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Research Article

Glycemic control effectiveness of treatment regimens containing sodium-glucose-cotransporter-2 inhibitors in Vietnamese outpatients with type 2 diabetes

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ABSTRACT

Sodium-glucose-agonist-2 (SGLT2) inhibitors are a new generation of oral hypoglycemic drugs that are often used in combination as a second or third-line hypoglycemic agent in the treatment of type 2 diabetes (T2D). However, the use of SGLT2 inhibitors for outpatient treatment of type 2 diabetes in Vietnam remains limited. This study aimed to investigate the drug use and glycemic control effectiveness of SGLT2 inhibitor-containing treatment regimens in T2D outpatients. A retrospective descriptive study was conducted over 3 months, compared pre- and post-treatment outcomes in 204 outpatients aged 18 years and older diagnosed with T2D treated with SGLT2 inhibitor-containing regimens at Dong Nai General Hospital from January 2023 to June 2024. The majority of patients were elderly with a median age of 67 (61.0–71.7) years, overweight and obese (over 53%), and had multiple comorbidities (hypertension and dyslipidemia were the most common). Metformin and dipeptidyl peptidase-4 inhibitors are often prescribed with SGLT2 inhibitors in combination regimens. After 3 months of treatment, fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) levels of T2D outpatients were decreased from 8.77±2.00 mmol/L to 7.8±1.51 mmol/L for FBG and from 8.3±1.41% to 7.8±1.31% for HbA1c ($p<0.001$). Initial HbA1c levels were associated with the ability to achieve HbA1c goals (95% CI 0.20 (0.11–0.35); $p<0.001$). In conclusion, therapeutic regimens with SGLT2 inhibitors improved HbA1c and FBG goals of T2D outpatients. Baseline HbA1c was associated with the ability to achieve glycemic goals after treatment with SGLT2 inhibitors.

Keywords:
SGLT2 inhibitors; Type 2 diabetes; HbA1c; Fasting blood glucose; Outpatient.

1. INTRODUCTION

Diabetes mellitus is a chronic condition characterized by hyperglycemia, a metabolic disorder of carbohydrates, lipids, and proteins due to relative or absolute insulin deficiency, impaired β-cell function, or a combination of both. The rise of diabetes has become a major global public health problem [1]. Type 2 diabetes (T2D) progresses silently, causing many dangerous chronic complications that leave severe sequelae and even death. T2D is often accompanied by related factors such as hypertension, dyslipidemia, overweight and obesity [2]. Therefore, controlling blood glucose, blood lipids, and related risk factors is always the treatment goal for patients with TD2 [3]. Many combined measures to prevent and treat T2DM, including lifestyle changes and medication to control blood glucose levels and prevent possible complications. The glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) levels are two important indicators in diagnosing and monitoring the effectiveness of treatment for type 2 diabetes mellitus (T2DM),[4]. The strategy for treating diabetes involves

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combining medications with different mechanisms of glycemic control to increase treatment effectiveness, reduce side effects, and prevent complications for patients [5]. Sodium-glucose-agonist-2 (SGLT2) inhibitors are a new generation of oral hypoglycemic drugs that work by inhibiting glucose reabsorption in the renal tubules, increasing urinary excretion, and are independent of blood insulin levels. These drugs are often used in combination as a second or third-line hypoglycemic agent in the treatment of type 2 diabetes, but can also be used as monotherapy when metformin is contraindicated. SGLT2 inhibitors, including canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin, are effective not only in lowering blood glucose but also in protecting the cardiovascular system and kidneys. SGLT2 inhibitors can be combined with metformin, GLP-1 RA (glucagon-like peptide-1 receptor agonists), or dipeptidyl peptidase-4 (DPP4) inhibitors, for glycemic control [6-8]. In fact, SGLT2 inhibitors are not widely used in outpatient treatment of type 2 diabetes at some local hospitals in Vietnam due to their high cost and insurance coverage issues [9,10]. SGLT2 inhibitors have been used in combination with other hypoglycemic drugs to enhance glycemic control in patients with type 2 diabetes at Dong Nai General Hospital. However, the efficacy of SGLT2 inhibitor-containing treatment regimens in outpatients in Vietnam have been limited. The objective of this study was to evaluate the degree of glycemic improvement in T2D outpatients treated with SGLT2 inhibitor regimens, in order to support physicians in optimizing treatment strategies and improving the quality of life of T2D outpatients.

2. MATERIALS AND METHODS

2.1. Study population

This retrospective descriptive study was approved by the Ethics Committee of Dong Nai General Hospital in Vietnam before the collection of data.

