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ORIGINAL RESEARCH ARTICLE

Effectiveness of Dapagliflozin as Add-On to Metformin with or without Other Oral Antidiabetic Drugs in Type 2 Diabetes Mellitus: A Multicentre, Retrospective, Real-World Database Study

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Abstract

Background Real-world Indian studies evaluating effectiveness of dapagliflozin as an add-on to other oral antidiabetic drugs (OAD) in patients with type 2 diabetes mellitus (DM) are scarce.

Methods An electronic medical record (EMR)-based, retrospective, multicentre study was conducted to evaluate the effectiveness of dapagliflozin as add-on therapy in adult patients with inadequately controlled DM on metformin with or without other OAD. Baseline characteristics (visit 1: metformin or metformin plus OAD treatment for at least 30 days) and treatment-related outcomes (visit 2: follow-up) considered between 60 and 140 days after adding/switching dapagliflozin [glycated haemoglobin (HbA1c), body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP)] were analysed.

Results A total of 3616 patients were screened from 478 centres. Most patients had received dapagliflozin (D) + metformin (M) + at least one other OAD [D + M + OAD, $n = 2907$ (80.4%), 408 followed-up with HbA1c reported], while 709 patients (19.6%, 138 followed-up with HbA1c reported) received dapagliflozin + metformin (D + M). Treatment with dapagliflozin as an add-on therapy resulted in significant change in HbA1c ($-1.1 \pm 1.44\%$; $p < 0.05$ for HbA1c subgroup $\geq 7.5\%$; $-1.6 \pm 1.41\%$; $p < 0.05$ for HbA1c subgroup $\geq 8\%$) at visit 2 compared with visit 1. Significant change in body weight (-1.4 ± 3.31 kg; $p < 0.05$ for HbA1c subgroup $\geq 7.5\%$; -1.5 ± 3.22 kg; $p < 0.05$ for HbA1c subgroup $\geq 8\%$) was observed at visit 2. Similarly, a significant change in BMI was noted for the HbA1c subgroup $\geq 7.5\%$ (-1.0 ± 8.38 kg/m^2). However, the change in BMI in the HbA1c subgroup $\geq 8\%$ was noted to be -1.4 ± 10.4 kg/m^2, which was not statistically significant ($p = 0.08$). In the overall study population, significant change in the SBP (-4.5 ± 14.9 mmHg; $p < 0.05$ for HbA1c subgroup $\geq 7.5\%$; -4.5 ± 15.1 mmHg; $p < 0.0001$ for HbA1c subgroup $\geq 8\%$) was observed at visit 2 compared with visit 1. On identical lines, significant change in DBP (-1.5 ± 8.94 mmHg; $p < 0.05$ for HbA1c subgroup $\geq 7.5\%$; -1.4 ± 8.91 mmHg; $p < 0.05$ for HbA1c subgroup $\geq 8\%$) was noted.

Conclusions Dapagliflozin showed significant improvement in glycemic parameter, BMI and BP when added to metformin, with or without other OADs in a real-world scenario.

1 Introduction

Globally and in emerging nations such as India, the burden of diabetes mellitus (DM) is large and rising, mostly due to soaring rates of overweight/obese individuals and poor lifestyle choices. In India, 101 million people were estimated to have DM and 136 million with pre-diabetes in 2021[1, 2]. Of the Indian population with DM, 76.6% has poor glycemic control [3]. Type 2 DM (T2DM) which makes up most cases, can cause microvascular and macrovascular problems that can affect several organ systems. Additionally, insulin resistance associated with obesity contributes to the development of other cardiovascular risk factors, including dyslipidemia, hypertension [4, 5]. These problems play a significant role in the rise in early morbidity and death among the patients with diabetes, which results in a reduction of life expectancy and a huge financial load on the Indian healthcare system as complications of DM increase the total cost [6, 7]. As a result, physicians, and researchers from all over the world are working to investigate novel therapeutic options

Extended author information available on the last page of the article

Key Summary Points

Dapagliflozin has been shown to be effective in controlling glycemic and non-glycemic parameters (weight and blood pressure) as add-on therapy in patients with type 2 DM in real-world clinical practice.

Dapagliflozin can be considered as one of the important SGLT-2 inhibitors in patients with type 2 diabetes mellitus (DM) associated with obesity/high BMI or hypertension.

for T2DM and to produce new data that will aid in improving the management of this chronic condition.

The current pharmacological therapy options for T2DM patients include metformin, sulfonylurea, thiazolidinedione, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose transport protein 2 (SGLT2) inhibitors, glucagon-like peptide 1 receptor agonist (GLP-1 RA), and insulin and insulin analogues [8]. Treatment of diabetes must be personalized according to the factors of the patient such as atherosclerotic cardiovascular disease (ASCVD), indicators of high cardiovascular (CV) risk, heart failure (HF), chronic kidney disease (CKD), weight and glycemic levels [8]. According to the American Association of Clinical Endocrinologists, criteria to consider while selecting a suitable agent include glycated hemoglobin (HbA1c) decrease, alteration in body weight, change in blood pressure (BP) and risk of hypoglycaemia [9]. The United States Food and Drug Administration (US FDA) authorised the use of dapagliflozin in January 2014, for use either alone or in conjunction with other anti-diabetic medications [10]. The Indian drug regulatory authorities also approved dapagliflozin for the same indication in 2015. [11–14] Additionally, dapagliflozin has been approved for heart failure (HF) and chronic kidney disease (CKD) based on cardiorenal benefits observed from landmark clinical trials such as Dapa HF and Dapa CKD studies. [10] The dapagliflozin effect on cardiovascular events—thrombolysis in myocardial infarction 58 (DECLARE-TIMI 58) trial showed that treatment with dapagliflozin in patients with T2DM who had or were at risk for ASCVD resulted in a lower rate of cardiovascular death or hospitalization for HF [15].

