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ORIGINAL ARTICLE

Effect of Sodium Glucose Co-transporter Type 2 Inhibitors on The Infract size among Diabetic Patients with ST Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Myocardial ischemia causes cell death, which sets off an inflammatory cascade that eventually leads to the formation of scars.Sodium-glucose co-transporter-2 inhibitors(SGLT2I) used in the management of patients with type 2 diabetes**.**

Aim: Is to evaluate the long-term treatment with SGLT2I on decreasing the infarct size in STEMI diabetic patientswho undergoing primary percutaneous coronary intervention.

Methods: This Comparative study included 30 patients who were admitted with STEMI undergoing Primary PCI. Patients were divided equally into group(1) included diabetic patients not on SGLT2I & group 2 included diabetic patients on SGLT2I for more than 6 months. Baseline characteristics, echocardiographic parameters , angiographic and procedural data, medication use, and outcome data were recorded prospectively.

Results: Regarding cardiac biomarkers, hs-TnI levels were significantly higher in non SGLT2I group compared to SGLT2I group (5467.4 ± 2210.42 Vs. 1325.7 ± 562.39, P<0.05, respectively).Furthermore, the angiography finding, TIMI flow after PCI was significantly improved in SGLT2I group compared to non SGLT2I group (2.1 ± 0.74 Vs. 1.4 ± 0.99, P=0.029, respectively), with no significant difference between both groups regarding other angiography findings. On hospital discharge, ST resolution and Ejection Fraction(EF) were significantly improved in SGLT2I group compared to non SGLT2I group (54.7 ± 1.87, 13 (86.67%)Vs. 50.3 ± 2.38, 8 (53.33%),P<0.001, 0.046, respectively) ,also WMSI on hospital discharge was significantly higher in non SGLT2I group compared to SGLT2I group (1.63 ± 0.38Vs. 1.30 ± 0.22, P=0.007 respectively). Mitral regurgitation was significantly different between both groups, being significantly improved in SGLT2I group compared to non SGLT2I group (2(13.33%) Vs. 8(53.33%),P=0.003,respectively). Baseline EF, Q wave, WMSI and mitral regurgitation were insignificantly different between both groups.

Conclusion: Diabetic patients with STEMI undergoing PPCI and treated with SGLT2I exhibited significantly decreased the infract size and improved cardiovascular outcomes compared to those not on SGLT2Itherapy.

Keywords: Infarction size, post PCI TIMI flow, wall motion Score Index.

INTRODUCTION

Globally, myocardial infarction (MI) and other ischemic heart disease are the leading causes of death. Myocardial ischemia, or MI, is usually caused by a thrombotic coronary artery blockage. Primary percutaneous coronary intervention (PCI) of the infarct-related coronary artery is typically done following a MI diagnosis in order to facilitate reperfusion, reduce tissue necrosis, and enhance clinical prognosis **[1]**.

Furthermore, with the elimination of dead cells and matrix debris, reperfusion sets off an

essentially regenerative signaling cascade by the immune system, which is designed to restore the damaged tissue**[2]**.

Nonetheless, strict regulation of this immune-mediated response is necessary to stop further

damage to cardiac tissue, which could lead to congestive heart failure **[1]**.

Since there are currently few effective treatments for reperfusion injury, and because the extent of a myocardial infarct is highly correlated with mortality, new medicines must be developed**[3]**.

SGLT2 inhibitors have been studied in a number of preclinical investigations and have been proven to minimize acute myocardial ischemia–reperfusion injury in the majority of instances due to their high efficacy, great tolerability, and capacity to prevent severe adverse cardiovascular events in big clinical trials **[4]**.

Therefore, this study aimed to evaluate the long-term treatment with SGLT2I on decreasing the infarct size in ST Segment Elevation Myocardial Infarction (STEMI) diabetic patients who were undergoing primary percutaneous coronary intervention.

METHODS

This Comparative study included 30 patients who admitted with STEMI undergoing Primary PCI, at Cardiology department, Zagazig University hospital, and Al-Ahrar teaching hospital in duration of one year.

Based on admission anti diabetic therapy patients were divided into two groups as follows:

Group1 (n=15): included diabetic patients not on SGLT2I. Group2 (n=15): included diabetic patients on SGLT2I (Empagliflozin 10mg or Dapagliflozin 10mg started at least 6months before hospitalization).

Inclusion criteria: Diabetic patients with ST segment elevation myocardial infarction (STEMI) undergoing Primary PCI.

Exclusion criteria: Individuals using insulin or those with insufficient knowledge about medical treatment, advanced renal impairment , need for emergent CABG and those with chronic heart failure.

Informed consent and ethics committee/IRB approval:

Written informed consent was obtained from all participants, the study was approved by the research ethical committee at faculty of medicine at Zagazig University under "ZU-IRB #10447". The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All studied cases were subjected to the following:

Detailed history taking: Including; personal history: age, sex, residence, occupation, and special habits including smoking or alcohol consumption. Present and Past history of any medical condition with emphasis on risk factors for coronary artery disease(CAD) as hypertension, smoking, dyslipidemia, Diabetes Mellitus (DM) ,AF, COPD, PAD, family history and previous history for Acute Coronary Syndrome (ACS) or Myocardial revascularization. Medical history of drugs taken including Statins, ACEI, ARBs, SGLT2 inhibitor and its duration of intake and DAPT.

Full clinical examination: General examination including vital signs (pulse, blood pressure, capillary filling time, respiratory rate, and temperature). Body mass index (BMI) .Signs of heart failure. Local cardiac examination for detection of any abnormality including abnormal heart sounds, murmurs, pulmonary rales, pericardial rub, thrills ,cardiomegaly , and previous surgery.

