# Medical Science

**Authors' Affiliation:**
[1]Resident at Family Medicine Department, King Abdulaziz Medical City Riyadh, Riyadh, Kingdom of Saudi Arabia
[2]Diabetes Clinical Fellow at university Diabetes Center, King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia
[3]Consultant, Family Medicine, King Abdulaziz Medical City, Riyadh, Saudi Arabia

[*]**Corresponding Author**
Resident at Family Medicine Department, King Abdulaziz Medical City Riyadh, Riyadh,
Kingdom of Saudi Arabia
Email: 7rb.khalid@gmail.com

**DISCOVERY**
**SCIENTIFIC SOCIETY**

# Change in HbA1c in Adults with type 2 diabetes mellitus using dapagliflozin 10mg and related side effects in King Abdulaziz Medical City, Saudi Arabia

**Khalid G Alharbi**[1*], **Hamad Alkanhal**[1], **Eman G Alharbi**[2], **Bader Altulaihi**[3]

## ABSTRACT

Diabetes is a common disease characterized by impaired glycemic control in the body. High blood glucose readings are any fasting blood glucose more than or equal to 126 mg/dl, random blood glucose more than or equal to 200 mg/dl, or A1c level greater than or equal to 6.5%. We used a retrospective, chart review study design to collect the A1c readings in patients using Dapagliflozin 10mg. The total sample size was 57 participants. Even though SGLT-2 inhibitors weakly reduce HbA1c, we have found in our study that Dapagliflozin has significantly decreased A1c in addition to a reduction in weight especially among females. Reported side effects were minimal with the majority having no side effects. However, 4 participants reported urinary side effects that were subsequently treated and improved.

**Keywords:** Type 2 diabetes mellitus, hba1c, semaglutide, dapagliflozin, sglt-2 inhibitors

## 1. INTRODUCTION

Diabetes is a worldwide disease characterized by dysregulate glycemic control in the blood and related organs (American Diabetes Association, 2024). In terms of its laboratory definitions, high glycemic levels are any fasting levels greater than or equal to 126 mg/dl, random blood glucose greater than or equal to 200 mg/dl, or A1c level greater than or equal to 6.5%, while a normal blood glucose level is anything lower than these cutoff with the exception or pre-diabetes state (FDA, 2024). In terms of pharmacological management, there are mainly 2 ways of treatment, either oral or injectable medications. Oral medication options are wide and include old commonly used sulfonylureas and newer agents such as the class

of Sodium-Glucose Transporter Protein 2 inhibitors (SGLT-2). Injectable agents include insulin and Glucagon Like Peptide-1 Receptor agonists (GLP-1). These oral and injectable agents vary in terms of their efficacy and side effect/safety profiles.

Efficacy as mentioned previously varies between oral agents. Furthermore, efficacy is mainly measured by degree of a1c reduction. For example, sulfonylureas whether started as monotherapy or add-on therapy lowered a1c by a range of 1-2% from the baseline compared to placebo (Wiviott et al., 2018). SGLT-2 agent Empagliflozin, on the other hand, decreases a1c by 0.7-0.9% from the baseline (Alguwaihes, 2021). Locally in Saudi Arabia, physicians vary in their choice of first and second-line oral or injectable hypoglycemic agents for the treatment of their patients with type 2 diabetes mellitus. The DISCOVER study was a prospective study over 3 year-period reported physician's choice of hypoglycemic agents in many countries including Saudi Arabia (Musso et al., 2012). Most common prescribed agents were metformin, gliclazide, and glibenclamide, respectively (Musso et al., 2012).

Although not commonly used as per this study, SGLT-2 inhibitors and GLP-1 agonists showed good efficacy and safety profiles as reported by many studies including a large study done in Saudi Arabia by (Alguwaihes, 2021; Clar et al., 2012.). Given that not so many studies highlighted efficacy of SGLT-2 agent Dapagliflozin in Saudi Arabia and no studies done in NGHA, Riyadh, we aim to investigate the efficacy and safety profile of Dapagliflozin in dose of 10mg for a duration of 1 year in patients treated in National Guard Hospital, Riyadh, Saudi Arabia.