Real-world data are crucial to confirm the effectiveness in the real-world scenario. Dapagliflozin decreased HbA1c level, body mass index (BMI) and BP after 6 months of starting treatment in clinical practice [16]. Similar results, such as improved glycemic profile, BP, BMI and lipid profile were demonstrated in another real-world PRECARE study which included 1402 patients of T2DM treated with dapagliflozin for 6 months. Also, there was an acute improvement in renal function with a reduction in albuminuria [17]. SOLD study has also proven the effectiveness of SGLT-2 inhibitors as an add-on therapy to metformin, insulin and other antidiabetic drugs for significant reduction in HbA1c and BMI in 739 elderly patients aged more than 70 years. In this study, dapagliflozin was used in 36% of SGLT-2-inhibitor users [18]. Although, dapagliflozin has been used in India in the last 8 years, there is scarcity of real-world clinical data for effect of dapagliflozin on glycemic and non-glycemic parameters such as weight and BP in the Indian population.

Hence, the current multicentric database study aims to assess the effectiveness of dapagliflozin added to metformin with or without other oral anti-diabetic drug (OAD) in Indian patients with type 2 DM.

The primary objective of the study is to evaluate the glycemic effectiveness of dapagliflozin as add on therapy to metformin with or without other OAD by assessing the change in HbA1c. The secondary objective of the study includes assessment of effectiveness of dapagliflozin on change in BMI/weight, SBP and DBP as an add-on therapy to metformin with or without other OAD.

2 Methods

2.1 Study Design

An electronic medical record (EMR)-based, retrospective, multicentre, longitudinal, database study was conducted, and the data were analysed for type 2 DM adult patients of either gender with HbA1c of $\geq$ 7.5%, receiving either dapagliflozin + metformin (D + M) or dapagliflozin + metformin + at least one other OAD (D + M + OAD) as per physician discretion. Patients with at least one record in EMR before and one record after 1-month to 3-month evaluation/follow-up period were included to ensure that each patient was continuous in the EMR system for the entire study period. The included patients were on metformin or metformin plus OAD treatment for at least 30 days with addition of dapagliflozin (baseline visit). Type 2 DM cases on insulin or other injectable therapy and patients diagnosed with gestational diabetes or pregnancy during baseline or follow-up periods were excluded.

The baseline visit was considered as visit 1, followed by visit 2/follow up visit which was considered between 60 and 140 days after adding/switching to dapagliflozin. Variables evaluated included demographic characteristics (gender and age), BMI, comorbidities, systolic BP (SBP) and diastolic BP (DBP), clinical and presentation of the patients. Since the current study was an observational and database study, no additional tests or interventions were suggested.

The primary outcome measure was mean change in HbA1c from visit 1 to visit 2. Secondary outcome measures included mean change in weight and BMI from visit 1 to visit 2, mean change in BP (SBP and DBP) from visit 1 to visit 2, in subsets of patients with HbA1c ≥ 7.5% and HbA1c ≥ 8%, respectively.

An informed consent waiver was obtained as this was a retrospective data analysis study. Data management was done in accordance with applicable regulatory requirements so that the integrity of the data can be ensured, e.g. removing errors and inconsistencies in the data. The data from the EMR was collected using the data collection forms.

2.2 Statistical Analysis

The data was analysed using descriptive statistics. For primary outcome analysis, actual values and mean change in HbA1c from visit 1 were summarized by visit with number (*n*), mean, standard deviation (SD), median, minimum and maximum. Similarly, for secondary outcome analysis, values and mean change in weight/BMI, SBP and DBP from visit 1 were noted by visit with *n*, mean, SD, median, minimum, maximum. Paired *t*-test was used to compare the post-baseline (visit 2) values with the visit 1 values for primary and secondary outcome measures.

