



Effectiveness of the combination of SGLT2 inhibitor and GLP-1 agonist on glycemic control and cardiorenal outcomes: A pilot real-world study in Indonesia

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ARTICLE HISTORY

Received on: 23/10/2025

Accepted on: 30/01/2026

Available Online: 05/03/2026

Key words:

Diabetes mellitus, type 2, glucagon-like peptide-1 receptor agonists, retrospective studies, sodium-glucose cotransporter-2 inhibitors.

ABSTRACT

The combined use of Sodium-Glucose Cotransporter-2 Inhibitor (SGLT2i) and Glucagon-like Peptide-1 Receptor Agonist (GLP-1 RA) offers potential cardiometabolic benefits in type 2 diabetes mellitus. However, real-world data on this strategy, particularly in Southeast Asian populations, remains scarce. This study assessed the effectiveness of the combination versus SGLT2i or other oral antidiabetic drugs (OADs) in Indonesian patients on glycemic control and cardiorenal outcomes. A retrospective cohort study was conducted over ≥ 12 months among three treatment groups. Data were analyzed using the Shapiro–Wilk test for normality, followed by ANOVA or Kruskal–Wallis tests. Among the 111 patients, a notable intergroup difference was detected in systolic blood pressure (-15.8 , -2.79 , -4.16 mmHg in combination, SGLT2i, and OADs group, respectively; $p = 0.011$) and diastolic blood pressure (-9.56 , $+1.06$, -2.24 mmHg; $p = 0.001$). No significant differences were observed in HbA1c, weight, body mass index, fasting plasma glucose, lipid composites, estimated glomerular filtration rate, or atherosclerotic cardiovascular disease risk score across the groups. GLP-1 RA and SGLT2i combination therapy was associated with improved blood pressure, suggesting added cardiovascular benefit. Larger prospective studies are warranted to confirm these findings.

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a progressive metabolic illness that often requires treatment intensification to

achieve glycemic targets and prevent long-term complications. Combination therapy for T2DM is increasingly recommended and employed to enhance glucose regulation and mitigate cardiovascular risks. Although metformin remains the primary therapeutic option for most T2DM patients, combined therapy may be necessary to achieve target outcomes and should be tailored to the specific characteristics of each patient [1]. Among available therapeutic options, the combination of a Sodium-Glucose Cotransporter-2 inhibitor (SGLT2i) with a

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Glucagon-like Peptide-1 Receptor Agonist (GLP-1 RA) has gained increasing attention. In general, this combination is generally advised for patients at high risk of atherosclerotic cardiovascular disease (ASCVD), those with chronic kidney disease, individuals necessitating weight reduction, or patients requiring potent glycemic control [2,3].

Although the effectiveness of the combination of SGLT2i and GLP-1 RA has been thoroughly examined in clinical studies, real-world data about their concurrent application, especially in Southeast Asian populations, is limited [4–7]. This study assesses the efficacy of combining SGLT2i with GLP-1 RA on glycemic control and cardiometabolic outcomes, relative to SGLT2 inhibitor or other oral antidiabetics (OADs) in a real-world Indonesian cohort.

2. METHODS

2.1. Study design

This pilot project employs a retrospective cohort study design across three diabetic patient care sites in Indonesia. It constitutes a component of a broader real-world investigation in Indonesia that evaluates the efficacy of SGLT2i in comparison to non-SGLT2i. The study design was approved by the Research Ethics Committee of FKIK Atma Jaya Catholic University of Indonesia (approval number: 01/05/KEP-FKIKUAI/2024; dated May 7, 2024) and by the Research Ethics Committee of FKUI – Dr. Cipto Mangunkusumo Hospital (approval number: KET-744/UN2.F1/ETIK/PPM.00.02/2024; dated May 24, 2024). The results of this study are reported in accordance with the STROBE guidelines for cohort studies.