All information from medical records of outpatients aged 18 years and older diagnosed with diabetes mellitus according to American Diabetes Association criteria [11] and type 2 diabetes according to the guidelines of the Viet Nam Ministry of Health [1] was collected in this study. Patients were diagnosed with T2D if fasting blood glucose (FBG) concentrations were ≥ 126 mg/dL (7.0 mmol/L) or HbA1C values were ≥ 6.5% (48 mmol/mol) [1]. Inclusion criteria included HbA1c > 7%, FBG > 7.2 mmol/L; prescription of SGLT2 inhibitor-containing regimens; complete test results (FBG, HbA1c, lipid profiles, eGFR, AST, ALT) on the day before using SGLT2 inhibitor-containing treatment regimens (T0) and at the time of follow-up (month T3). Exclusion criteria included type 1 diabetes or gestational diabetes or other types other than T2D; patients < 18 years, pregnant, or breastfeeding; conditions affecting HbA1c test results (hemodialysis, hemoglobin disorders, etc.); cirrhosis; severe acute illnesses (shock, severe infection, sepsis, acute heart failure, etc.); malignancies; prescription of SGLT2 inhibitor-containing treatment regimens for 3 months.

2.2. Sample size

The sample size (N) was calculated using the formula $N = (Z_{1-\alpha/2})^2\ p\ (1-p)/d^2$, where p is the prevalence of of diabetes patients achieving maximum improvement (optimal HbA1c) from 22% to over 40% [12]; d is the acceptable margin of error; Z is the confidence coefficient (Z = 1.96 if the level of confidence is 95%). Therefore, the minimum sample size was determined to be 184 patients.

2.3. Place and time

This study was conducted at the Department of Endocrinology, Dong Nai General Hospital on June 2024.

2.4. Study design

This retrospective descriptive study was conducted over 3 months and compared pre- and post-treatment outcomes in 204 outpatients aged 18 years and older diagnosed with T2D treated with SGLT2 inhibitor-containing regimens.

2.4.1. Evaluation of study population characteristics

Medical information of T2D patients was collected through eHOSPITAL software and handwritten medical records, including age, sex, weight, height, laboratory parameters, and clinical status. Variables on study population characteristics include age (divided into 2 groups: ≤ 65 years and > 65 [1]), gender (male/female); smoking; number of drugs in prescription; comorbidities, body mass index (BMI), etc. BMI in kg/m² is calculated by dividing body mass by the square of body height recorded from the patient's medical records. BMI was classified according to WHO standards for Asians: underweight (< 18.5 kg/m^2), normal weight (18.5 – 22.9 kg/m^2), overweight (23 – 24.9 kg/m^2), and obese (≥ 25 kg/m^2) [13].

2.4.2. Evaluation of drug use in outpatients with T2D

The drugs prescribed for T2D patients in this study will be surveyed in terms of the number of drugs prescribed for T2D and combination regimens containing SGLT2 inhibitors for T2D treatment.

2.4.3. Evaluation of treatment effectiveness of T2D outpatients

Changes in fasting blood glucose and HbA1c of type 2 diabetic patients at the time of the most recent follow-up visit (T3 months) were compared with the baseline time of SGLT2 inhibitor use according to the goals of the Viet Nam Ministry of Health. Furthermore, changes in other biochemical parameters of outpatients with T2D, such as blood lipid levels (triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) concentrations), uric acid levels, AST and ALT enzymatic activities, and estimated glomerular filtration rate (eGFR), were assessed at baseline (T0) and 3 months after diabetes treatment with an SGLT2 inhibitor. Patients with T2D are considered to have achieved the HbA1c target if HbA1c < 7% (53 mmol/mol) or FBG is 80-130 mg/dL (4.4 – 7.2 mmol/L) after treatment period [1]. T2D patients were also assessed to have achieved the target blood lipid concentration, specifically LDL-C concentrations < 70 mg/dL (1.8 mmol/L) if they have atherosclerotic cardiovascular disease; triglyceride concentrations < 150 mg/dL (1.7 mmol/L); and HDL-C concentrations > 40 mg/dL (1.0 mmol/L) in men and > 50 mg/dL (1.3 mmol/L) in women [1]. Furthermore, the adverse effects of SGLT2 inhibitor-containing regimens used for T2D patients have been evaluated.

2.4.4. Assessment of factors related to the effectiveness of glycemic control of outpatients with T2D

Each factor associated with achieving the HbA1c or FBG target was assessed. Factors that were significantly associated with glycemic control outcomes ($p < 0.05$) in univariate analysis were included in multivariate logistic analysis.

2.5. Variables

Quantitative variables, including biochemical parameters, were divided into groups before and after 3 months of treatment with SGLT2 inhibitor-containing regimens. Independent variables included age, gender, smoking, number of comorbidities, combination regimen, initial eGFR, and initial HbA1c (T0). Dependent variables included achieving glycemic goals.