3 Results

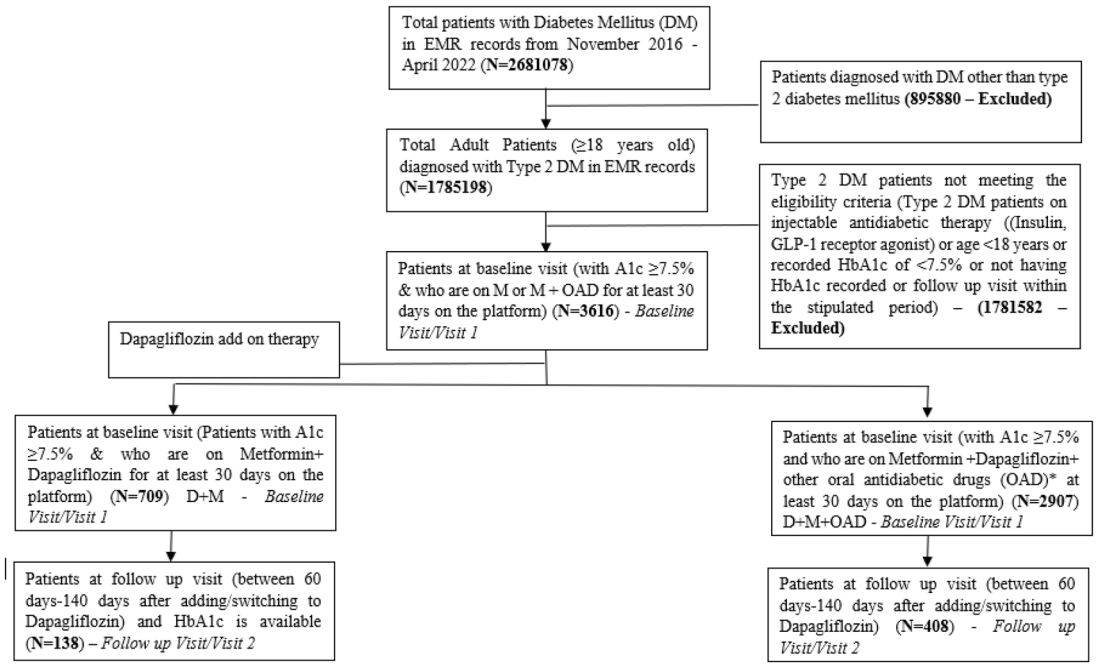
3.1 Patient Characteristics

The total of 3616 patients were identified from 478 centres (visit 1). Of all the identified patients at visit 1, the number of patients on D + M combination treatment was noted to be 709, while those on D + M + OAD combination was found to be 2907. A total of 138 out of 709 patients had reported follow-up HbA1c values between 60 days and 140 days after adding/switching to dapagliflozin. In the (D + M + OAD) group, 408 of these 2907 patients had follow-up HbA1c recorded at the follow-up visit between 60 days and 140 days after adding/switching to dapagliflozin (visit 2).

The patient flow has been explained below in Fig. 1.

3.2 Demographic and Other Baseline Characteristics

Majority of the patients were male (55.7%) with mean age of 51 years. In the group of patients on the combination therapy, 1174 (40.39%) patients in the HbA1c ≥ 7.5% group had hypertension. Around 11.76% patients in the HbA1c ≥ 7.5% group were seen to be affected by dyslipidemia. A majority of the patients weighed between 76 and 100 kg



**Other OADs* – *Oral Antidiabetic drugs other than Metformin and Dapagliflozin- Sulfonylureas/Thiazolidinediones/ Alpha Glucosidase inhibitors/DPP-4 inhibitors/ Glinides*

(A1c/HbA1c= glycated haemoglobin, D=dapagliflozin, M=metformin, OAD=oral antidiabetic drug)

Fig. 1 Consort diagram for the study

[$n = 1209$ (41.59%) for the HbA1c ≥ 7.5% group]. Similar findings were noted in the D + M group and D + M + OAD group separately, as mentioned in Table 1.

3.3 Change in Outcome Parameters at Follow-up

3.3.1 HbA1c Change

In overall study population, significant change in HbA1c (−1.1 ± 1.44%; $p < 0.05$ for HbA1c subgroup ≥ 7.5%; −1.6 ± 1.41%; $p < 0.05$ for HbA1c subgroup ≥ 8%) were observed at visit 2 compared with visit 1. Similar trends were observed in study subgroups D + M and D + M + OAD (Fig. 2).

3.3.2 Weight and BMI Changes

In overall study population, significant change in body weight (−1.4 ± 3.31 kg; $p < 0.05$ for HbA1c subgroup ≥ 7.5%; −1.5 + 3.2 kg; $p < 0.05$ for HbA1c subgroup ≥ 8%) was observed at visit 2 compared with visit 1. Similar trends were observed in study subgroups D + M and D + M + OAD. (Fig. 3)

Similarly, a significant change in BMI was noted for the HbA1c subgroup ≥ 7.5% (−1.0 ± 8.38 kg/m^2). However, the change in BMI in the HbA1c subgroup ≥ 8% was noted to be −1.4 ± 10.4 kg/m^2, which was not statistically significant ($p = 0.08$). A similar trend was calculated for the study subgroups D + M and D + M + OAD (Fig. 4).

Change in BMI was assessed for different subgroups of BMI (≤ 24.9, 25–29.9 and ≥ 30 kg/m^2; Table 2). A statistically significant (< 0.05) reduction in BMI was observed in patients of D + M arm compared with baseline visit/visit 1 irrespective of the BMI subgroups.