Routine laboratory investigations: Cardiac enzymes: total creatinine kinase (CK), CK-MB isoenzyme (MB) and troponin T are dynamically measured before the procedure and until 48 hours after procedure. CRP(mg/dL). Liver function tests ALT(U/L),AST(U/L). Kidney function testes (Serum creatinine (mg/dL), Urea(mg/dL)). Lipid profile within 1st 24hours(mg/dL). HbA1c(normal up to 6.5%), and RBS. INR, PT (Sec) and PTT (Sec). Complete blood count (Hemoglobin, White Blood Cells, Platelets).

Baseline electrocardiography(ECG) : Diagnostic ST elevation in absence of left ventricular hypertrophy or left bundle branch block(LBBB).≥ 1.5 mm (0.15 mV) in women or ≥ 2 mm (0.2 mV) in males in leads V2-V3. ≥ 1 mm (0.1 mV) in two more contiguous chest leads or limb leads. New or presumed new LBBB is thought to be a STEMI comparable**[5]**;.

Echocardiography: Echocardiography can be utilized in a number of ways to calculate LVEF. The left ventricular (LV) volumes are calculated using formulae that vary depending on the type of echocardiographic image (three-, two-, or M-mode) and the technique employed. One-dimensional (linear), two-dimensional (area), or three-dimensional (volume) measurements can be produced. For LVEF assessment, the currently preferred in our study two-dimensional method is the biplane method of disks (modified Simpson's rule) **[6].**

Wall motion score index(WMSI) : Each segment is then scored, using the following criteria:

Normal endocardial excursion and wall thickening are considered normokinesia (1 point). Hypokinesia (2 points): decreased endocardial excursion, decreased wall thickening. Akinesia (3 points): no endocardial excursion nor wall thickening is present. Four points for dyskinesia:

systolic outward thinning or stretching. Then, the sum of the previously indicated segmental values is divided by the total number of myocardial segments (16) to determine the wall motion score index. A WMSI of 3.0 correlates with an ejection fraction of 12% and is regarded as akinetic, whereas a WMSI of 1.0 (16/16) is considered normokinetic. Mild hypokinesia, hypokinesia, and severe hypokinesia are the designations given to WMSIs of 1.5, 2.0, and 2.5, respectively**[7]**.

Percutaneous coronary intervention: Using conventional interventional procedures, coronary angiography and stent implantation were carried ,every baseline and procedural cine coronary angiography was examined and subjected to quantitative analysis. TIMI flow grades were evaluated before and after PCI. The final angiography was used to determine the myocardial blush grade (MBG) [8]..

Statisticalanalysis:

Microsoft Excel was utilized to gather and examine the data. The Statistical Package for the Social Sciences (SPSS version 20.0) program was then used to import the data and analyze it. Contingent on the nature of the data, the quantitative group is represented by mean± SD, while the qualitative data is expressed as a number and percentage. variations between independent multiples that are quantified using ANOVA. For significant results, the P value was set at <0.05, and for highly significant results, at <0.001.

RESULTS

The present study showed SGLT2I group had significantly higher age compared to non SGLT2I group (P=0.008). The other baseline characteristics (sex, weight, height, and BMI)were not significantly different between both groups**(Table 1).**

The HR was significantly higher in non SGLT2I group compared to SGLT2I group(P=0.001), with no significant difference between both groups regarding SBP and DBP**.** There was an insignificant difference between the studied groups regarding the risk factors(smoking, hypertension, dyslipidemia, angina, CKD, PAD, COPD, family history of CAD,previousPCI, prior CABG and prior MI)**(Table2).**

Regarding the laboratory investigations, neutrophil, NLR, TG and CRP were significantly higher in non SGLT2I group compared to SGLT2I group (P<0.001,0.004,<0.001respectively). Level of urea was significantly higher in SGLT2I group compared to non SGLT2I group (P=0.005). Other laboratory findings (Hb, PLT, WBCs, lymphocytes, HbA1c, serum creatinine, ALT, and AST) were insignificantly different between both groups **(Table3).**

After 24 hours, lymphocytes count was significantly higher in SGLT2I group compared to non SGLT2I group (P=0.017). Neutrophil, NLR and CRP were significantly higher in non SGLT2I group compared to SGLT2I group (P=0.011, 0.005, <0.001 respectively). Other laboratory findings (Hb, PLT, WBCs, HbA1c and serum creatinine) were in significantly different between both groups **(Table 4).**

Regarding cardiac biomarkers, hs-TnI levels were significantly higher in non SGLT2I group compared to SGLT2I group (5467.4 ± 2210.42 Vs. 1325.7 ± 562.39, P<0.05, respectively) **(Table 5).**

Regarding the angiography finding, TIMI flow after PCI was significantly higher in SGLT2I group compared to non SGLT2I group (P=0.029), with no significant difference between both groups regarding other angiography finding**(Table 6).**

On hospital discharge, ST resolusion and EF was significantly higher in SGLT2I group compared to non SGLT2I group (P<0.001, 0.046). WMSI on discharge was significantly higher in non SGLT2I group compared to SGLT2I group (1.63 ± 0.38 Vs. 1.30 ± 0.22, P=0.007 respectively).Mitral regurgitation was significantly different between both groups, being significantly improved in SGLT2I group compared to non SGLT2I group (P=0.003). Baseline EF, WMSI and mitral regurgitation were insignificantly different between both groups**(Table7).**

Table1: Baseline characteristics of the studied groups

		Total (n=30)	Non SGLT2I group (n=15)	SGL T2I group (n=15)	P value
Age(years)	**Mean±SD**	69.2±4.75	67.0±3.98	71.5± 4.5	**0.008***
	Range	61-79	61-73	66-79	
Sex	**Male**	25(83.3%)	13(86.67%)	12(80%)	1.00
	Female	5(16.7%)	2(13.33%)	3 (20%)	
Weight(Kg)	**Mean±SD**	71.1±6.68	70.5±7.49	71.8±5.95	0.594
	Range	56-84	56-84	64-82	

		Total (n=30)	Non SGLT2I group (n=15)	SGL T2I group (n=15)	P value
Height(m)	Mean±SD	1.6 ±0.04	1.7 ±0.03	1.6 ±0.04	0.164
	Range	1.59-1.7	1.6-1.7	1.59-1.7	
BMI(Kg/m^2)	Mean±SD	26.3±2.41	25.7±2.87	26.8±1.78	0.231
	Range	19.38-30.8	19.38-30.85	23.53-28.65	

BMI:body mass index,*:statistically significant as pvalue<0.05.