2.6. Measurements

The concentrations of biochemical parameters and HbA1c values of T2D outpatients in this study were determined at the Department of Biochemistry, Dong Nai General Hospital. The concentrations of biochemical parameters, including blood glucose, blood lipids, enzyme activity, and uric acid, were quantified by the photometric method on the AU680 biochemical analyzer system (Beckman Coulter). The HbA1c value was measured using the ADAMS A1c HA-8190V Automated HbA1c Analyzer (Arkray). Reagent kits for the determination of plasma concentrations of biochemical parameters were obtained from Beckman Coulter. Reagent kits for the determination of HbA1c levels were purchased from Arkray. Plasma AST and ALT activities were determined by the kinetic photometric method. Plasma total protein concentrations were determined by the biuret method. Plasma triglyceride, glucose, total cholesterol, HDL-C, LDL-C, and uric acid concentrations were determined by the enzymatic-colorimetric method. Normal values of biochemical parameters included HbA1c 4.0 –6.0%, FBS 3.9 –5.6 mmol/L, triglycerides 0.46 –1.88 mmol/L, total cholesterol 3.9 – 5.2 mmol/L, HDL-C > 1.0 mmol/L for men and > 1.3 mmol/L for women, LDL-C < 2.6 mmol/L, uric acid 180 –420 µmol/L for men and 150 –360 µmol/L for women, aspartate transaminase (AST) < 37 U/L, alanine transaminase (ALT) < 40 U/L, and estimated glomerular filtration rate (eGFR) ≥ 60 ml/min/1.73m^2.

2.7. Statistical method

Collected data was entered into Excel 2021 software and statistically processed using SPSS 20.0 software, using appropriate statistical methods. The chi-square test is used to compare two or more groups for differences in proportions of categorical variables. The Wilcoxon signed-rank test (if non-normal distribution) and paired sample t-test (if normal distribution) were used to evaluate changes in FBS and HbA1c in the same group before and after treatment. The Kruskal-Wallis test (if non-normal distribution) and the One-way ANOVA test (normal distribution) were used to compare the average results of 3 or more independent groups. Results were considered statistically significant when $p < 0.05$.

3. RESULTS

3.1. Demographic characteristics of outpatients with T2D

The study collected 204 outpatient medical records that met the sampling criteria at the Department of Endocrinology, Dong Nai General Hospital, from January 2023 to June 2024. The median age of the patient population was 67 (61 - 71.75) years old. The proportion of female patients (53.9%) was 7 (5 –8). Patients with 3-4 comorbidities accounted for the highest percentage (49.5%). Dyslipidemia (89.7%) was the comorbidity with the highest proportion in the study sample, followed by hypertension (86.3%) and chronic kidney disease (52.5%). The characteristics of the patients in this study were presented in table 1.

Table 1. Demographic characteristics of outpatients with type 2 diabetes

Variables	Number (n)	Percentage (%)
Age (years)		
≤ 65	116	56.9
> 65	88	43.1
Sex (Male/Female)	94/110	46.1/53.9
Smoking (Yes/No)	11 / 193	5.4 / 94.6
BMI (kg/m^2)		
Underweight (< 18.5)	6	3
Normal (18.5 - 22.9)	88	43.1
Overweight (23 - 24.9)	80	39.2
Obese (≥ 25)	30	14.7
Number of drugs in the prescription		
< 5	34	16.7
≥ 5	170	83.3
Numbers of comorbidities		
0	1	0.5
1-2	44	21.6
3-4	101	49.5
≥ 5	58	28.4
Comorbitities		
Lipid disorders	183	89.7
Hypertension	176	86.3
Chronic kidney disease (CKD)	107	52.5
Atherosclerosis	106	52.0
Varicose veins	40	19.6
Neurological disease	40	19.6
Ischemic heart disease	23	11.3
Osteoporosis	18	8.8
Other diseases	58	28.4

3.2. Evaluation of drug use in T2D outpatients

Most T2D outpatients were prescribed SGLT2 inhibitors in combination with other hypoglycemic agents, most commonly dipeptidyl peptidase-4 (DPP-4) inhibitors (73.5%), metformin (66.2%), and insulin (59.8%). The SGLT2 inhibitors prescribed to T2D outpatients were empagliflozin (80.4%) at doses of 10 mg and 25 mg and dapagliflozin (19.6%) at a dose of 10 mg (see Table 2).