3.3.3 BP Changes

In overall study population, significant change in the SBP (−4. ± 14.9 mmHg; $p < 0.05$ for HbA1c subgroup ≥ 7.5%; −4.5 ± 15.1 mmHg; $p < 0.05$ for HbA1c subgroup

Table 1 Demographic characteristics—patients with HbA1c ≥ 7.5% on dapagliflozin + metformin (D + M) or on dapagliflozin + metformin + at least one other OAD (D + M + OAD)

Characteristic (unit)	Dapagliflozin + metformin (D + M) (*N* = 709)	Dapagliflozin + metformin + at least one other OAD* (D + M + OAD) (*N* = 2907)
Age groups		
18–39 years	161 (22.71)	410 (14.1)
40–64 years	481 (67.84)	2109 (72.55)
≥ 65 years	67 (9.45)	388 (13.35)
Gender distribution		
Male	348 (49.08)	1667 (57.34)
Female	361 (50.92)	1240 (42.66)
Comorbidity		
Hypertension (HTN)	248 (34.98)	1174 (40.39)
Hypothyroidism	145 (20.45)	342 (11.76)
Dyslipidemia	125 (17.63)	485 (16.68)
Coronary artery disease (CAD)	72 (10.16)	189 (6.5)
Chronic kidney disease (CKD)	145 (20.45)	25 (0.86)
Weight (kg)		
< 50 kg	0	42 (1.44)
50–75 kg	245 (34.56)	1204 (41.42)
76–100 kg	280 (39.49)	1209 (41.59)
> 100 kg	57 (8.04)	72 (2.48)
Body mass index (BMI) distribution		
Normal (BMI 18.5–24.99)	38 (5.36)	282 (9.7)
Overweight (25–29.99)	161 (22.71)	611 (21.02)
Class 1 (BMI 30–34.99)	99 (13.96)	352 (12.11)
Class 2 (BMI 35–39.99)	42 (5.92)	103 (3.54)
Class 3 (BMI ≥ 40)	30 (4.23)	29 (1)

Values are expressed as a number (percentage)

*Other oral antidiabetic drugs (OADs): OADs other than metformin and dapagliflozin–sulfonylureas/thiazolidinediones/alpha glucosidase inhibitors/dpp-4 inhibitors/glinides

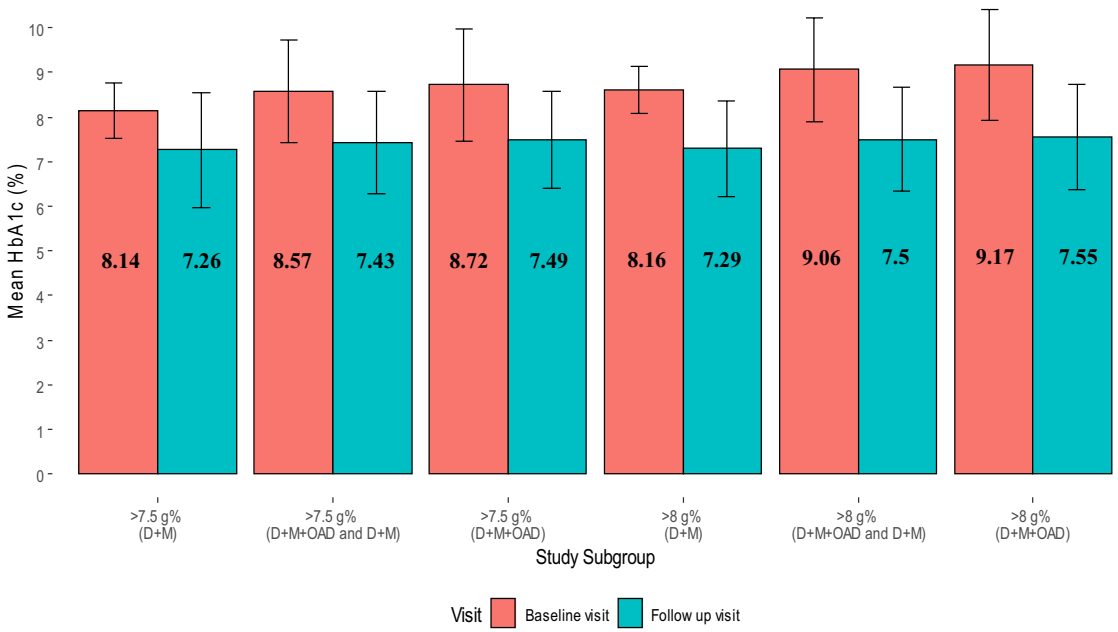


Fig. 2 Mean HbA1c in study subgroups. *HbA1c* glycated haemoglobin, *D* dapagliflozin, *M* metformin, *OAD* oral antidiabetic drug