2.2. Patients and treatments

The eligibility criteria for this study encompass T2DM patients who are at least 18 years of age, regardless of whether they are on SGLT2i or GLP-1 RA, at any dosage. Exclusion criteria included SGLT2i use for less than 12 months, incomplete documentation of primary outcome data in medical records, and discrepancies in the duration of follow-up measurements exceeding 24 months. This study compared the clinical outcomes of groups receiving SGLT2i and GLP-1 RA combination (Group 1) versus SGLT2i alone (Group 2) versus other OADs (Group 3). In the combination group, therapy was administered simultaneously.

2.3. Variables and data collection

The primary variable assessed in this study was the change in HbA1c from baseline. Secondary variables included changes in ASCVD risk, estimated using the Revised Pooled Cohort Equation calculator [8], along with fasting plasma glucose (FPG), systolic and diastolic blood pressure (SBP and DBP), body weight, body mass index (BMI), estimated glomerular filtration rate (eGFR), and lipid composite parameters consisting of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and total cholesterol. Body weight and BMI data were measured at the same visit. In addition to primary and secondary outcomes, variables with potential confounding effects were also evaluated. These included age, sex,

smoking status, duration of diabetes, number of antidiabetic medications, and presence of comorbid conditions such as hypertension, dyslipidemia, a history of cardiovascular disease, microvascular complications, and prior occurrence of related adverse events. Data were collected between July and December 2024 at SS Diabetes Care, Eka Hospital BSD, and Dr. Cipto Mangunkusumo Hospital. The dataset included clinical outcomes and potential confounding factors categorized as primary, secondary, or demographic/confounding variables.

2.4. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics, Version 22. The Shapiro–Wilk test was used to analyze the normality of the data. We utilized ANOVA for normally distributed data and employed the Kruskal–Wallis test for non-normally distributed data. The chi-square test was used for binomial data types, but Fisher’s exact test was used when 50% of the cells had an expected count of less than 5. Linear regression was used to adjust for the confounders, which comprises two stages: the initial stage involves identifying variables that may serve as confounding factors for each of the outcomes. This step was followed by a linear regression analysis of variables exhibiting a significant correlation (p -value < 0.25) with the outcome, and the relevant standard covariates, including age, gender, and baseline values. Lipid composite data that were missing were estimated using the Sampson-NIH formula. Missing values were imputed utilizing a combination of approaches based on data availability. These approaches were used to maintain intra-patient trends while reducing data loss. Linear extrapolation was used to predict intermediate or endpoint missing values, while linear interpolation was employed when missing values occurred at the beginning of a patient’s observation period. For variables lacking a recognizable temporal trend, missing data were substituted with the mean of the observed values.

3. RESULTS

The study comprised 111 participants, with 37 patients allocated to each group. Table 1 displays the patient demographics for each group. The table indicates significant differences across groups for the number of diabetic drugs, treatment histories, medical histories, body weight, BMI, SBP, LDL-C, and triglycerides ($p < 0.05$). Nonetheless, for other components, there are comparable characteristics among groups. In the combination group, the utilization of GLP-1 RA included liraglutide (13.51%), semaglutide (59.46%), dulaglutide (16.22%), and lixisenatide (10.81%), whereas the use of SGLT2 inhibitors comprised dapagliflozin (40.54%) and empagliflozin (59.46%). In the SGLT2i group, dapagliflozin was administered to 35.14% of patients, while empagliflozin was utilized for the remaining 64.86%.

A comparative analysis of the three groups revealed a significant difference in SBP ($p = 0.011$) and DBP ($p = 0.001$), with the most substantial reduction observed in the GLP-1 RA and SGLT2i combination group for both parameters. No significant variations were observed in the remaining variable components, with the mean observation time being 14.18 months. The findings of this analysis are presented in Table 2.

Table 1. Demographics of patients between groups.