## 2. METHODS

This study implemented a retrospective, chart review study design and a non-probability convenient sampling technique to collect the A1c levels in patients using Dapagliflozin before and after 1 year of starting these medications. Included patients were those who started these medications from period of 1/1/2023 and reviewed their charts until 1/1/2024 to check for A1c reduction degree and occurrence of urinary side effects. Data was collected and cleaned in an Excel sheet and then imported to R software (version 4.2.2). The normality of data was assessed using a histogram and the Shapiro-Walik test. Continuous variables were presented in median and interquartile ranges, while categorical were presented in numbers and percentages. Wilcoxon rank-sum test was used to assess the association between changes in Hemoglobin A1C, demographic and medical characteristics of participants. A paired Wilcoxon rank sum test was used to assess the significance of the change in weight and Hemoglobin A1C before and after 1 year of using the Dapagliflozin. A p-value of less than 0.05 was considered significant.

## 3. RESULTS

The study included 57 participants with a median age of 58 years (interquartile range 52-64). Of these, 67% were female. Only 7% reported having side effects from diabetes medication. Regarding complications of diabetes mellitus, 37% were documented clinically to have complications directly related to type 2 diabetes mellitus. In terms of medication, all included participants were on Dapagliflozin in dosage of 10mg. The median Hemoglobin A1C level before intervention was 9.20 (interquartile range 8-10.2), which decreased to 8.2 (interquartile range 7.4-9) after intervention. The median weight before intervention was 86 kg (interquartile range 81-103), and 80 kg after intervention (interquartile range 78-98.5).

Table 1 shows a summary of our participants' demographic data. Table 2 shows that 73% of participants were found to have no complications of diabetes mellitus. However, out the 27% who had complication, 22.8%, 10.5% and 7% reported having retinopathy, nephropathy and ischemic heart disease, respectively. In terms of side effects, 4 participants had side effects after using Dapagliflozin 10mg. 2 of them had positive nitrates on urinalysis and urine dipstick but no reported symptoms and, hence, not treated and improved with increased water intake on follow-ups, 1 of them had candida urinary tract infection and 1 participant had recurrent vaginal candidiasis. Statistically, were have found that age and gender have not played a significant role in its effect on change of hemoglobin A1c after 1 year of starting either Dapagliflozin 10mg (Table 3).

Furthermore, we have observed that there is no statistically significant change in Hemoglobin A1c in those who had complications of type 2 diabetes mellitus versus those without complications. The median Hemoglobin A1C was significantly decreased after using Dapagliflozin compared to before using it (median=9.2 vs median=8.2, p<0.001) as seen in (Figure 1). The median weight was significantly decreased after using Dapagliflozin compared to before using it (median=86 vs median=80, p<0.001) as seen in (Figure 2).

**Table 1** Demographic and medical characteristics of participant

| Characteristic | N = 571 |
|---|---|
| Age | 58 (52, 64) |
| Gender | |
| Female | 38 (67%) |
| Male | 19 (33%) |
| Side effects | |
| Yes | 4 (7%) |
| No | 53 (93%) |
| Complications of DM | |
| Yes | 21 (37%) |
| No | 36 (63%) |
| Hemoglobin A1C before starting Dapagliflozin 10mg | 9.20 (8.00, 10.20) |
| Hemoglobin A1C after 1 year of starting Dapagliflozin 10mg | 8.20 (7.40, 9.00) |
| Weight before | 86 (81, 103) |
| Weight after | 80 (78, 98.5) |

1Median (IQR); n (%)

**Table 2** Reported Complications of diabetes mellitus

| Characteristic | N = 571 |
|---|---|
| Complications of diabetes mellitus* | |
| Ischemic heart disease | 4 (7.0%) |
| Nephropathy | 6 (10.5%) |
| Neuropathy | 2 (3.5%) |
| Retinopathy | 13 (22.8%) |
| Recurrent vaginal candidiasis | 1 (0.9%) |
| None | 36 (63%) |

1Median (IQR); n (%)

*Multi-choice question

**Table 3** Association between change in Hemoglobin A1C among Dapagliflozin 10mg users and demographic and clinical characteristics

| Characteristic | N = 571 | p-value2 |
|---|---|---|
| Age | - | >0.9 |
| 30-52 | -0.95 (-1.73, -0.43) | - |
| 53 and above | -0.80 (-1.60, -0.30) | - |
| Gender | - | 0.5 |
| Female | -1.00 (-1.60, -0.30) | - |
| Male | -0.70 (-1.35, -0.40) | - |
| Complications of diabetes mellitus | - | 0.3 |
| No | -0.80 (-1.28, -0.25) | - |
| Yes | -1.20 (-2.40, -0.50) | - |