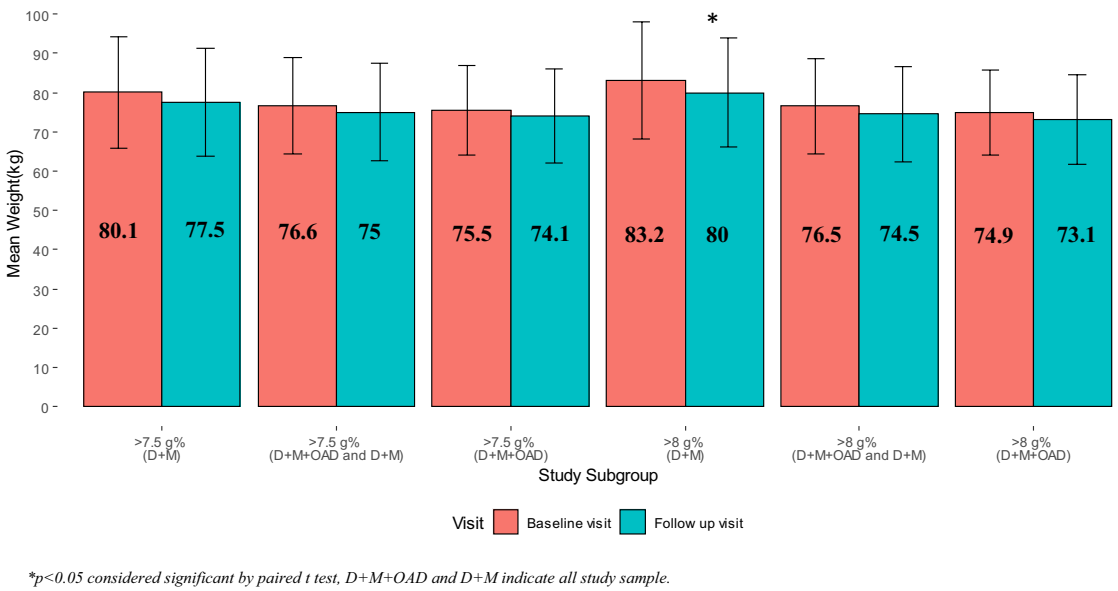
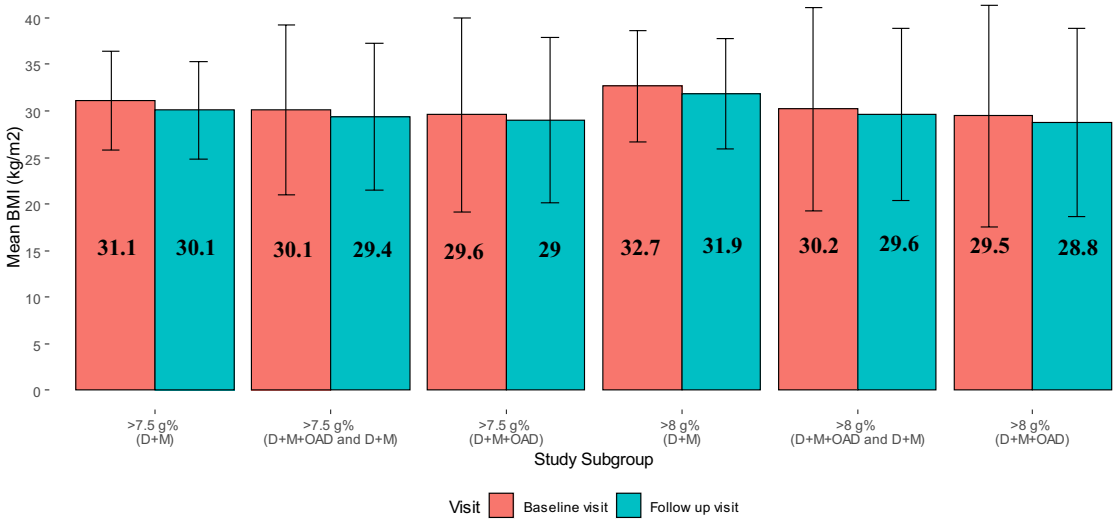


Fig. 3 Mean body weight in the study subgroups. *D* dapagliflozin, *M* metformin, *OAD* oral antidiabetic drug

≥ 8%) was observed at visit 2 compared with visit 1. Similar trends were observed in study subgroups D + M and D + M + OAD (Fig. 5). On identical lines, significant change in DBP (−1.5 ± 8.94 mmHg; $p < 0.05$ for HbA1c subgroup ≥ 7.5%; −1.4 ± 8.91 mmHg; $p < 0.05$ for HbA1c subgroup ≥ 8%) was noted, which was similar in study subgroups D + M and D + M + OAD (Fig. 6).

4 Discussion

Maintaining glycemic control is difficult in the context of insulin resistance and typically requires adjunct medications because cell function diminishes. Due to metformin's ability to increase insulin sensitivity, the addition of



**p<0.05 considered significant by paired t test, D+M+OAD and D+M indicate all study sample.*

Fig. 4 Mean BMI in various subgroups of study. *BMI* body mass index, *D* dapagliflozin, *M* metformin, *OAD* oral antidiabetic drug)

Table 2 Change in BMI from baseline (visit 1) to follow-up (visit 2) in subgroups by BMI category