Components	Group 1 (n = 37)*	Group 2 (n = 37)*	Group 3 (n = 37)*	p-value
Age	61.93 ± 9.63	55.33 ± 11.238	57.11 ± 9.887	0.581
Gender (male)	23 (33.33%)	20 (28.986%)	26 (37.68%)	0.356
Smoking history	3 (37.50%)	1 (12.5%)	4 (50%)	0.528
Diabetes duration	4 (2–5)	3 (1–4)	4 (2–5)	0.138
Number of diabetes medications	4 (3–5)	3 (3–4)	2 (2–3)	0.000
Medication history:				
Metformin	30 (33.33%)	31 (34.444%)	29 (32.22%)	0.838
Sulfonylurea	15 (34.09%)	9 (20.455%)	20 (45.46%)	0.033
DPP-4 inhibitor*	20 (27.03%)	24 (32.432%)	30 (40.54%)	0.046
Metiglinide	0 (0%)	0 (0%)	0 (0%)	–
Thiazolidinedione	5 (83.33%)	1 (16.667%)	0 (0%)	0.046
Acarbose	0 (0%)	1 (100%)	0 (0%)	1.000
Insulin	13 (48.15%)	10 (37.037%)	4 (14.82%)	0.046
ACE inhibitor / ARB*	22 (48.89%)	13 (28.889%)	10 (22.22%)	0.013
Beta blocker	11 (73.33%)	2 (13.333%)	2 (13.33%)	0.002
Aldosterone antagonist	0 (0%)	0 (0%)	0 (0%)	–
Statin	31 (38.27%)	29 (35.802%)	21 (25.93%)	0.022
Aspirin	8 (57.14%)	2 (14.286%)	4 (28.57%)	0.131
History of Illness:				
Coronary Arterial Disease (CAD)	15 (83.33%)	3 (16.67%)	0 (0%)	0.000
Stroke	1 (100%)	0 (0%)	0 (0%)	1.000
Peripheral Arterial Disease (PAD)	4 (100%)	0 (0%)	0 (0%)	0.033
Hypertension	29 (45.31%)	17 (26.56%)	18 (28.13%)	0.007
Dyslipidemia	35 (38.89%)	32 (35.56%)	23 (25.56%)	0.001
Heart failure	1 (100%)	0 (0%)	0 (0%)	1.000
Diabetic nephropathy	8 (44.44%)	9 (50%)	1 (5.56%)	0.023
Diabetic neuropathy	6 (75%)	2 (25%)	0 (0%)	0.026
Diabetic retinopathy	4 (80%)	1 (20%)	0 (0%)	0.125
HbA1c (%)*	8.48 ± 1.04	8.57 ± 1.63	8.62 ± 2.47	0.589
Weight (kg)	79.74 ± 17.37	75.30 ± 9.97	68.89 ± 11.92	0.001
BMI (kg/m ²)*	30.040 ± 5.499	28.435 ± 4.132	25.832 ± 4.139	0.002
FPG (mg/dL)*	139.36 ± 43.56	148.27 ± 47.85	168.06 ± 66.27	0.527
SBP (mmHg)*	143.71 ± 19.14	138.40 ± 19.90	130.22 ± 15.66	0.029
DBP (mmHg)*	74.00 ± 10.95	78.83 ± 9.77	80.67 ± 7.83	0.707
LDL-C (mmHg)*	107.50 ± 40.23	130.70 ± 50.77	115.94 ± 32.39	0.011
HDL-C (mmHg)*	41.36 ± 12.29	44.35 ± 11.88	50.07 ± 15.39	0.288
Triglycerides (mmHg)	440.21 ± 791.83	138.42 ± 81.87	138.71 ± 75.28	0.011
Total cholesterol (mmHg)	188.49 ± 45.04	191.38 ± 47.50	196.85 ± 38.35	0.805
eGFR (mL/minute/1.73 m ²)*	71.57 ± 26.94	88.08 ± 22.92	85.61 ± 27.22	0.612
ASCVD Risk (%)*	22.17 ± 18.14	12.88 ± 11.61	12.87 ± 10.75	0.485