Table2:Clinical examination , vital signs &Risk factors of the studied groups

	Total (n=30)	Non SGLT2I group (n=15)	SGL T2I group (n=15)	P value
HR(beats/min)	82.7±6.83 71-95	86.6±6.32 75-95	78.9±4.97 71-85	**0.001***
SBP(mmHg)	134.7±14.1 110 -160	134.0± 16.39 110 -160	135.3± 11.87 120 -160	0.800
DBP(mmHg)	81.3±8.19 70-90	79.3±8.84 70-90	83.3±7.24 70-90	0.186
Riskfactors(%)				
Smoking	20(66.67%)	11(73.33%)	9 (60%)	0.699
Hypertension	23(76.67%)	12(80%)	11(73.33%)	1.00
Dyslipidemia	21(70%)	11(73.33%)	10(66.67%)	1.00
Angina	20(66.67%)	11(73.33%)	9 (60%)	0.699
CKD	3 (10%)	1 (6.67%)	2(13.33%)	1.00
PAD	6 (20%)	4(26.67%)	2(13.33%)	0.651
COPD	3 (10%)	2(13.33%)	1 (6.67%)	1.00
FamilyhistoryofCAD	7(23.33%)	3 (20%)	4(26.67%)	1.00
PreviousPCI	8(26.67%)	5(33.33%)	3 (20%)	0.682
PriorCABG	4(13.33%)	2(13.33%)	2(13.33%)	1.00
PriorMI	2 (6.67%)	1 (6.67%)	1 (6.67%)	1.00
AF	3 (10%)	2(13.33%)	1 (6.67%)	1.00

HR: heart rate ,SBP: systolic blood pressure, DBP: diastolic blood pressure,*:statistically significant as p value<0.05. CKD: chronic kidney disease, PAD: peripheral artery disease, COPD: chronic obstructive pulmonary disease, CAD: coronary artery disease, PCI: percutaneous coronary intervention, CABG: coronary artery by pass graft, MI: myocardial infarction, AF: atrial fibrillation.

Table3: Laboratory investigations of the studied groups

	Total (n=30)	Non SGLT2I group (n=15)	SGL T2I group (n=15)	P value
Hb(g/dL)	13.04±1.03 11.5-14.5	13.1± 1.11 11.5 -14.5	12.99±0.97 11.6-14.3	0.808
PLT(*10^9/L)	292.1±38.9 209 -348	288.9± 42.95 209-348	295.2± 35.71 226 -342	0.667
WBCs(*10^9/L)	9.4 ±1.74 6.7-13	9.7±1.66 7.2-12.7	9.1 ±1.81 6.7-13	0.317
Lymphocytes(*10^9/L)	2.01±0.43 1.3-2.9	1.9 ±0.43 1.3-2.4	2.1 ±0.41 1.6-2.9	0.164
Neutrophil(*10^9/L)	6.96±1.19 5.4-9.3	7.7 ±1.17 5.4-9.3	6.3 ±0.69 5.4-7.4	**<0.001***
NLR	3.7±1.21 1.9 -6.54	4.3±1.33 2.48-6.54	3.1±0.67 1.9 -4.11	**0.004***
HbA1c(%)	7.7 ±0.6 6.7-8.9	7.7 ±0.56 6.8-8.5	7.8 ±0.65 6.7-8.9	0.613
CPR(mg/dL)	3.4 ±0.76 2.2-4.5	4.0 ±0.42 3.1-4.5	2.7 ±0.34 2.2-3.5	**<0.001***

Serum creatinine(mg/dL)	1.1 ±0.15 0.8-1.3	1.03±0.15 0.8-1.3	1.1 ±0.14 0.8-1.3	0.222
Urea(mg/dL)	67.2±8.81 52-85	62.8±8.48 52-78	71.5±6.94 61-85	**0.005***
ALT(U/L)	46.5±11.74 27-65	43.1±12.38 27-62	49.9±10.35 32-65	0.111
AST(U/L)	39.5± 9.8 21-55	38.2±8.54 21-55	40.9±11.06 21-55	0.466
Total cholesterol(mg/dL)	255.5± 36.5 195 -320	257.3± 38.71 195-320	253.7± 35.51 200 -318	0.796
Triglycerides(mg/dL)	203.0±17.2 172 -227	209.3± 16.31 178-227	196.7±16.3 172 -227	**0.043***
HDL(mg/dL)	45±7.09 35-60	44.1±6.33 36-57	45.9± 7.9 35-60	0.513
LDL(mg/dL)	134.1± 9.7 112 -150	131.5±9.16 113-147	136.7±9.85 112 -150	0.151

Hb: hemoglobin, PLT: platelets, WBCs: white blood cells, NLR: neutrophil lymphocyte ratio, CPR: C-reactive protein, ALT: alanine amino transferase, AST: aspartate amino transferase,*:statistically significant as p value<0.05. HDL: high density lipoprotein, LDL: low density lipoprotein, *:statistically significant as pvalue<0.05.