1difference in Hemoglobin A1C: Median (IQR)
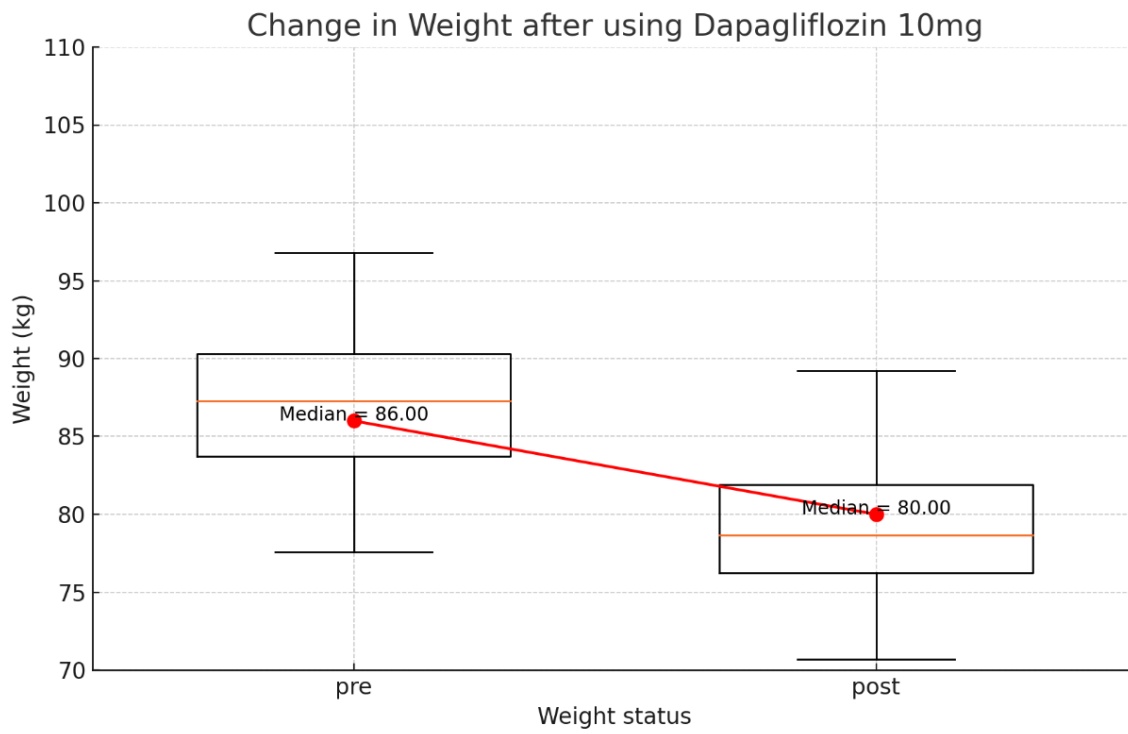
2Wilcoxon rank sum test

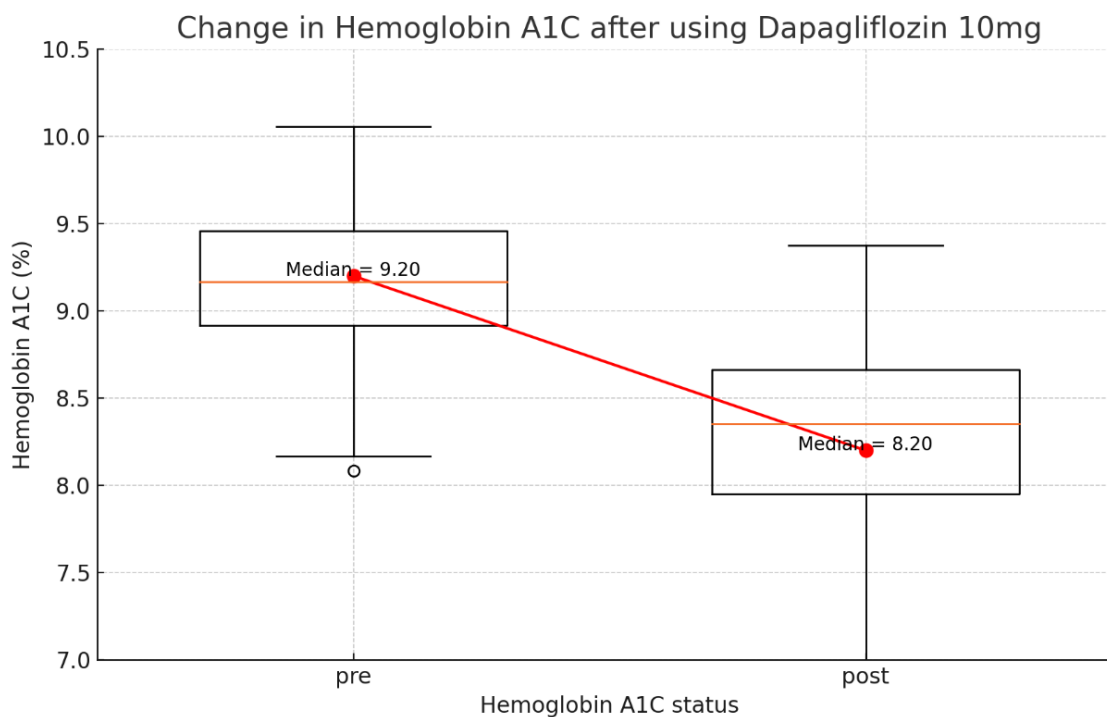**Figure 1** Change in Hemoglobin A1C level after using Dapagliflozin 10mg

