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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE EFFECT OF DAPAGLIFLOZIN ON THYROID FUNCTION TEST IN DIABETIC PATIENTS

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Abstract.

Background: Hyperglycemia brought on by insulin resistance and decreased insulin secretion is a hallmark of type II diabetes mellitus (T2DM), a common metabolic disease. By increasing the excretion of glucose in the urine, dapagliflozin, an inhibitor of the sodium–glucose cotransporter-2 (SGLT2), lowers blood glucose levels and may have other systemic effects. **Aim:** The purpose of this study was to assess how dapagliflozin affected glycemic control, thyroid function, and serum vitamin D_3 levels while looking into potential age and gender effects. **Methods:** Thirty T2DM patients who had previously received metformin treatment (18 men and 12 women, ages 31 to 70) were enlisted. In addition to metformin, each participant received 10 mg of dapagliflozin daily for eight weeks. Using chemiluminescent and ELISA assays, serum levels of HbA_1c, triiodothyronine (T_3), thyroxine (T_4), thyroid-stimulating hormone (TSH), and vitamin D_3 were assessed both before and after treatment. **Results:** Although, changes in T_4, TSH, and vitamin D_3 were not statistically significant, dapagliflozin significantly decreased HbA_1c and T_3 levels. While HbA_1c showed a near-borderline difference between sexes ($p \approx 0.10$) and vitamin D_3 showed a mild age-related trend ($p \approx 0.07$), neither gender nor age significantly affected any of the parameters. **Conclusion:** Dapagliflozin's main effect appears to be on peripheral metabolic regulation rather than endocrine hormone synthesis, as evidenced by the fact that it successfully improved glycemic control without substantially changing thyroid or vitamin D_3 levels. Dapagliflozin's stable therapeutic profile is highlighted by the consistent biochemical responses across age and gender, which calls for additional research with bigger sample sizes and longer follow-up periods.

Key words. Dapagliflozin, diabetes mellitus, metformin, thyroid hormones, thyroid stimulating hormones.

Introduction.

Elevation of blood sugar is a deleterious abnormality that could happen in the body. If the situation persists, this will lead to a state of metabolic disorder called diabetes mellitus (DM). According to the sources of such abnormality, which could be a decreased insulin activity and/or insulin secretion, this disease is subdivided into two types [1]. Type I, which is insulin-dependent and treated through insulin replacement therapy, while type II DM is treated with oral hypoglycemics, as this type mostly occurs due to the malfunction of pancreatic beta cells and resistance to insulin in peripheral tissues [2].

Type II DM is one of the most common and widely spread metabolic disorders in the world, affecting approximately 415 million adults, which accounts for 9.1% of the population [3-4]. DM in general and special type II has many serious complications, such as nephropathy, retinopathy, and cardiovascular complications. Some of these complications could lead to organ damage, impairments in functions, and even death [5-6]. Thus, suitable treatment, controlling patients' status, and supportive efforts to prevent its complications are the primary responsibilities of many researchers and medical teams worldwide.

One of the oral hypoglycemic medications that has recently been used in the treatment of Type II DM is sodium-glucose cotransporters 2 inhibitors (SGLT2). Dapagliflozin is a famous agent from this group, which studies showed that it has a very interesting way in the reduction of glucose level in the blood via inhibition of the reabsorption of filtered glucose in the kidney and thus will enhance glucose excretion [7]. Besides the glycemic control, a recent study revealed that dapagliflozin and other agents from the same group could also have an additional beneficial outcome on the cardiovascular and renal system via reduction of the rate of mortality, although the exact mechanism is still unclear [8]. Moreover, another study demonstrates that dapagliflozin and other agents could also have a protective effect on the central nervous system via reducing the rate of cognitive impairment and improving the cerebral microvascular function in diabetic and Alzheimer's patients [9]. All of these and more give a suggestion that dapagliflozin and related agents could have a protective role for different organs, glands, and systems in diabetic and non-diabetic patients, but these need more digging to find out where and how with reasonable explanations.

The thyroid gland is similar to other glands and organs in the body, and its function could deteriorate if any elevation or reduction happens to its hormones [10]. First of all, this study aimed to check HbA1c in human serum to confirm the hypoglycemic role of dapagliflozin. The second target was to find out if dapagliflozin could have any modifying effect on thyroid function test {triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH)} when used in type II DM patients through checking the level of these hormones and enzymes before taking dapagliflozin therapy and after taking it for 3 months. On the other hand, we have vit D, which contributes to determining the state of bone health; therefore, lowering the serum level 1,25-dihydroxyvitamin D [1,25(OH)2D] and increasing levels of PTH could have a bad impact on the bone status [11-12]. As a consequence, vitamin D level was also checked before and after treatment to find out if dapagliflozin could modulate its level or if there is no connection at all.

Materials and Methods.