*Group 1 = Combination of GLP-1 RA and SGLT2i; Group 2 = SGLT2i; Group 3 = other OADs. Data in means (SD) or numbers (%) or median (IQR range) for ordinal data type. DPP-4 inhibitor = Dipeptidyl Peptidase-4 inhibitor; ACE inhibitor = Angiotensin Converting Enzyme inhibitor; ARB = Angiotensin Receptor Blocker; HbA1c = glycated hemoglobin; BMI = Body Mass Index; FPG = Fasting Plasma Glucose; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; LDL-C = Low-Density Lipoprotein Cholesterol; HDL-C = High-Density Lipoprotein Cholesterol; eGFR = estimated Glomerular Filtration Rate; ASCVD risk = Atherosclerotic Cardiovascular Disease risk.

Table 2. Comparative analysis between groups.

Component	Mean ± SD Group 1	N Group 1	Mean ± SD Group 2	N Group 2	Mean ± SD Group 3	N Group 3	p-value
HbA1c difference (%)	-0.988 ± 1.731	37	-1.126 ± 1.692	37	-0.570 ± 2.308	37	0.215
Weight difference (kg)	-1.973 ± 5.407	26	0.034 ± 3.639	37	-0.027 ± 3.240	37	0.106
BMI difference (kg/m ²)	-0.685 ± 2.101	26	-0.036 ± 1.354	37	-0.027 ± 1.212	37	0.181
FPG difference	-12.636 ± 52.227	22	-10.657 ± 51.096	37	-14.514 ± 65.084	37	0.557
SBP difference (mmHg)	-15.800 ± 16.238	25	-2.789 ± 18.161	37	-4.162 ± 16.741	37	0.011
DBP difference (mmHg)	-9.560 ± 10.905	25	1.06 ± 9.947	36	-2.243 ± 9.998	37	0.001
LDL-C difference (mg/dl)	-19.680 ± 37.138	25	-22.248 ± 55.312	37	-16.903 ± 32.658	37	0.870
HDL-C difference (mg/dl)	-3.831 ± 12.296	16	0.624 ± 8.768	37	-2.965 ± 9.851	37	0.158
Triglyceridedifference (mg/dl)	-134.460 ± 579.574	21	-5.503 ± 69.801	37	-3.911 ± 74.595	37	0.544
Total cholesterol difference (mg/dl)	-28.594 ± 48.146	16	-20.897 ± 54.714	37	-18.283 ± 42.732	37	0.751
eGFR difference (ml/minute/1.73 m ²)	0.139 ± 18.482	18	-0.249 ± 14.335	37	4.222 ± 13.902	37	0.442
ASCVD risk difference (%)	-2.240 ± 9.530	15	-0.762 ± 8.295	37	-0.608 ± 3.630	37	0.491

Group 1 = Combination of GLP-1 RA and SGLT2i; Group 2 = SGLT2i; Group 3 = other OADs. HbA1c = glycated hemoglobin; BMI = Body Mass Index; FPG = Fasting Plasma Glucose; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; LDL-C = Low-Density Lipoprotein Cholesterol; HDL-C = High-Density Lipoprotein Cholesterol; eGFR = estimated Glomerular Filtration Rate; ASCVD risk = Atherosclerotic Cardiovascular Disease risk.

Table 3. Adjustment to confounding results.