Table 2. Prescription of hypoglycemic drugs for treatment of outpatients with type 2 diabetes

Prescription for T2D outpatients (N = 204)	Number (n)	Percentage (%)
Antidiabetic drugs combined with SGLT2i		
DPP4i	150	73.53
Metformin	135	66.18
Insulin	122	59.80
SU	38	18.63
Acarbose	1	0.49
SGLT2i		
Empagliflozin 10 mg	29	14.22
Empagliflozin 25 mg	135	66.17
Dapagliflozin 10 mg	40	19.61

SGLT2i: Sodium-glucose-agonist-2 inhibitor; DPP4i: dipeptidyl peptidase-4 inhibitor; SU: sulfonylurea

Table 3. Combination of hypoglycemic drugs indicated for outpatients with type 2 diabetes

Treatment regimens	Antidiabetic drugs (N = 204)	Number (n)	Percentage (%)
Monotherapy	SGLT2i	2	1
	Total	**2**	**1**
2-drug regimens	SGLT2i + insulin	16	7.8
	SGLT2i + DPP4i	7	3.4
	SGLT2i + metformin	6	2.9
	Total	**29**	**14.2**
3-drug regimens	SGLT2i + insulin + DPP4i	41	20.1
	SGLT2i + DPP4i + metformin	29	14.2
	SGLT2i + insulin + metformin	13	6.4
	SGLT2i + metformin + SU	12	5.9
	SGLT2i + DPP4i + SU	2	1
	Total	**97**	**43.1**
4-drug regimens	SGLT2i + insulin + DPP4i + metformin	47	23
	SGLT2i + DPP4i + metformin + SU	23	11.3
	SGLT2i + insulin + metformin + SU	4	2
	SGLT2i + acarbose + metformin + SU	1	0.5
	SGLT2i + insulin + DPP4i + SU	1	0.5
	Total	**76**	**37.7**

SGLT2i: Sodium-glucose-agonist-2 inhibitor; DPP4i: dipeptidyl peptidase-4 inhibitor; SU: sulfonylurea
p: Chi-square test

3.3. Evaluation of treatment effectiveness of T2D outpatients

3.3.1. Evaluation of glycemic control effectiveness of treatment regimens containing SGLT2 inhibitors

After 3 months using SGLT2 inhibitor-containing regimens, the mean HbA1c and FBG levels of patients decreased significantly ($p < 0.001$). The proportion of patients with HbA1c ≥ 8% decreased significantly at time point T3m (-13.1%). The proportion of patients achieving HbA1c, fasting blood glucose, and both HbA1c and fasting blood glucose targets increased significantly compared to baseline, by +9.9%, +11.3%, and 8.9%, respectively (see table 4).

After 3 months of treatment with SGLT-2i-containing regimens, the mean HbA1c and FBG levels of patients decreased compared to the baseline time. However, the monotherapy regimens did not improve HbA1c and FBG levels. Conversely, combination regimens improved HbA1c and FBG, with the four-drug regimen improving HbA1c and FBG better than the two- and three-drug regimens containing an SGLT-2 inhibitor (see figure 1).

3.3.2. Evaluation of the impact of SGLT2 inhibitor-containing regimens on changes in other biochemical parameters of T2D outpatients

The mean concentrations of triglycerides, LDL-C, uric acid concentrations, AST, and ALT in T2D patients at T3m decreased compared to the time before using the SGLT2 inhibitor (T0). The mean concentrations of HDL-C and cholesterol increased slightly but not statistically significantly compared to the baseline ($p > 0.05$). Most patients had a normal eGFR at T0 and T3m after treatment with SGLT2 inhibitors (see table 5).

Table 4. Results of fasting blood glucose and HbA1c control in T2D outpatients

	T0	T3m	p
Concentrations	**Mean ± SD**	**Mean ± SD**	
HbA1c (%)	8.3 ± 1.41	7.8 ± 1.31	< 0.001*
FBG (mmol/L)	8.77 ± 2.00	7.8 ± 1.51	< 0.001 *
Patients	**Number (%)**	**Number (%)**	
HbA1c ≥ 8%	121 (59.2%)	94 (46.1%)	< 0.001**
HbA1c goals	29 (14.2%)	49 (24.1%)	< 0.001**
FBG goals	41 (20.1%)	64 (31.4%)	0.001**
HbA1c and FBG goals	17 (8.3%)	35 (17.2%)	< 0.001**

T0: the time before using an SGLT2 inhibitor; T3m: 3 months of treatment with SGLT2 inhibitor-containing regimens; P*: Wilcoxon test; p**: Chi-square test

