038/nrendo.2016.105
3. Rodgers A, Ezzati M, Vander Hoorn S, Lopez AD, Lin RB, Murray CJ. Distribution of major health risks: findings from the Global Burden of Disease study. PLoS Med. 2004 Oct 19;1(1):e27. DOI: 10.1371/journal.pmed.0010027
4. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine. 2015 Nov 26;373(22):2117-28. DOI: 10.1056/NEJMoa1504720
5. Packer M, Anker SD, Butler J, Filippatos G, Zannad F. Effects of sodium-glucose cotransporter 2 inhibitors for the treatment of patients with heart failure: proposal of a novel mechanism of action. JAMA cardiology. 2017 Sep 1;2(9):1025-9. DOI: 10.1111/dom.13678
6. Zelniker TA, Braunwald E. Cardiac and renal effects of sodium-glucose cotransporter 2 inhibitors in Diabetes: JACC state-of-the-art review. Journal of the American College of Cardiology. 2018 Oct 9;72(15):1845-55. DOI: 10.1016/j.jacc.2018.06.040
7. Meng W, Ellsworth BA, Nirschl AA, McCann PJ, Patel M, Girotra RN, et al. Discovery of dapagliflozin: a potent, selective renal sodiumdependentglucosecotransporter2 (SGLT2) inhibitor for the treatment of type2 Diabetes. J Med Chem. 2008;51:1145–1149. https://doi.org/10.1021/jm701272q
8. Thomson SC, Rieg T, Miracle C, Mansoury H, Whaley J, Vallon V, et al. Acute and chronic effects of SGLT2 blockade on glomerular and tubular function in the early diabetic rat. Am J PhysiolRegulIntegr Comp Physiol. 2012;302:R75–R83. DOI: 10.1152/ajpregu.00357.2011
9. Brater DC. Clinical pharmacology of loop diuretics. Drugs. 1991;41:14–22. DOI:10.2165/00003495-199100413-00004
10. Fitchett DH, Udell JA, Inzucchi SE. Heart failure outcomes in clinical trials of glucose-lowering agents in patients with Diabetes. Eur J Heart Fail.2017;19:43–53. DOI: 10.1002/ejhf.633
11. Kanai Y, Lee WS, You G, Brown D, Hediger MA. The human kidney low affinityNa+/glucose cotransporter SGLT2: delineation of the major renal reabsorptive mechanism for D-glucose. J Clin Invest. 1994;93:397–404. DOI: 10.1172/JCI116972
12. Rahman A, Kittikulsuth W, Fujisawa Y, Sufiun A, Rafiq K, Hitomi H, et al. Effects of diuretics on sodium-dependent glucose cotransporter 2 inhibitor-induced changes in blood pressure in obeserats suffering from the metabolic syndrome. J Hypertens. 2016;34:893–906. doi: 10.1097/HJH.0000000000000871.
13. Oliva RV, Bakris GL. Blood pressure effects of sodium-glucose co-transport 2(SGLT2) inhibitors. J Am Soc Hypertens. 2014;8:330–339. DOI: 10.1016/j.jash.2014.01.007
14. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin,cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med.2015;373:2117–2128. DOI: 10.1056/NEJMoa1504720.
15. Glovaci D, Fan W, Wong ND. Epidemiology of Diabetes mellitus and cardiovascular disease. Current cardiology reports. 2019 Apr;21(4):1-8. DOI: 10.1007/s11886-019-1107-y
16. Doenst T, Nguyen TD, Abel ED. Cardiac metabolism in heart failure: Implications beyond atp production. Circ Res. 2013;113:709–724. DOI: 10.1161/CIRCRESAHA.113.300376
17. Karwi QG, Uddin GM, Ho KL, Lopaschuk GD. Loss of metabolic flexibility in the failing heart. Front Cardiovasc Med. 2018;5:68. DOI: 10.3389/fcvm.2018.00068
18. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Bonaca MP, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. The Lancet. 2019 Jan 5;393(10166):31-9. doi: 10.1016/S0140-6736(18)32590-X.
19. Drexel H, Leiherer A, Saely CH, Brandtner EM, Geiger K, Vonbank A, et al. Are SGLT2 polymorphisms linked to diabetes mellitus and cardiovascular disease? Prospective study and meta-analysis. Bioscience reports. 2019 Aug 30;39(8). https://doi.org/10.1042/BSR20190299
20. Neuen BL, Young T, Heerspink HJ, Neal B, Perkovic V, Billot L, et al. SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis. The lancet Diabetes & endocrinology. 2019 Nov 1;7(11):845-54. doi: 10.1016/S2213-8587(19)30256-6
21. Li WJ, Chen XQ, Xu LL, Li YQ, Luo BH. SGLT2 inhibitors and atrial fibrillation in type 2 diabetes: a systematic review with meta-analysis of 16 randomized controlled trials. Cardiovascular diabetology. 2020 Dec;19(1):1-4. DOI:10.1186/s12933-020-01105-5
22. Cardoso R, Graffunder FP, Ternes CM, Fernandes A, Rocha AV, Fernandes G, et al. SGLT2 inhibitors decrease cardiovascular death and heart failure hospitalizations in patients with heart failure: a systematic review and meta-analysis. EClinicalMedicine. 2021 Jun 1;36:100933. doi: 10.1016/j.eclinm.2021.100933.
23. Chambergo-Michilot D, Tauma-Arrué A, Loli-Guevara S. Effects and safety of SGLT2 inhibitors compared to placebo in patients with heart failure: a systematic review and meta-analysis. IJC Heart & Vasculature. 2021 Feb 1;32:100690. doi: 10.1002/ehf2.13169.

24. Falkentoft AC, Andersen J, Malik ME, Selmer C, Gæde PH, Staehr PB, et al. Impact of socioeconomic position on initiation of SGLT-2 inhibitors or GLP-1 receptor agonists in patients with type 2 diabetes–a Danish nationwide observational study. The Lancet Regional Health-Europe. 2022 Mar 1;14:100308. doi: 10.1016/j.lanepe.2022.100308.
25. Kato ET, Silverman MG, Mosenzon O, Zelniker TA, Cahn A, Furtado RH et al. Effect of dapagliflozin on heart failure and mortality in type 2 diabetes mellitus. Circulation. 2019 May 28;139(22):2528-36. doi: 10.1161/CIRCULATIONAHA.119.040130.
26. Woo V, Connelly K, Lin P, McFarlane P. The role of sodium glucose cotransporter-2 (SGLT-2) inhibitors in heart failure and chronic kidney disease in type 2 diabetes. Current medical research and opinion. 2019 Jul 3;35(7):1283-95. DOI: 10.3390/diseases8020014
27. Tromp J, Ponikowski P, Salsali A, Angermann CE, Biegus J, Blatchford J, et al. Sodium–glucose cotransporter 2 inhibition in patients hospitalized for acute decompensated heart failure: rationale for and design of the EMPULSE trial. European journal of heart failure. 2021 May;23(5):826-34. doi: 10.1002/ehf2.12759.