No.	Parameter	Adjustment components	Group 1	Group 2	Group 3	Adjusted p-value
1	HbA1c difference (%)	Group, age, gender, number of diabetes medications, history of CAD, history of dyslipidemia, history of diabetic neuropathy, BMI baseline, and HbA1c baseline	-1.012 (-1.766 to -0.258)	-1.169 (-1.673 to -0.664)	-0.336 (-0.957 to 0.286)	0.123
2	Weight difference (kg)	Group, age, gender, body weight baseline	-1.120 (-2.734 to 0.495)	0.104 (-1.178 to 1.387)	-0.697 (-2.028 to 0.634)	0.460
3	BMI difference (kg/m ²)	Group, age, gender, BMI baseline	-0.387 (-0.977 to 0.203)	0.040 (-0.439 to 0.519)	-0.312 (-0.808 to 0.184)	0.450
4	FPG difference (mg/dl)	Group, age, gender, number of diabetes medications, FPG baseline, and BMI baseline	-12.421 (-39.933 to 15.091)	-18.576 (-33.944 to -3.209)	-7.772 (-26.414 to 10.870)	0.652
5	SBP difference (mmHg)	Group, age, gender, history of PAD, history of hypertension, history of diabetic nephropathy, SBP baseline, and BMI baseline	-11.082 (-16.932 to -5.233)	-1.705 (-6.241 to 2.830)	-8.433 (-13.115 to -3.751)	0.030
6	DBP difference (mmHg)	Group, age, gender, history of CAD, history of hypertension, history of diabetic nephropathy, DBP baseline, and BMI baseline	-9.740 (-13.685 to 5.794)	1.348 (-1.528 to 4.224)	-2.402 (-5.454 to 0.650)	0.000
7	LDL-C difference (mg/dl)	Group, age, gender, and LDL-C baseline	-30.982 (-43.568 to -18.396)	-10.639 (-21.068 to -0.209)	-20.876 (-31.132 to -10.620)	0.056
8	HDL-C difference (mg/dl)	Group, age, gender, history of dyslipidemia, and HDL-C baseline	-5.675 (-9.705 to -1.644)	0.142 (-2.522 to 2.806)	-1.416 (-4.147 to 1.315)	0.058
9	Triglycerides difference (mg/dl)	Group, age, gender, TG baseline, and BMI baseline	14.357 (-30.812 to 59.527)	-46.741 (-76.671 to -16.812)	-40.459 (-71.277 to -9.641)	0.078
10	Total cholesterol difference (mg/dl)	Group, age, gender, total cholesterol baseline, and BMI baseline	-23.594 (-44.477 to -2.710)	-18.767 (-31.851 to -5.682)	-19.754 (-33.187 to -6.321)	0.925
11	eGFR difference (mL/minute/1.73 m ²)	Group, age, gender, history of hypertension, and eGFR baseline	-21.181 (-46.125 to 3.762)	-20.136 (-35.772 to -4.500)	-22.250 (-37.950 to -6.550)	0.982
12	ASCVD risk difference (%)	Group, history of CAD, history of hypertension, and ASCVD risk baseline	-0.116 (-4.175 to 3.943)	-1.105 (-3.334 to 1.124)	-1.127 (-3.414 to 1.160)	0.910

Bold values indicate statistically significant results after adjustment for confounding factors ($p < 0.05$).

The linear regression analysis yielded robust results for all test variables. The findings of this investigation demonstrated significant results regarding the difference in SBP and DBP, even after adjustment for confounding risks and standard covariates; with the cohort utilizing the combination of GLP-1 RA and SGLT2i exhibiting superior reductions in SBP and DBP, as seen in [Table 3](#).

4. DISCUSSION

The combination therapy of GLP-1 RA and SGLT2i showed a notable decrease in SBP and DBP compared to other groups. A positive tendency towards greater SBP and DBP reduction in the combination group remained evident even after adjustment for relevant covariates, indicating a potential therapeutic advantage. To strengthen future analyses, it is advisable to utilize a bigger sample size, implement a prospective design, and gather compliance and lifestyle factors. A double-blind RCT (DURATION-8) showed enhancements in blood pressure compared to monotherapy at 28 weeks [5]. Two meta-analyses yielded results analogous to this study and the DURATION-8 trial, which encompassed a greater number of participants than the other studies, hence producing a bigger effect size, indicating a significant enhancement in SBP, ranging from 0.93 to 1.17 mmHg, without a significant effect on DBP [9,10]. The AWARD-10 trial demonstrated that the dosage magnitude determines the effectiveness of this combination in reducing SBP. Administration of dulaglutide at a dosage of 1.5 mg per day resulted in a reduction of SBP by -4.5 mmHg from baseline in the combination group with SGLT2i compared to placebo; however, no decrease in SBP was observed at lower dosages [4].