BMI categories	Visits	D + M		D + M + OAD		D + M and D + M + OAD	
		Number of patients	BMI	Number of patients	BMI	Number of patients	BMI
≤ 24.9	Baseline visit/visit 1	12	24.02±0.54	39	23.58±1.30	51	23.68±1.18
	Follow up visit/visit 2	12	23.21±0.38	39	23.55±1.79	51	23.47±1.58
	Change in BMI	12	**−0.81**	39	**−0.03**	51	**−0.21**
	p-Value		**0.0005**		**0.83**		**0.2838**
25–29.9	Baseline visit/visit 1	30	27.26 ± 1.60	80	27.48 ± 1.36	110	27.42 ± 1.42
	Follow-up visit/visit 2	30	26.60 ± 1.76	80	27.17 ± 2.15	110	27.01 ± 2.07
	Change in BMI	30	**−0.66**	80	**−0.31**	110	**−0.4**
	p-Value		**0.0003**		**0.1191**		**0.0082**
≥30	Baseline visit/visit 1	44	35.40 ± 3.44	74	35.07 ± 15.31	118	35.20 ± 12.27
	Follow-up visit/visit 2	44	34.47 ± 3.26	74	32.51 ± 2.79	118	33.24 ± 3.11
	Change in BMI	44	**−0.93**	74	**−2.57**	118	**−1.96**
	p-Value		**< 0.0001**		**0.1733**		**0.979**

p-Values were obtained by comparing BMI at visit 2 with visit 1. p < 0.05 was consider significant by paired t test. BMI values are expressed as mean ± SD in unit kg/m^2

BMI body mass index, *D + M* dapagliflozin + metformin, *D + M + OAD* dapagliflozin + metformin + other oral antidiabetic drugs

a medication that uses an insulin-independent mechanism may be beneficial [19]. The latest American Diabetes Association (ADA) 2023 guidelines mention that for achieving the glycemic goals in a patient with DM, metformin can be combined with a pharmacological agent with adequate efficacy. SGLT2 inhibitors have been categorised under "high" glucose lowering capacity and thus become a potential option for combination therapy with metformin. Additionally, in DM cases with heart failure, chronic kidney disease or CVD, SGLT2 inhibitors with proven benefit can be chosen, independent of the background use of metformin. SGLT2 inhibitors have been noted to have CV as well as renal benefits which extends to elderly population [8]. In a DAPA HF trial, the patients with heart failure and having reduced ejection fraction who received dapagliflozin had a lower risk of aggravating heart failure and cardiovascular death [20]. A review by Parikh et al. evaluated the 10-mg dapagliflozin data across 19 clinical trials. In treatment-naïve DM cases, dapagliflozin decreased the HbA1c (−1.45%) similarly

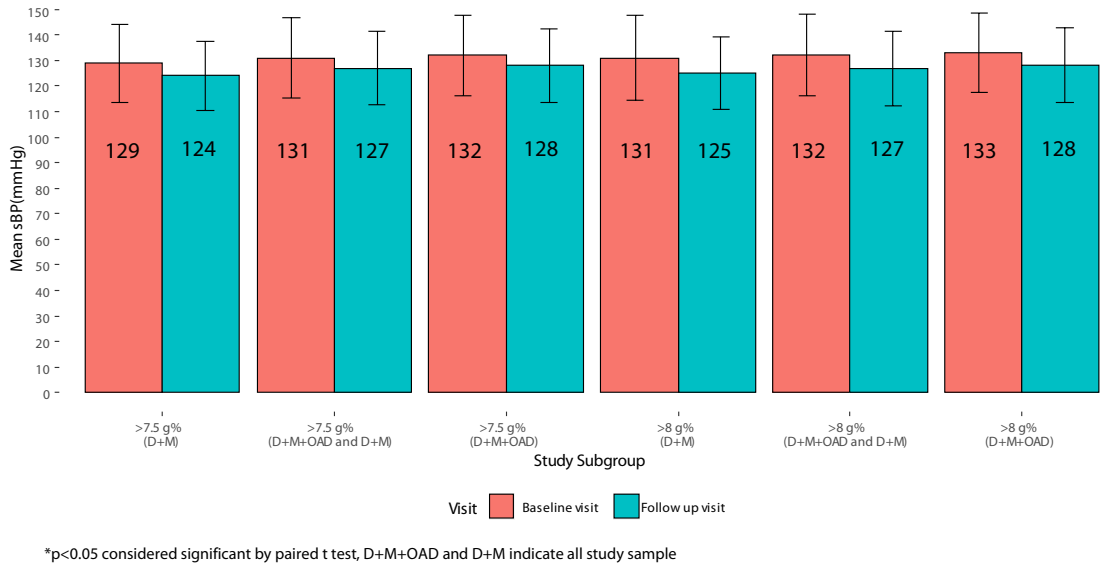


Fig. 5 Mean SBP in study subgroups. *D* dapagliflozin, *M* metformin, *OAD* oral antidiabetic drug, *SBP* systolic blood pressure