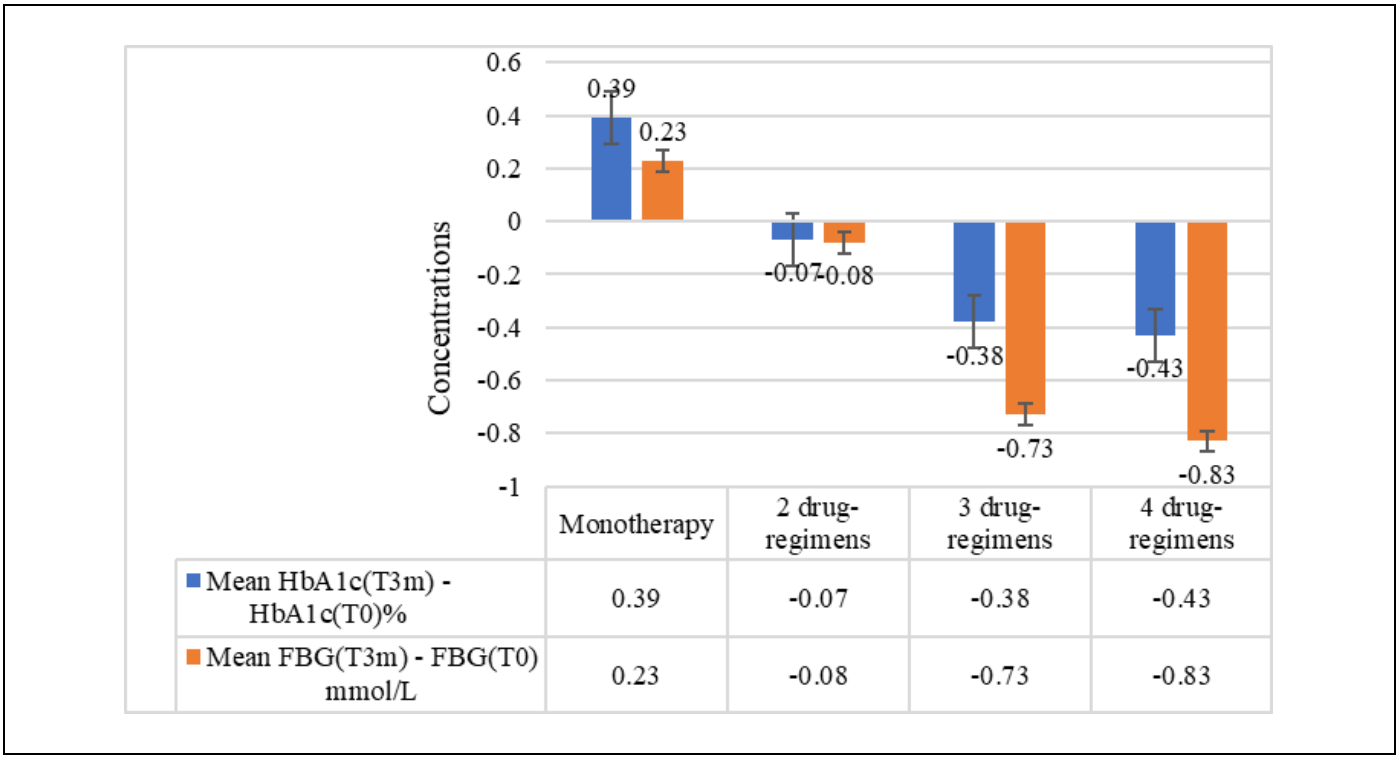

Figure 1. Changes in HbA1c and FBG after 3 months of treatment with regimens containing SGLT-2i (Mean $HbA1c_{(T3m)}$ - $HbA1c_{(T0)}$: difference between %HbA1c after 3 months and the baseline; Mean $FBG_{(T3m)}$ - $FBG_{(T0)}$: difference between fasting blood glucose (mmol/L) after 3 months and the baseline).

The proportion of patients achieving HDL-C, LDL-C, and triglyceride goals was significantly higher at 3 months after treatment with SGLT2 inhibitor-containing regimens than at baseline without SGLT2 inhibitor, but the difference was not statistically significant (p>0.05) (see figure 2).

3.3.3. Adverse events

95% of T2D outpatients did not experience adverse events when using SGLT2 inhibitor-containing regimens. Adverse events were recorded in only 10/204 patients using SGLT2 inhibitors, of which urinary tract infections accounted for the highest proportion (2.5%) (see figure 3). Most cases of urinary tract infections responded to antibiotics and did not require discontinuation of SGLT2 inhibitors. There were 2 patients with hypoglycemia when using a regimen containing insulin and SU concurrently. The study also recorded additional events of acute kidney injury and allergy caused by empagliflozin.

Table 5. Changes in other biochemical parameters compared to baseline time.