Table4: Laboratory investigations after 24hours of the studied groups

	Total(n=30)	**NonSGLT2I group(n=15)**	**SGLT2Igroup (n=15)**	**Pvalue**
Hb(g/dL)	12.9± 0.93 11.5 -14.3	12.6± 0.8 11.5-14	13.2± 0.99 11.6 -14.3	0.104
PLT(*10^9/L)	284.1±41.1 213-347	285.0± 31.81 229 -336	283.3± 49.77 213 -347	0.910
WBCs(*10^9/L)	8.8 ±1.34 6.6-11	8.80±1.21 7 -10.7	8.77± 1.5 6.6-11	0.958
Lymphocytes(*109/L)	1.99± 0.5 1.2-3.1	1.8 ±0.37 1.2-2.3	2.2 ±0.53 1.5-3.1	**0.017***
Neutrophil(*109/L)	6.8 ±0.97 5.5-8.8	7.3 ±1.04 5.7-8.8	6.4 ±0.68 5.5-7.3	**0.011***
NLR	3.7±1.24 1.94-6.67	4.3±1.26 2.85-6.67	3.1 ±0.9 1.94-4.73	**0.005***
HbA1c(%)	7.3 ±0.77 5.8-8.9	7.2 ±0.82 5.8-8.3	7.4 ±0.73 6.6-8.9	0.390
CPR(mg/dL)	4.3 ±1.85 2.1-7.6	5.9 ±1.1 4.3-7.6	2.6 ±0.38 2.1-3.3	**<0.001***
Serum creatinine(mg/dL)	0.9 ±0.11 0.7-1.1	0.87±0.13 0.7-1.1	0.88± 0.1 0.7-1	0.876

Hb:hemoglobin,PLT:platelets,WBCs:white blood cells,NLR:neutrophil lymphocyte ratio , CPR:C-reactive protein,*:statistically significant as p value<0.05.

Table 5: Cardiac biomarkers of the studied groups

		Total (n=30)	**Non SGLT2I group (n=15)**	**SGLT2I group (n=15)**	**P value**
CK-MB (U/L)	**Mean± SD**	169.9 ± 38.8	159.0 ± 42.1	180.7 ± 33.08	0.127
	Range	103 - 223	103 - 223	107 - 222	
I hs-TnI (ng/L)	**Mean± SD**	651.9 ± 492.5	960.8 ± 514.76	343.1 ± 181.91	**<0.001***

	Range	131 - 1904	147 - 1904	131 - 649	
II hs-TnI (ng/L)	**Mean± SD**	3512.7± 2752.2	5853.8 ± 1912.29	1171.5 ± 537.25	**<0.001***
	Range	233 - 8786	1205 - 8786	233 - 1747	
III hs-TnI (ng/L)	**Mean± SD**	2749.2± 2837.6	4762.9 ± 2810.7	735.4 ± 298.24	**<0.001***
	Range	224 - 8893	580 - 8893	224 - 1262	
hs-TnI peak (ng/L)	**Mean± SD**	3396.6± 2635.8	5467.4 ± 2210.42	1325.7 ± 562.39	**<0.001***
	Range	297 - 9053	1989 - 9053	297 - 2208	

Table 6: Angiography findings and risk score of the studied groups

		Total(n=30)	**NonSGLT2I group(n=15)**	**SGLT2I group(n=15)**	**P value**
Baseline TIMI flow	**0**	13(43.33%)	6 (40%)	7(46.67%)	0.815
	1	6 (20%)	3 (20%)	3 (20%)	
	2	6 (20%)	4(26.67%)	2(13.33%)	
	3	5(16.67%)	2(13.33%)	3 (20%)	
	Mean ± SD Range	1.1 ±1.16 0 -3	1.1 ±1.13 0 -3	1.1 ±1.22 0-3	0.878
TIMI flow after PCI	**0**	3 (10%)	3 (20%)	0 (0%)	0.163
	1	8(26.67%)	5(33.33%)	3 (20%)	
	2	12(40%)	5(33.33%)	7(46.67%)	
	3	7(23.33%)	2(13.33%)	5(33.33%)	
	Mean ±SD Range	1.8 ±0.94 0 -3	1.4 ±0.99 0 -3	2.1 ±0.74 1-3	**0.029***
Affected vessel number	**1vessel**	6 (20%)	4(26.67%)	2(13.33%)	0.658
	2vessel	13(43.33%)	6 (40%)	7(46.67%)	
	3vessel	11(36.67%)	5(33.33%)	6 (40%)	
Affected vessel	**LM lesion**	3 (10%)	2(13.33%)	1 (6.67%)	0.811
	LAD lesion	16(53.33%)	7(46.67%)	9 (60%)	
	LCX lesion	7(23.33%)	4(26.67%)	3 (20%)	
	RCA lesion	12(40%)	5(33.33%)	7(46.67%)	
Killip Class	**Class1**	17(56.67%)	8(53.33%)	9 (60%)	0.684
	Class2	8(26.67%)	5(33.33%)	3 (20%)	
	Class3	5(16.67%)	2(13.33%)	3 (20%)	
GRACE Score	**Mean ±SD Range**	153.2± 25.81 112 -194	151.8± 26.29 112 -187	154.5± 26.17 120-194	0.777
Myocardial blush grades	**Grade0**	12(40%)	4(26.67%)	5(33.33%)	0.868
	Grade1	13(43.33%)	6 (40%)	7(46.67%)	
	Grade2	3 (10%)	3 (20%)	2(13.33%)	
	Grade3	2 (6.67%)	2(13.33%)	1 (6.67%)	

TIMI:thrombolysis in myocardial infarction, LM: left main,LAD:left anterior descending artery,LCX:left circumflex artery ;RCA:right coronary artery*:statistically significant as p value<0.05.