**Figure 2** Change in weight level after using Dapagliflozin 10mg

## 4. DISCUSSION

Dapagliflozin is a sodium-glucose cotransporter 2 (SGLT2) inhibitor that has multiple uses and indications. For example, maintain or improving eGFR in chronic kidney disease, reducing risk of cardiovascular death, reducing hospitalization and mortality in patients with heart failure. More importantly, it is mainly used for the treatment of type 2 diabetes mellitus as it works at lowering blood sugar levels by blocking renal tubes from reabsorbing glucose back into the blood, thereby promoting its excretion through urine (American Diabetes Association, 2024; FDA, 2024). Hemoglobin A1c (HbA1c) is a key marker used to estimate long-term blood glucose control in individuals with diabetes. Dapagliflozin efficacy was proven by The American Diabetes Association (ADA) in reducing HbA1c levels. Furthermore, several studies have demonstrated that dapagliflozin can significantly lower HbA1c levels when used as monotherapy or in combination with other antidiabetic agents.

The approximate reduction of HbA1c levels upon initiating Dapagliflozin for several months is between 0.5% to 1%, this typically determined by baseline level of HbA1c, and other medication used along with Dapagliflozin. (American Diabetes Association, 2024; FDA, 2024). Dapagliflozin has another desired effect which is promoting weight loss. This effect provides major benefit for diabetic patients as they typically suffer from obesity and facing difficulties in losing weight as demonstrated and proved by ADA to be a beneficial side effect of using Dapagliflozin. However, the weight loss observed with dapagliflozin use is generally limited, as they usually lose about 2-3% of their total body weight over long-term treatment. Losing weight in adults using dapagliflozin can be explained by caloric loss associated with glucose excretion through urine. (American Diabetes Association, 2024; FDA, 2024).

In this study, we found significant improvement in glycemic control by measuring HbA1c levels and losing weight by using dapagliflozin for a course of 1 year. Statistically, the median Hemoglobin A1C level decreased from 9.20 to 8.2 after completing 1 year with dapagliflozin. This change was statistically significant with a p-value of <0.001. Furthermore, the median weight of the participants has a statistically significant decrease from 86 kg to 80 kg with a p-value of <0.001. Moreover, this study included 67% female participants and 33% male participants and a median age of 58. Our analysis showed no significant impact on glycemic control or weight loss in comparison of both gender and age following use of dapagliflozin for 1 year. Furthermore, this study included 37% with type 2 diabetic complications.

However, there was no significant difference in glycemic control between participants with and without complications of type 2 diabetes mellitus. Thus, these findings suggest that Dapagliflozin 10mg is equally effective in reducing Hemoglobin A1C levels and promoting weight loss regardless of diabetes related complications. Our study correlates with other studies findings in measuring the efficacy of long-term glycemic control and weight loss following use of dapagliflozin 10mg. The DECLARE-TIMI 58 trial was a large-scale study that evaluated the cardiovascular outcomes and safety of Dapagliflozin in patients with type 2 diabetes. The trial showed that Dapagliflozin significantly reduces Hemoglobin A1C levels, with an average reduction of 0.9% compared to placebo. Additionally, the study reported a significant weight loss, with participants having an average weight loss of around 2-3 kg (Wiviott et al., 2018).