Concentrations	T0 (mean ± SD)	T3m (mean ± SD)	P
Triglyceride (mmol/L)	2.17 ± 1.17	1.95 ± 1.03	**0.018***
Total cholesterol (mmol/L)	3.9 ± 1.05	3.96 ± 1.09	0.484*
HDL-C (mmol/L)	1.04 ± 0.19	1.06 ± 0.20	0.486*
LDL-C (mmol/L)	2.1 ± 0.90	2.03 ± 0.92	0.317*
Uric Acid (µmol/L)	397.12 ± 63.93	390.27 ± 59.86	0.228**
AST (U/L)	25.7 ± 7.89	24.7 ± 8.02	0.683*
ALT (U/L)	27.7 ± 11.67	26 ± 11.77	0.425*
eGFR (ml/min/1.73 m^2)	66.24 ± 31.72	64.43 ± 32.40	0.244*

T0: the time before using an SGLT2 inhibitor; T3m: 3 months of treatment with SGLT2 inhibitor-containing regimens; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; AST: aspartate transaminase; ALT: alanine transaminase; p*: Wilcoxon test; p**: t-test

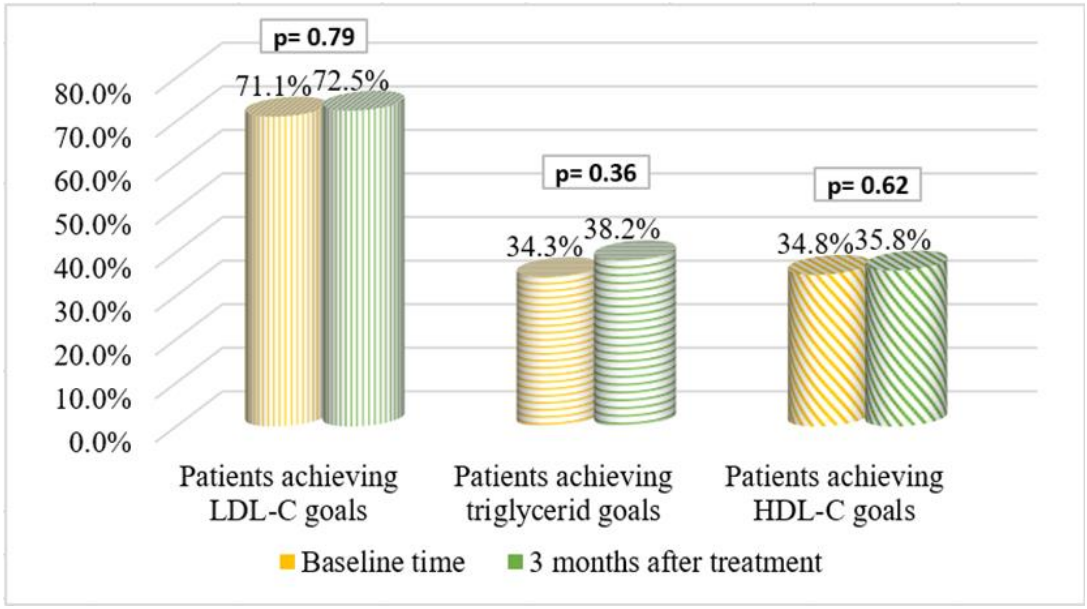

Figure 2. Percentage of type 2 diabetes outpatients achieving lipid goals after 3 months with SGLT2 inhibitor-containing regimens

3.4. Evaluation of factors related to glycemic control goals after 3 months of treatment with SGLT2 inhibitor-containing regimens

The results of univariate logistic analysis showed that factors associated with the ability to achieve the HbA1c target in this study included baseline HbA1c (95% CI 0.373 (0.23 – 0.60); $p < 0.001$) and SGLT2 inhibitor-containing regimens (95% CI 0.37 (0.23 – 0.60); $p < 0.001$). These independent variables were further evaluated in a multivariate logistic analysis. Other factors such as age, gender, smoking, glomerular filtration rate, and number of comorbidities did not affect the effectiveness of glycemic control ($p > 0.05$). Multivariate logistic analysis showed that the baseline HbA1c values were very important in achieving the glycemic control target after 3 months of treatment with SGLT2 inhibitor-containing regimens (95% CI 0.20 (0.11 –0.35); $p< 0.001$) (see table 6).