Table7:Echocardiographic and ECG assessment of the studied groups

		Total (n=30)	Non SGLT2I group (n=15)	SGLT2I group (n=15)	P value
Baseline					
EF (%)	**Mean± SD**	50.2±2.51	50.1 ± 2.66	50.3 ± 2.44	0.777
	Range	47 - 55	47 - 55	47 - 55	
Q wave		6 (20%)	2 (13.33%)	4 (26.67%)	0.361
WMSI	**Mean± SD**	1.81±0.48	1.91 ± 0.45	1.72 ± 0.5	0.292
	Range	1.1 - 2.5	1.1 - 2.4	1.1 - 2.5	
Mitral regurgitation	**Trivial**	18 (60%)	7 (33.33%)	11 (26.67%)	0.135
	Moderate	9 (30%)	5 (20%)	4 (0%)	
	Severe	3 (10%)	3 (0%)	0 (0%)	
On hospital discharge					
EF (%)	**Mean± SD**	52.5±3.07	50.3 ± 2.38	54.7 ± 1.87	**<0.001***
	Range	47 - 58	47 - 54	51 - 58	
ST resolution		21 (70%)	8 (53.33%)	13 (86.67%)	**0.046***
WMSI	**Mean± SD**	1.46±0.35	1.63 ± 0.38	1.30 ± 0.22	**0.007***
	Range	1 - 2.2	1.1 - 2.2	1 - 1.7	
Mitral regurgitation	**Trivial**	19 (46.67%)	7 (26.67%)	12 (66.67%)	**0.020***
	Moderate	8 (23.33%)	6 (40%)	2 (6.67%)	
	Severe	3 (10.00%)	3 (20%)	0 (0%)	
	No	6 (20.00%)	2 (13.33%)	4 (26.67%)	

EF:ejection fraction,WMSI:regional wallmotion abnormalities,*:statistically significantas p value<0.05.