SGLT2i function by obstructing glucose reabsorption in the proximal tubule, resulting in natriuresis, which may influence the hypotensive effect [11]. Concurrently, GLP-1 RA induces natriuresis by inhibiting the Na⁺/H⁺ Exchanger 3, located in the proximal tubule, which is crucial for the reabsorption of sodium and bicarbonate [12]. Another mechanism by which this combination therapy exerts its hypotensive effect is weight reduction, which is achieved by appetite suppression and the inhibition of hepatic glucose synthesis [13]. Other than that, a meta-analysis of 26 publications ($n = 668$ individuals) showed that SGLT2i enhanced vascular function by enhancing flow-mediated dilation, while GLP-1 RA improved pulse wave velocity [14], indicating that both therapies can improve endothelial function and arterial stiffness. This combination is believed to influence the Renin-Angiotensin-Aldosterone System (RAAS). The diuretic and natriuretic actions of SGLT2i lead to RAAS activation, in contrast to GLP-1 RA, which limits RAAS activation by suppressing angiotensin II production [15]. This combined therapy induces natriuresis and volume reduction without compensatory vasoconstriction, and these and other antihypertensive effects serve as cardioprotective agents. A meta-analysis indicated that the reduction of blood pressure with SGLT2i and GLP-1 RA correlated with decreased risks of mortality, cardiovascular death, heart failure, myocardial infarction, and renal failure [16].

Numerous clinical studies and meta-analyses have demonstrated enhancements in glycemic control and weight

reduction by the concomitant administration of GLP-1 RA and SGLT-2 inhibitors [4,5,9,10]. A meta-analysis comprising 5 RCTs and 5 non-RCTs ($n = 1,604$ participants) demonstrated a reduction in HbA1c of 1.32% and a weight loss of 0.93 kg relative to control/placebo [9]. Nonetheless, discrepancies in outcomes exist among different real-world investigations [13], as evidenced by the present real-world study conducted in Indonesia. These discrepancies may arise from variations in study design, treatment compliance, and the characteristics of T2DM patients in Indonesia. Indonesia has a comparatively younger diabetes population than Western countries; nonetheless, many individuals are diagnosed at a more advanced stage, displaying higher baseline HbA1c levels, perhaps due to inadequate screening and awareness. The average BMI of Indonesian patients with T2DM is frequently lower, with many individuals displaying the “lean diabetes” phenotype [17–19]. Variations in adiposity may influence the efficacy of drugs like GLP-1 RA, which function partially through appetite suppression and weight reduction [14]. Another factor that can diminish the efficacy of the combination therapy is the rising physical inactivity among the Indonesian population, which adversely affects therapeutic outcomes [20]. An extensive cross-sectional study consists of 30,940 respondents, revealed that the majority of respondents mostly consumed rice (99.8%) and frequently ingested instant noodles, fried snacks, and sugary snacks. Nearly half of the respondents (44.8%) exhibited poor levels of physical activity [21]. Furthermore, an earlier qualitative investigation identified various obstacles to the utilization of SGLT2i, such as drug availability and accessibility [22], which may result in noncompliance, a factor challenging to evaluate in retrospective observational studies.

Results from a meta-analysis studying the efficacy of the combination therapy, consisting of four studies ($n = 1,610$ participants), indicate potential favorable effects on lipid metabolism, particularly in lowering LDL-C (-0.13 mmol/l) and total cholesterol levels (-0.17 mmol/l), compared to SGLT2i monotherapy [10]. Nevertheless, the findings of this meta-analysis exhibit significant heterogeneity ($I^2 \geq 50\%$), and the extent of these lipid-related benefits remains inconsistent across studies, highlighting the need for further investigation to elucidate the mechanisms and magnitude of the combination therapy's impact on lipid parameters. This study found no improvement in ASCVD risk with advancing age and no enhancement in SBP, HDL-C, or total cholesterol levels.