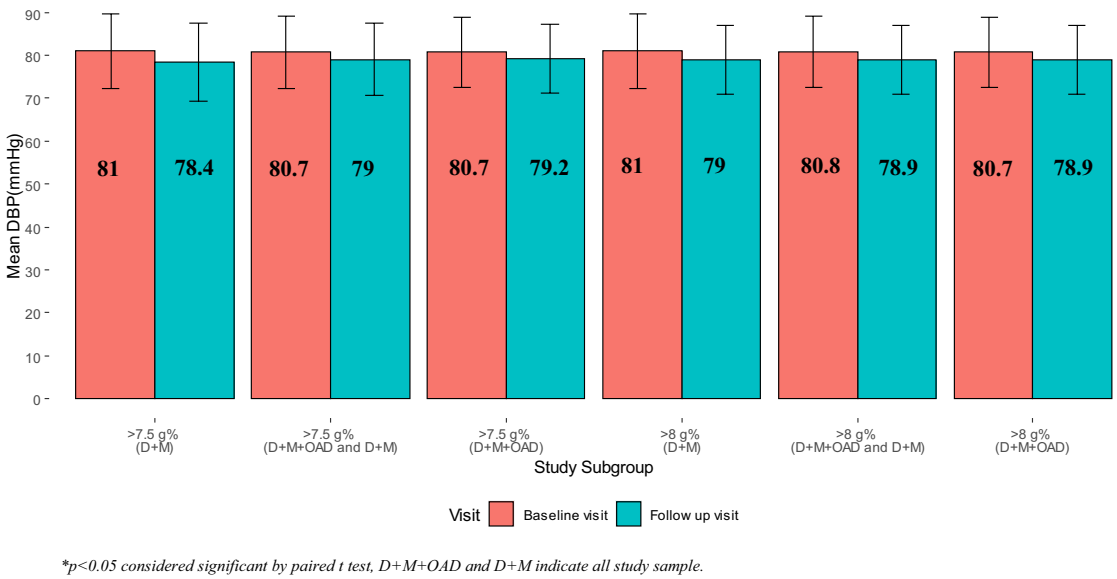


Fig. 6 Mean DBP in study subgroups. *D* dapagliflozin, *DBP* diastolic blood pressure, *M* metformin, *OAD* oral antidiabetic drug

to metformin-extended-release formulation (−1.44%). In metformin-treated patients as well, dapagliflozin led to significant reduction (−0.52%). In pooled 24-week analyses, dapagliflozin versus placebo changes in HbA1c, weight and SBP were noted to be −0.60%, −1.61 kg and −3.6 mmHg, respectively [21]. Based on pooled analysis, a recently published meta-analysis by Xu et al. noted a significant reduction of HbA1c with dapagliflozin alone [mean difference (MD) = −0.46, $p < 0.05$] and with dapagliflozin plus metformin (MD = −0.45, $p < 0.05$) versus placebo. Similarly, the weight changes with dapagliflozin alone (MD = −1.95, $p < 0.05$] and with dapagliflozin plus metformin (MD = −2.06, $p < 0.05$) versus placebo were significant [22]. Another meta-analysis by Pinto et al. noted that the MD for HbA1c (MD = −0.59) and body weight (MD = −1.88) was both significant for dapagliflozin 10 mg versus placebo and similar to other SGLT2 inhibitors [23].

Observational data can be utilised to reproduce the findings to demonstrate that patients experience the advantages of dapagliflozin as reported in clinical trials. Dapagliflozin's clinical effectiveness studies from Europe have demonstrated

that these improvements were equivalent to those seen in dapagliflozin clinical trials and that the drug decreased HbA1c level, weight and BP at 6 months after starting treatment [24]. However, a literature search indicated that there is a paucity of such real-world research from Indian hospitals. This retrospective cohort research examined individuals with type 2 DM receiving dapagliflozin plus metformin combination treatment, with or without additional OADs (D + M + OAD group), to determine the HbA1c decrease, weight and BMI changes and change in BP.

The study's findings demonstrate that, when combined with metformin, individuals treated with dapagliflozin had considerably greater reductions in HbA1c levels, weight, SBP and DBP. According to data from clinical studies, individuals who combined dapagliflozin and other OADs saw HbA1c reductions between −0.4% and −1.2% at 1 year follow-up [25–28]. In the present study, group of patients getting D + M showed mean reductions at follow-up ranging from 0.88 to 1.3%, whereas in the group of patients getting D + M + OAD, the mean reductions ranged from 1.2 to 1.6%. The average HbA1c reduction for complete patient set ranged from 1.1 to 1.6%. In comparison with the subgroup of patients with HbA1c ≥ 7.5 g%, the subset of patients with HbA1c ≥ 8 g% saw a larger mean HbA1c reduction. The possible reason is that HbA1c reduction with SGLT-2 inhibitors may be directly related to visit 1 HbA1c. Some recently published real-world Indian studies have explored the effect of dapagliflozin on glycemic control in Indian patients. A study by Ghosh et al. published in 2022 noted that after 120 days of dapagliflozin treatment, a significant decrease in the blood glucose and HbA1c was noted in line with our study findings [29]. A study by Bhosle et al. had evaluated and compared the effectiveness of SGLT2 inhibitors in type 2 DM management. It noted that all SGLT2 inhibitors led to significant reduction in the levels of HbA1c, fasting blood sugar (FBS), post prandial blood sugar (PPBS), SBP and DBP at week 12 and 24, and there was no significant difference between the four SGLT2 inhibitors on these aspects. The authors had concluded that gliflozins can be the best choice to start early in patients with inadequately controlled type 2 DM receiving triple-drug therapy which helps in controlling the parameters of glycemia [30].