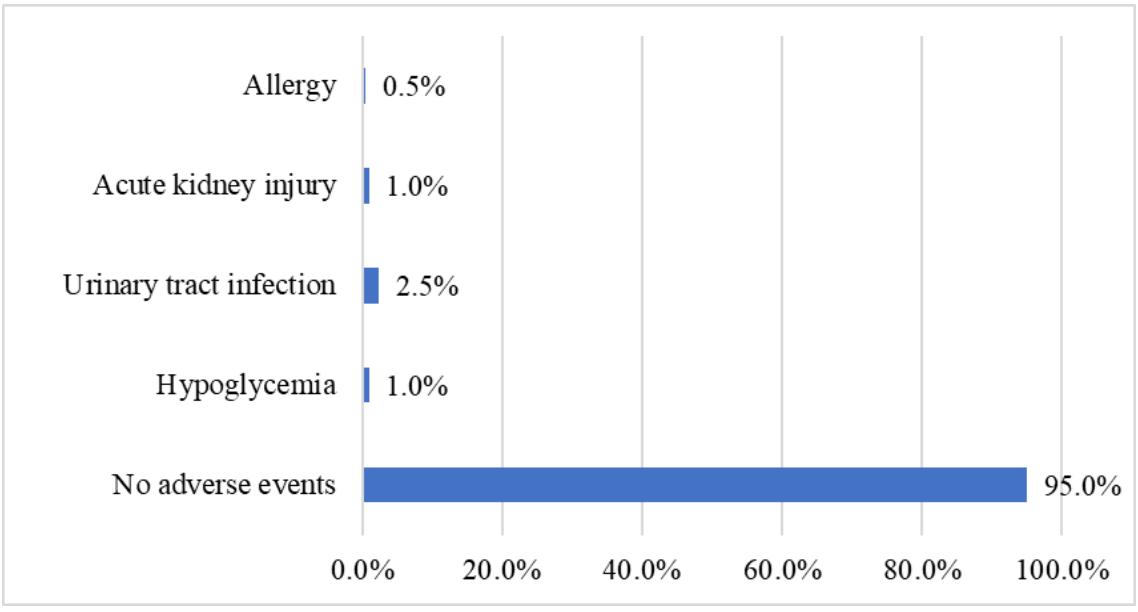

Figure 3. Adverse events observed in type 2 diabetes outpatients receiving SGLT2 inhibitor-containing regimens

Table 6. Results of logistic regression analysis of factors related to glycemic control goals

Factors		Univariable analysis		Multivariable analysis	
		OR (95% CI)	**P**	**OR (95% CI)**	**p**
Age (years)		0.98 (0.95 – 1.01)	0.314	-	-
Sex	Male	1		-	-
	Female	0.62 (0.32 – 1.18)	0.148	-	-
Smoking	No	1		-	-
	Yes	0.83 (0.21 – 3.27)	0.795	-	-
Number of comorbidities	0 - 2	1		-	-
	3 – 4	0.95 (0.38 – 2.37)	0.924	-	-
	≥ 5	0.95 (0.45 – 1.98)	0.895	-	-
BMI		1.23 (0.97 – 1.56)	0.080	-	-
SGLT2 inhibitor-containing regimens		0.37 (0.23 – 0.60)	< **0.001**	0.74 (0.40 – 1.38)	0.354
Baseline HbA1c (%)		0.18 (0.11 – 0.31)	< **0.001**	0.20 (0.11 – 0.35)	< **0.001**
eGFR at T0		0.99 (0.97 – 1.00)	0.165	-	-

"-": no analysis

4. DISCUSSION

The majority of outpatients with T2DM at the Endocrinology clinics of Dong Nai General Hospital were elderly (67 (61 –71.75) years old). This patient group is at high risk for cardiovascular complications, renal impairment, and severe hypoglycemia. Therefore, the use of SGLT2 inhibitors offers significant benefits in protecting the heart and kidneys, but close monitoring of dehydration and renal function is necessary [14]. Diabetes often increases the risk of complications and multimorbidity in the elderly. Hypertension and dyslipidemia are common comorbidities that increase the incidence of cardiovascular disease and lead to increased mortality in patients with T2D [11]. In this study, the percentages of hypertension (86.3%) and dyslipidemia (89.7%) were different from the study by Lee D-H et al. (51% and 57%, respectively) [15]. The difference between the study results may be due to the duration of diabetes, age, gender, and BMI [16]. Therefore, the hypolipidemic drugs prescribed to type 2 diabetes outpatients in this study were statins to prevent the progression of cardiovascular disease [11]. Among cardiovascular medications, angiotensin II receptor blockers were the most commonly used. The median number of drugs in a prescription of diabetic patients in this study was 7 drugs, higher than the study by Al-Taani GM et al. (6.5 drugs) [17]. The percentage of outpatients using 5 or more drugs was 83.7%, higher than higher than the study by Alwhaibi M et al. (78%) [18]. Overuse of medication can lead to a range of negative consequences, including: increased risk of adverse drug reactions and drug interactions, increased treatment costs, reduced quality of life, and decreased adherence to treatment [19]. DPP4 inhibitors, metformin, and insulin were most commonly combined with SGLT-2 inhibitors to improve glycemic control in T2D outpatients [20]. Metformin exerts its hypoglycemic effect primarily by reducing glucose production in the liver through inhibition of gluconeogenesis, enhancing the inhibitory effect of insulin on endogenous glucose production, and reducing glucose absorption in the intestine. DPP4i increases insulin secretion via GLP-1. SGLT2 inhibitors increase glucose excretion by blocking the SGLT2 protein in the renal proximal tubule. Many studies have shown that this combination helps reduce weight, increase the rate of achieving treatment goals, and improve blood pressure and blood lipids [21]. The majority of outpatients with T2DM in this study were overweight and obese. Therefore, they are primarily prescribed combination regimens containing SGLT2 inhibitors, and very few patients are treated alone with SGLT2 inhibitors [15].