A retrospective analysis indicated comparable outcomes concerning renal protection, with no significant difference in eGFR improvement between combination therapy and monotherapy. In the group receiving both SGLT2i and GLP-1 RA with SGLT2i initiated six months prior, there is a notable enhancement in the annual reduction of eGFR (-3.5 to -0.4 ml/min/1.73 m²/year), whereas the GLP-1 RA-preceding group exhibits no significant deceleration in eGFR decline, indicating that the preceding medications substantially influence renal outcomes [23]. The present real-world study was unable to do a subgroup analysis due to insufficient participation.

This study has several notable strengths. It is a multicenter investigation, which enhances the representativeness of the study population by capturing a wide range of clinical profiles and

treatment practices. Moreover, including comparator groups receiving other OADs—without GLP-1 RA or SGLT2i—enables a more comprehensive evaluation of treatment effectiveness across different therapeutic strategies. Nevertheless, several limitations should be acknowledged. As a retrospective study, it is inherently susceptible to missing data; although appropriate data imputation methods were applied, some uncertainty remains. Baseline characteristics differed significantly across treatment groups, which may introduce confounding; however, statistical adjustments were made to mitigate this effect on outcome comparisons. The study also could not account for unmeasured changes in medication dosage, which are common in routine clinical practice. Another limitation is the inability to accurately assess patient adherence to therapy, which may bias the estimation of treatment effects. Finally, due to insufficient data, the current study in Indonesia cannot be compared to GLP-1 RA monotherapy. Due to its elevated cost and administration, GLP-1 RA prescriptions in Indonesia are generally utilized as adjunctive therapy to SGLT2i. Furthermore, due to the pilot nature of this research, a study with more advanced statistical power is necessary. However, this study has a power of 83.9%, indicating adequate statistical power.

5. CONCLUSION

Patients receiving the combined treatment of GLP-1 RA and SGLT2i experienced more pronounced blood pressure reductions than those treated with SGLT2i alone or other oral antidiabetic agents, even after controlling for several confounders. However, no statistically significant differences were found in other metabolic parameters. These preliminary findings highlight the potential benefit of combination therapy, particularly for individuals with heightened cardiovascular risk, though validation through prospective, larger, more powerful studies is warranted.

6. ACKNOWLEDGMENTS

The researchers sincerely acknowledge the support provided by the pharmacy and medical records units at Dr. Cipto Mangunkusumo National Referral Hospital, Eka Hospital BSD, and SS Diabetes Care, whose cooperation and permission were essential for data access and the smooth conduct of this study.

7. AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

8. FINANCIAL SUPPORT

This study is sponsored by Indonesian Education Scholarship (BPI), Center for Higher Education Funding and Assessment (PPAPT), and Indonesian Endowment Fund for Education (LPDP) under grant number “00169/BPPT/

BPI.06/9/2023”. The grant is allocated for data collection and publication activities.

9. CONFLICT OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

10. ETHICAL APPROVALS

Ethical approval details are given in the ‘Methods’ section.

11. DATA AVAILABILITY

All the data is available with the authors and shall be provided upon request.

12. PUBLISHER’S NOTE

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13. USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declare that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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How to cite this article:

Cokro F, Sauriasari R, Tahapary DL, Setiawan H, Tricaesario C, Hidayati N, Soegondo S. Effectiveness of the combination of SGLT2 inhibitor and GLP-1 agonist on glycemic control and cardiorenal outcomes: A pilot real-world study in Indonesia. *J Appl Pharm Sci.* 2026;16(04):153-159. DOI: 10.7324/JAPS.2026.266181