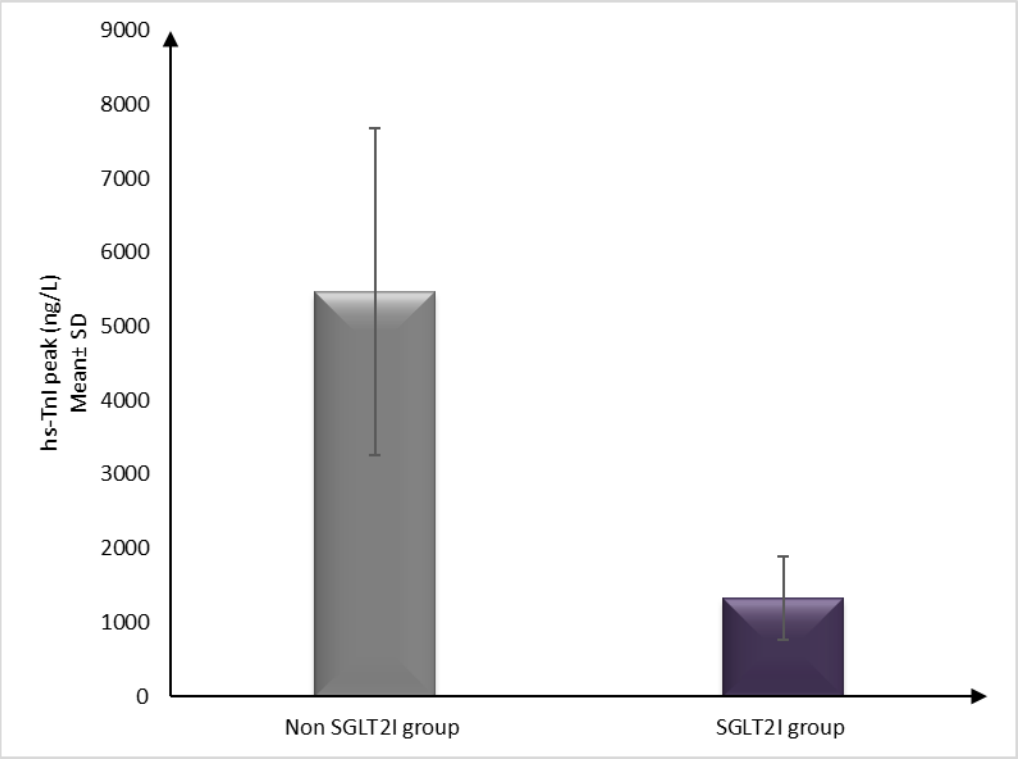

Figure 1: hs-TnI peak of the studied groups

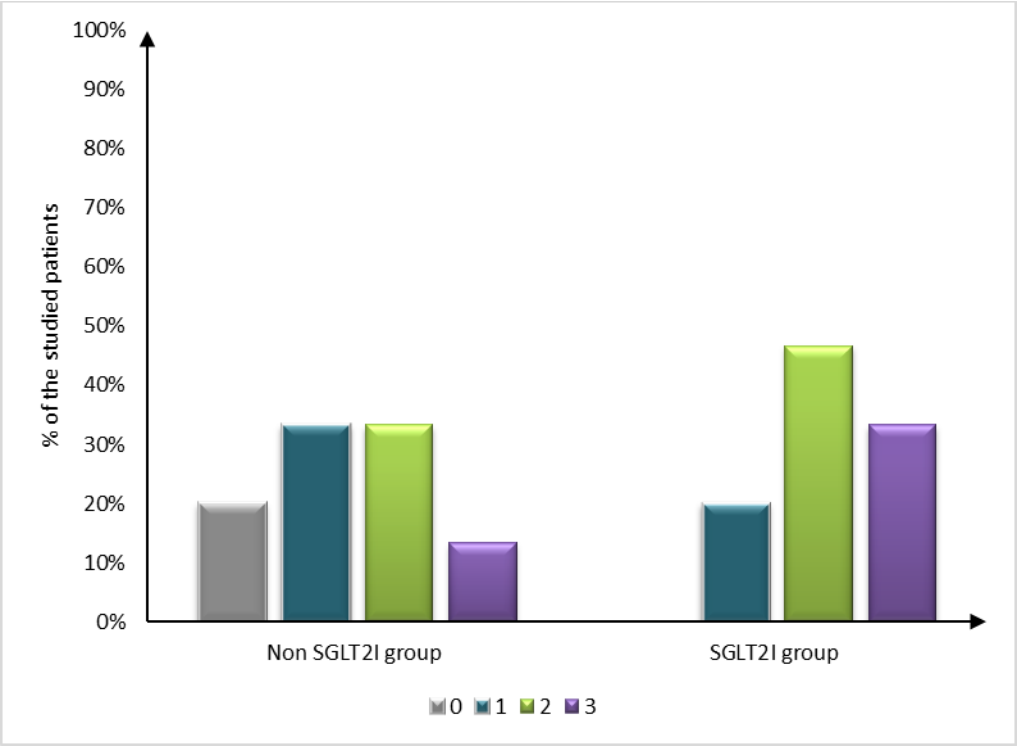

Figure 2: TIMI flow after PCI of the studied groups

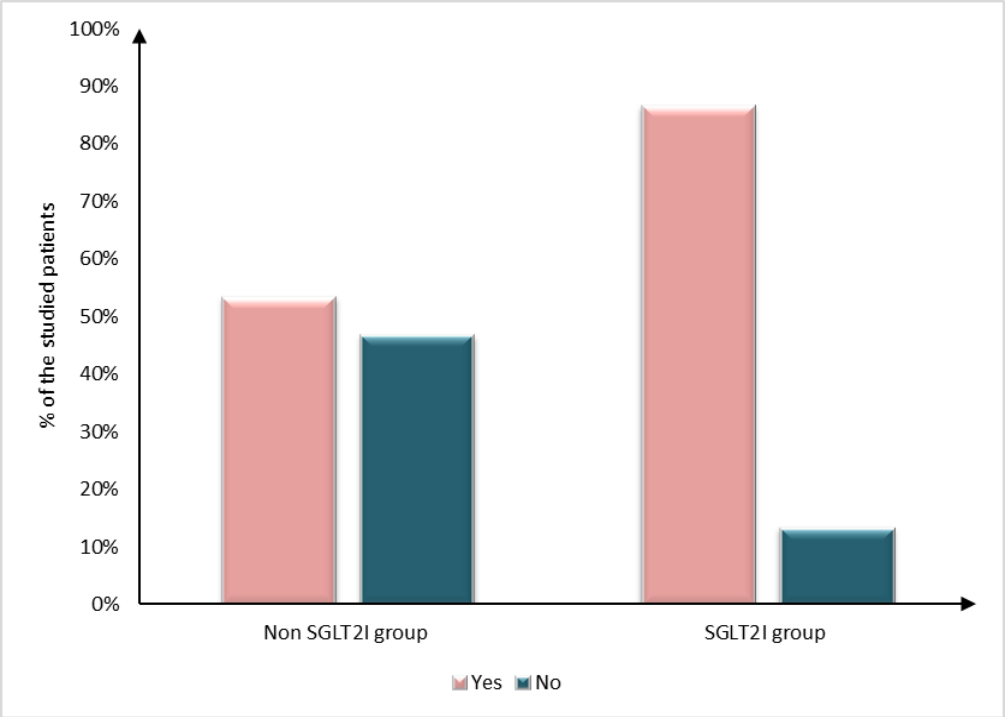

Figure 3: ST resolution on hospital discharge of the studied groups

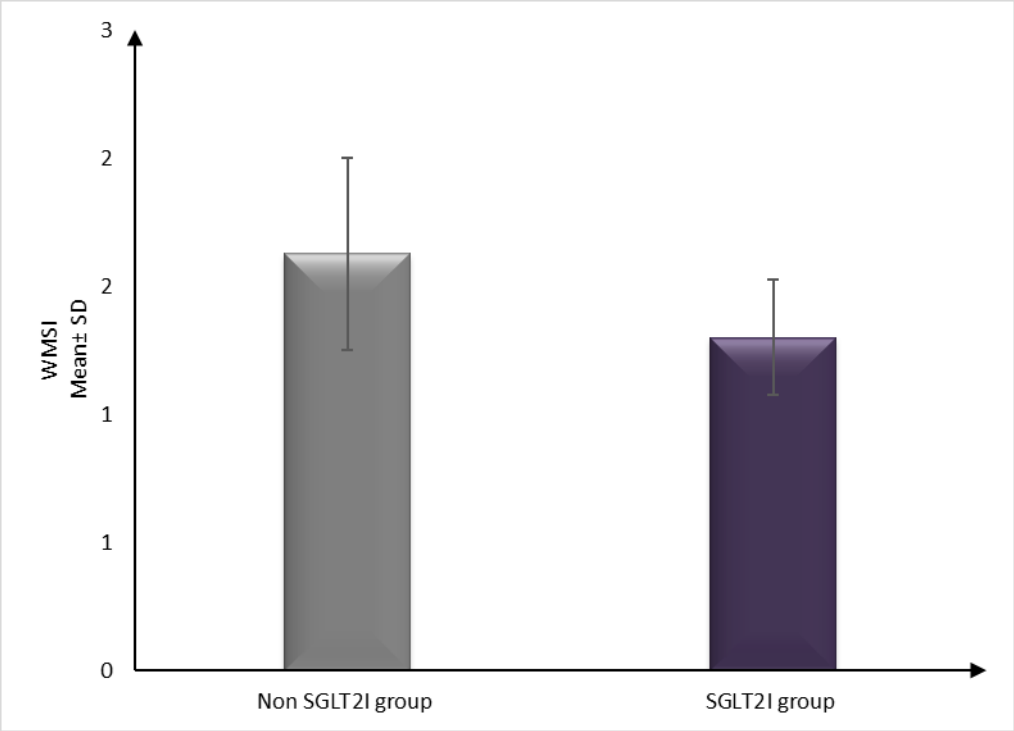

Figure 4: WMSI on hospital discharge of the studied groups

DISCUSSION:

SGLT2 inhibitors are a new class of oral glucose-lowering medications that were initially developed to help people with type 2 diabetes manage their blood sugar levels. Their ability to reduce blood sugar is dependent on SGLT2 blockage in the kidney's first segment of the proximal convoluted tubule, which causes glucosuria **[9]**.