Because the patient initially did not achieve glycemic control goals, it was recommended to measure HbA1c levels every 3 months to optimize diabetes management and reduce the risk of complications [22]. Many studies have shown that controlling HbA1c < 7% not only helps reduce complications due to diabetes but also reduces treatment costs [23]. Moreover, the higher the initial HbA1c value, the greater the reduction in HbA1c [24]. However, the difference between HbA1c and FBG after 3 months in this study were not statistically significant compared to the baseline. This may be due to insufficient duration of treatment with SGLT2 inhibitors to demonstrate effective results in T2D outpatients. Additionally, all patients in this study were elderly, had multiple chronic diseases, and had been ill for a long time, making it difficult to achieve treatment goals.

The mechanism of SGLT2 inhibitors on lipid changes remains largely unknown. A previous study concluded that SGLT2 inhibitors reduced total cholesterol but did not significantly change triglyceride,

LDL-C, and HDL-C values [25]. In contrast, a meta-analysis showed that SGLT2 inhibitors increased total, LDL-C, and HDL-C while decreasing triglycerides, depending on drug dose and race [26]. Uric acid levels in T2D outpatients in this study decreased after treatment. The reason may be that SGLT2 inhibitors increase uric acid excretion through the kidney, leading to a decrease in serum uric acid concentration [27]. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities have been found to be increased in T2D patients and are associated with comorbidities including hypertension, myocardial infarction, and chronic kidney disease. AST and ALT from T2D outpatients in this study were both reduced compared to baseline levels. A meta-analysis showed that SGLT2 inhibitor treatment was associated with a reduction in serum ALT and AST [28]. SGLT2 inhibitor drugs have been shown to restore and stabilize eGFR after long-term treatment when compared with other hypoglycemic drugs [29]. Most outpatients in this study had relatively high baseline mean eGFR values, which did not change after 3 months of treatment compared to baseline levels. The results of multivariate logistic analysis related to the ability to achieve glycemic control goals showed that the initial HbA1c value was more statistically significant than the number of drugs in the prescription. According to the UKPDS study, a 1% reduction in HbA1c will reduce microvascular complications by 37%, myocardial infarction by 18%, and diabetes-related mortality by 21% [30]. Other factors such as disease duration, education level, awareness level, treatment compliance, comorbidities, and the maintenance of non-pharmacological regimens such as physical exercise or healthy eating also greatly affected the glycemic control of patients.

This was the first retrospective study to evaluate the effectiveness of SGLT2 inhibitor-containing regimens in outpatients at Dong Nai General Hospital. Limitations of this study include small sample size and lack of information on patient weight and blood pressure changes in medical records. Further clinical studies may be conducted with larger sample sizes and longer follow-up periods to evaluate adverse events of regimens containing SGLT2 inhibitor drugs and other factors that may influence the indication for SGLT2 inhibitor drugs, such as health insurance and treatment costs.

5. CONCLUSIONS

SGLT2 inhibitors are a new generation of hypoglycemic drugs recommended for prescription in T2D patients due to their safety profile and protective effects on cardiovascular and renal function in these patients. The use of SGLT2 inhibitor-containing regimens improved the percentage of outpatients achieving HbA1c and fasting glucose goals after 3 months of treatment. Quadruple combination regimens help patients achieve HbA1c and FBG goals in T2D outpatients better than two- or three-drug regimens. Baseline HbA1c was associated with the ability to reach glycemic goals after treatment with an SGLT2 inhibitor.

6. ACKNOWLEDGMENT

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Authors contribution

Thuan Thi Minh Nguyen: Conceptualization, Methodology, Formal analysis, Project administrator, Supervision, Writing - original draft, Writing-reviewing and editing.

Huy Van Pham: Data curation, Formal analysis, Methodology, Investigation, Software, Writing-reviewing and editing.

Ngoc Thi Bao Le: Investigation, Writing-reviewing and editing.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval

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