Weight control is a crucial component of DM management. The most recent ADA guidelines on treating type 2 DM state that there is substantial evidence to show that controlling obesity can postpone the onset of type 2 DM and is extremely helpful in managing type 2 DM. ADA 2023 guidelines mention that evidence exists that obesity management can delay the progression from pre-diabetes to type 2 DM and is highly beneficial in treating type 2 DM. The guidelines mention that SGLT2 inhibitors have intermediate effect on weight reduction in type 2 DM population [8]. A review by Lazzaroni et al. noted that metformin, acarbose, empagliflozin and exenatide lead to mild weight loss (< 3.2% of initial weight); canagliflozin, ertugliflozin, dapagliflozin and dulaglutide induce moderate weight loss (3.2–5%); and liraglutide, semaglutide and tirzepatide result in strong weight loss based on evidence (> 5%) [31]. Weight reduction enhances glycemic control and decreases the requirement for glucose-lowering drugs. Clinical research findings showed that individuals using dapagliflozin along with other OADs demonstrated weight reduction ranging from 0.69 to 3.2 kg after a year [13, 25, 28]. The current study revealed that, for the full patient set, the mean weight loss was reported to be between 1.4 and 1.6 kg, which was consistent with the findings of the earlier clinical studies. Additionally, it was reported that the mean BMI decreased generally by 1–1.4 kg/m^2. The mean weight reductions for the subset of patients getting the D + M combination ranged from 2 to 2.4 kg, which was greater than the reduction range of 1.2–1.3 kg found with the D + M + OAD subgroup. The fact that the amount of weight loss was smaller in the D + M + OAD subgroup may be because certain OADs (such sulphonylurea) have questionable effects on weight. Some recent Indian studies have been published which have explored the effect of dapagliflozin on weight reduction. A study by Ghosh et al. published in 2022 noted that after 120 days of dapagliflozin treatment, a significant decrease in the weight, BMI, body fat and all skin fold thickness were noted. Interestingly, the study found that dapagliflozin reduced pancreatic as well as liver fat and increased insulin sensitivity in Asian–Indian patients with type 2 DM [29]. The study by Bhosle et al. also noted a significant reduction in body weight by all gliflozins, which is an added advantage of the drug class, especially when considering it for combination therapy [30].

Type 2 DM and hypertension (HTN) raise the risk of microvascular complications and cardiovascular outcomes by a significant amount. Although antihypertensive medication and lifestyle changes are necessary to lower cardiovascular risk, some anti-hyperglycaemic medications may have an added advantage in helping patients reach BP targets [15]. Published data indicate that treatment with glucagon-like peptide-1 (GLP-1) receptor agonists reduce SBP by 2–5 mmHg, while their effect on DBP is less clear. Administration of SGLT-2 inhibitors reduces SBP by 3–4 mmHg and DBP by 1–2 mmHg [32]. In the current investigation, the full patient set had a mean SBP reduction of 4.5 mmHg and a mean DBP reduction of 1.4–1.5 mmHg. A mean SBP reduction of 4.7 mmHg was seen in the group of patients who were prescribed D + M + OAD, which was larger than the reduction seen in the D + M subgroup (3.9 mmHg). Mean DBP decrease was comparable (1.2–1.5 mmHg) in both, the D + M and D + M + OAD groups. The difference in SBP and DBP reductions between the groups in the DECLARE-TIMI 58 study was 2.7 and 0.7 mmHg, respectively [33].

This decrease in BP varied from 0.5 to 1.2 mmHg for DBP and from 1.8 to 5.1 mmHg for SBP in other phase III clinical studies [13]. Even though dapagliflozin consistently reduced BP levels in all clinical trials, there may be some variation in weight loss that contributes to the differences.

The study had a few limitations, for example, possible missing data associated with retrospective medical records database analysis. The long-term impact of dapagliflozin could not be evaluated due to short duration of follow-up; further long-term real-world studies are required to confirm the trend. The study focused only on evaluation of effectiveness and the safety parameters could not be assessed.

5 Conclusions

Dapagliflozin showed significant improvement in glycemic parameter, BMI and BP when added to metformin, with or without other OADs in real-world scenario. These findings complement the findings noted in dapagliflozin clinical trials. This study supports the use of dapagliflozin as an add-on therapy to metformin ± other OADs in patients with type 2 DM in real-world clinical practice.

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Availability of Data and Material All the data is available in the manuscript.

Code Availability Not Applicable

Declarations

Conflict of Interest Dr. Bipin Sethi, Dr. Rakesh Sahay, Dr. Mangesh Tiwaskar, Dr. Vijay Negalur, and Snehal Shah have declared no conflicts of interest. Dr. Rajnish Dhediya, Dr. Kumar Gaurav, Dr. Rahul Rathod, Dr. Bhavesh Kotak and Gauri Dhanaki are employees of Dr. Reddy's Laboratories Ltd.

Ethics Approval Ethical approval was obtained from Suraksha Ethics Committee (ECR/644/Inst/MH/2014/RR-20).

Consent to Participate Informed consent waiver was obtained from the ethics committee as this was a non-experimental, retrospective data analysis study.

Consent for Publication Not Applicable.

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