SGLT2 inhibitors were found to be more effective than a placebo in four sizable cardiovascular outcome trials involving people with type 2 diabetes **[10]**.

More so than metrics of left ventricular systolic performance, myocardial infarct size was directly associated with left ventricular remodeling and subsequent occurrences **[11]**.

Our study provides that the long-term treatment with SGLT2I can decrease the infarct size in STEMI diabetic patients undergoing primary percutaneous coronary intervention.

SGLT2I group had significantly higher age and lower HR compared to non SGLT2Igroup (P=0.008). The other baseline characteristics (sex, weight, height, BMI, SBP, and DBP)were insignificantly different between both groups. The older age of patients in the SGLT2Igroup might initially suggest a higher baseline cardiovascular risk; however, the associated lower HR in the same group could indicate an improved cardiovascular response or a protective physiological effect induced by SGLT2I therapy. Lower HR is often associated with reduced cardiac workload and improved myocardial efficiency, which are beneficial inthe context of cardiovascular disease management, especially in patients with diabetes andincreasedcardiovascular risk.

Regarding the laboratory investigations, neutrophil, NLR, CRP, and triglycerides were significantly higher in non SGLT2I group compared to SGLT2I group(P<0.001,0.004,<0.001 respectively). Level of urea was significantly higher in SGLT2I group compared tononSGLT2Igroup (P=0.005).

The elevated inflammatory markers and triglycerides in the non-SGLT2I group may reflect an increased inflammatory and atherogenic state, which is associated with worse cardiovascular outcomes. Incontrast, the SGLT2I group showing lower levels of these markers indicates a potential mechanism through which SGLT2Is exert cardioprotective effects, likely by reducing systemic inflammation, improving lipid metabolism, and therebydecreasing cardiovascular risk. The increased urea levels in the SGLT2I group could be related to the hemodynamic changes induced by these drugs, such as increased diuresis and natriuresis, which might affect renal function parameters without necessarily indicating harm.

After 24 hours, lymphocytes count was significantly higher in SGLT2I group compared to non SGLT2I group (P=0.017). Neutrophil, NLR

and CRP were significantly higher in nonSGLT2I group compared to SGLT2I group (P=0.011, 0.005, <0.001 respectively). Other laboratory findings (Hb, PLT, WBCs, HbA1c and serum creatinine) were in significantly different between both groups.

Similarly**, Paolisso et al. [12]** conducted a study on results in diabetic individuals receiving PCI who have an acute myocardial infarction and are treated with SGLT2-Inhibitors. The patients were split into non-SGLT2-I users and SGLT-I users. They found that non-SGLT2-I users had a greater inflammatory burden at admission and 24 hours later than the SGLT2-I group.

Regarding cardiac biomarkers, hs-TnI levels (I hs-TnI, II hs-TnI, III hs-TnI and hs-TnI peak) were significantly higher in non SGLT2I group compared to SGLT2I group (P<0.05), with no significant difference between both groups regarding CK-MB.

This can be attributed to the effect of SGLT 2I on infarct size and limitation of progression of ischemia. Previous research has shown that the use of SGLT2 inhibitors during the early stages of AMI lowers the extent of the myocardial infarct by activating transcription factor 3 and down regulating inflammatory responses inside the infarcted myocardium **[13]**. Furthermore, SGLT2 inhibitors decrease oxidative stress in diabetic mice by lowering reactive oxygen species generation and nicotinamide-adenine dinucleotide phosphate activity**[14]**. Additionally, it has been demonstrated that SGLT2 inhibitors decrease oxidative stress by raising endothelial nitric oxide synthase and nitric oxide production in porcine endothelial cells**[15]**.

Regarding the angiography finding, TIMI flow after PCI was significantly higher in SGLT2I group compared to non SGLT2I group (P=0.029), with no significant difference between both groups regarding other angiography findings. The observation of superior TIMI flow in the SGLT2 inhibitor group compared to non-SGLT2I group post-PPCI in STEMI patients highlights SGLT2Is' potential to enhance myocardial reperfusion and protect against reperfusion injury, possibly due to their anti-inflammatory and antioxidative properties. This suggests a valuable role for SGLT2Is in improving cardiovascular outcomes in diabetic patients with acute myocardial infarction, warranting the increased incorporation into clinical practice and guidelines for comprehensive cardiovascular risk management.

On hospital discharge, ST resolution and EF were significantly higher in SGLT2I group compared to non SGLT2I group (P<0.001, 0.046). WMSI was significantly higher in non SGLT2I group compared to SGLT2I group (1.63 ± 0.38) Vs. 1.30±0.22, P=0.007 respectively). Mitral regurgitation was significantly different between both groups, being significantly improved in SGLT2I group compared tonon SGLT2I group (P=0.003). Baseline EF, WMSI and mitral regurgitation were insignificantly different between both groups.