Another local study evaluated the safety of dapagliflozin and its outcomes in patients with type 2 diabetes. It showed that dapagliflozin has significantly decreased HgbA1c levels with an average of 1.23% after 12 months. Furthermore, the study showed a significant reduction in lipid profiles after 12 months, including LDL, Triglycerides, Total cholesterol. However, no weight follow-up was done in this study. The result of the study is also in line with the present study, confirming the efficacy of Dapagliflozin in glycemic control and it might give a clue that participant lost weight after having significant reductions in lipid profile (Alguwaihes, 2021). In Table 2, Four participants experienced side effects from Dapagliflozin 10mg, including positive nitrates on urinalysis, candida urinary tract infection, and recurrent vaginal candidiasis.

Genital infections are among the frequent complaints of type 2 diabetes. Patients with type 2 diabetes (T2DM) who have inadequate glycemic control may experience hyperglycemia and glucosuria, which can exacerbate vulvovaginitis in this patient population. While glucosuria promotes the adhesion of bacteria to vaginal epithelial cells, hyperglycemia impairs the body's defense mechanisms and creates an ideal environment for microorganisms to flourish. As was previously noted, SGLT2 inhibitors raise the risk of genital infections by increasing the amount of glucose excreted in the urine, which normalizes blood glucose levels. When comparing 10 mg of dapagliflozin with a placebo, there was a small increase in the rate of genitourinary tract infections, including vulvovaginal candida infections and UTIs, in multiple meta-analyses and systematic reviews (Musso et al., 2012; Clar et al., 2012; Zhang et al., 2014).

Although monitoring, assessing and long-term follow up among participants. Our study has some limitations that need to be considered. For example, with only 57 participants, the sample size is relatively small as it could limit the statistical power of the study and the generalization of its findings. This can be explained by single-centered study (National Guard Hospital, Riyadh). Thus, it may limit the applicability of the results to other settings or regions. Also, the study was conducted in retrospective-chart review design and data was collected from patient records, which might not capture all relevant variables. Accordingly, addressing these limitations in future research will help provide a more comprehensive understanding of the efficacy of Dapagliflozin on glycemic control and weight reduction.

## 5. CONCLUSION

The study demonstrates that Dapagliflozin (10mg) significantly improves glycemic control and reduces weight in patients with type 2 diabetes mellitus at the National Guard Hospital in Riyadh. The medication's efficacy in lowering Hemoglobin A1C levels and promoting weight loss was consistent across different ages, genders, and the presence of diabetes-related complications. These findings support the use of Dapagliflozin as a valuable treatment option for managing type 2 diabetes mellitus, contributing to better patient outcomes and overall metabolic health. Further research with larger sample sizes and longer follow-up periods is recommended to confirm these results and explore additional benefits and risks associated with Dapagliflozin

**Author Contributions**

Bader Altulaihi: Author, Supervisor

Khalid Alharbi: Co-Author

Hamad Alkanhal: Co-Author

Eman Al Harbi: Co-Author

**Ethical approval**

The study was approved by the Medical Ethics Committee of King Abdullah International Medical Research Center (Ethical approval code: IRB/1081/24).

**Informed consent**

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

**Funding**

This study has not received any external funding.

**Conflict of interest**

The authors declare that there is no conflict of interests.

**Data and materials availability**

All data sets collected during this study are available upon reasonable request from the corresponding author.

## REFERENCES

1. Alguwaihes AM. Safety of dapagliflozin in patients with type 2 diabetes mellitus in Saudi Arabia: A Post Authorization Safety Study. Diabetes Ther 2021; 12(5):1979-1992. doi: 10.1007/s13300-021-01092-0

2. American Diabetes Association. Diabetes Technology: Standards of Medical Care in Diabetes—2024. Diabetes Care 2024; 47(Supplement_1):S126-S144. doi: 10.2337/dc24-S007

3. Clar C, Gill JA, Court R, Waugh N. Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes. BMJ Open 2012; 2(5):e001007. doi: 10.1136/bmjopen-2012-001007

4. FDA. Farxiga® (dapagliflozin) tablets, for oral use. FDA Prescribing Information for Dapagliflozin, 2024.

5. Musso G, Gambino R, Cassader M, Pagano G. A novel approach to control hyperglycemia in type 2 diabetes: sodium glucose co-transport (SGLT) inhibitors: systematic review and meta-analysis of randomized trials. Ann Med 2012; 44(4):375-93. doi: 10.3109/07853890.2011.560181

6. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2018; 380(4):347-357.

7. Zhang M, Zhang L, Wu B, Song H, An Z, Li S. Dapagliflozin treatment for type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. Diabetes Metab Res Rev 2014; 30(3):204-211. doi: 10.1002/dmrr.2479