Consistently, **Paolisso et al. [12]** reported the same findings as follows; the SGLT2-I group had a higher frequency of ST-segment resolution after PCI (p = 0.001). The two study groups' admission values for left ventricular volume, ejection fraction (LVEF), and regional wall motion abnormalities (RWMA) were comparable. After the revascularization, the LVEF increased considerably in both groups with significant defference between admission and discharge (p<0.001). On the other hand, SGLT2-I users had a substantially greater rise in EF than non-SGLT2-I users (p < 0.001). Furthermore, RWMA were considerably lower at discharge in the SGLT2-I users (81.1 % against 62.2 %, p = 0.003) in comparison to non-SGLT2-I (83.6 % versus 79.8 %, p = 0.133). SGLT2-I users had a decreased rate of discharge moderate-to-severe mitral regurgitation when compared to hospital admission.

There was some limitation of our study:small sample size with only 30 participants,the study's findings may not be widely generalizable to all diabetic patients with ST segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention(PCI).Conducting the study in only two departments within the same geographical region may limit the applicability of the findings to broader populations due to regional variations in patient demographics, healthcare practices, and access to care. Finally,the absence of a control group with non-diabetic STEMI patients undergoing primary PCI, it's challenging to isolate the effect of diabetes and SGLT2 inhibitors from the effects of STEMI and primary PCI in the observed outcomes.

CONCLUSION:

Our study conclusively demonstrated that diabetic patients with STEMI undergoing PPCI and treated with SGLT2I exhibited significantly decreased the infract size and improved cardiovascular outcomes compared to those not on SGLT2I therapy.

Further research is needed to better elucidate the mechanistic pathways by which SGLT-2 inhibitors may protect the heart. MRI is also needed to assess infarction size.

Conflict of Interest: No conflict of interest to disclose.

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References:

1- **van Zuylen VL, den Haan MC, Geutskens SB, Roelofs H, Fibbe WE, Schalij MJ, et al.** Post-myocardial infarct inflammation and the potential role of cell therapy.Cardiovasc Drugs Ther. 2015 Feb;29:59-73.

2- **Jiang B and Liao R.** The paradoxical role of inflammation in cardiac repair and regeneration. J CardiovascTransl Res. 2010 Aug;3:410-6.

3- **Stone GW, Selker HP, Thiele H, Patel MR, Udelson JE, Ohman EM, *et al*.** Relationship between Infarct Size and Outcomes Following Primary PCI. J Am CollCardiol.2016; 67: 1674–83.

4- **Schulz R, Andreadou I, Hausenloy DJ, Ferdinandy P.** Risk factors, co-morbidities, and co-medications in cardioprotection: Importance for translation. Br J Pharmacol.2020; 177: 5249–51.

5- **Yildiz M, Wade SR, Henry TD.** STEMI care 2021: Addressing the knowledge gaps. American Heart Journal Plus: Cardiol Res Pract. 2021 Nov 1;11:100044.

6- **Redfors B, Shao Y, Omerovic E.** Myocardial infarct size and area at risk assessment in mice. Experim & Clin Cardiol. 2012;17(4):268.

7- **Savage ML, Hay K, Anderson B, Scalia G, Burstow D, Murdoch D et al.** The Prognostic Value of Echocardiographic Wall Motion Score Index in ST-Segment Elevation Myocardial Infarction. Crit Care Res Pract. 2022 Nov 10;2022.

8- **Rencuzogullari I, Çagdas M, Karabag Y, Karakoyun S, Yesin M, Gürsoy MO et al.** Association of the SYNTAX Score II with cardiac rupture in patients with ST-segment elevation myocardial infarction undergoing a primary percutaneous coronary intervention. Coronary Art Dis. 2018 Mar 1;29(2):97-103.

9- **Zelniker TA and Braunwald E.** Mechanisms of cardiorenal effects of sodium-glucose cotransporter 2 inhibitors: JACC state-of-the-art review. J Am CollCardiol. 2020 Feb 4;75(4):422-34.

10- **Inzucchi SE, Zinman B, Wanner C, Ferrari R, Fitchett D, Hantel S et al.** SGLT-2 inhibitors and cardiovascular risk: proposed pathways and review of ongoing outcome trials. DiabVasc Dis Res. 2015 Mar;12(2):90-100.

11- **Małek ŁA, Śpiewak M, Kłopotowski M, Petryka J, Mazurkiewicz Ł, Kruk M et al.** Influence of left ventricular hypertrophy on infarct size and left ventricular ejection fraction in ST-elevation myocardial infarction. Eur J Radiol. 2012 Mar 1;81(3):e177-81.

12- **Paolisso P, Bergamaschi L, Gragnano F, Gallinoro E, Cesaro A, Sardu C et al.** Outcomes in diabetic patients treated with SGLT2-Inhibitors with acute myocardial infarction undergoing PCI: The SGLT2-I AMI PROTECT Registry. Pharmacol Rese. 2023 Jan 1;187:106597.

13- **Andreadou I, Efentakis P, Balafas E, Togliatto G, Davos CH, Varela A et al.** Empagliflozin limits myocardial infarction in vivo and cell death in vitro: role of STAT3, mitochondria, and redox aspects. Front Physiol. 2017 Dec 19;8:1077.

14- **Ganbaatar B, Fukuda D, Shinohara M, Yagi S, Kusunose K, Yamada H et al..** Empagliflozin ameliorates endothelial dysfunction and suppresses atherogenesis in diabetic apolipoprotein E-deficient mice. Eur J Pharmacol.**2020**; 875, 173040.

15- **Park SH, Belcastro E, Hasan H, Matsushita K, Marchandot B, Abbas M et al.** Angiotensin II-induced upregulation of SGLT1 and 2 contributes to human microparticle-stimulated endothelial senescence and dysfunction: protective effect of gliflozins. CardiovascDiabetol. 2021 Dec;20:1-7.

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