Patients: Thirty diabetic patients taking metformin as a monotherapy were recruited in this study (18 male and 12

female) in the age range of 31-70 years. Diagnosis of diabetes was made by one specialist physician. All patients gave written informed consent to participate in this study. Patients with the following criteria were excluded from the study (patients with drug abuse, patients with diseases other than diabetes, patients with diabetes who used multiple therapies, and other exclusion criteria, including pregnant and lactating women).

Study protocol: This is a prospective observational study conducted in Mosul City from October 2024 to April 2025. The patients initially were on metformin monotherapy 1000mg/day (Glucophage, MERCK®, Germany) for several months, then all patients received Dapagliflozin 10mg/day (Divinus, Hikma® Jordan) as an add-on therapy, and the combination was used together for 8 weeks.

Sampling: Five milliliters of venous blood were withdrawn from the patients initially before adding dapagliflozin after overnight fasting. The blood sample was divided into two parts; one was used for HbA1C measurement, and the other was allowed to clot in a plain tube at room temperature, and then the serum was separated by centrifugation at 3000 rpm for 10 min and kept frozen for bending analysis. This serum was used for the determination of HbA1c, T3, T4, TSH, and D3 levels. At the end of the study (after 8 weeks), another blood samples were taken from the patients (collected and processed in the same way), and the assessment of the same parameters (HbA1c, T3, T4, TSH, and D3) was done.

Analytical methods.

T3, T4, TSH and Vitamin D measurement:

The CL-series T3, T4, TSH, and Vitamin D assay is a Chemiluminescent immunoassay (CLIA) for the quantitative determination of T3, T4, TSH, and Vitamin D in human serum or plasma. The kit is supplied by Mindray Bio-Medical Electronics Co., Ltd, catalog No. 105-004210-00, 105-004211-00, 105-004212-00, and VD-T112, respectively.

HbA1c measurement:

HbA1c ELISA Kit supplied by Antibodies-online is a competitive inhibition enzyme immunoassay technique for the in vitro quantitative measurement of HbA1c in human serum, plasma, and erythrocyte lysates.

Statistical analysis: GraphPad Prism version 8 (GraphPad Software, San Diego, CA, USA) was used to analyze the data. The mean±SD was used to express the results. Data normality was evaluated using the Shapiro-Wilk test. Pre- and post-treatment values were compared using paired t-tests (or Wilcoxon signed-rank tests for non-parametric data). One-way ANOVA and independent t-tests were used to assess the effects of age group and gender, respectively. $0.05 \leq p < 0.10$ was interpreted as a trend toward significance, and a $p < 0.05$ was deemed statistically significant.

Results.

Effect of Dapagliflozin on HbA1c level: To confirm the hypoglycemic effect of Dapagliflozin, we add it as additional therapy in a dose of 10mg/day. As expected, Dapagliflozin caused a significant reduction in HbA1c (Pre=8.267±0.2149, compared to the Post=6.550±1.717) as shown in Figure 1.

Table 1. *Effect of Dapagliflozin on TSH, T3 and T4 levels.*

Parameters	Before	After	P-value
TSH	2.67±0.60	2.56±0.35	0.7580
T3*	1.44±0.024	1.27±0.070	0.0223*
T4	96.03±9.46	95.60±4.94	0.9304

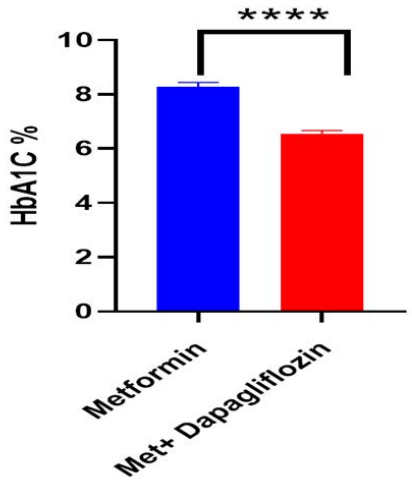

Figure 1. *Representative graph showing the effects of Dapagliflozin on HbA1C. There is a significant reduction in HbA1C level. Data were pooled from 30 participants (n=30) and presented as mean±SEM Statistical significance was determined by paired t-test, ****p<0.0001 is a significant value.*

Effect of Dapagliflozin (as an additional therapy) on TSH, T3, and T4 levels: To test the effect of Dapagliflozin on liver function test, we added it as additional therapy in a dose of 10mg/day. The results showed that there is no significant effect on both TSH and T4 levels, while the T3 level reduced significantly, as shown in Table 1 and Figure 2.

Effect of Dapagliflozin (as an additional therapy) on vitamin D3 level: To test the effect of Dapagliflozin on Vitamin D3, we add it as additional therapy in a dose of 10mg/day. The results showed that there is no significant reduction in the serum level of vitamin D3, as shown in Figure 3.

The effect of Gender and age group on Vitamin D3, thyroid function tests, and HbA1C: The complete characteristics of the parameters under investigation are shown in Table 2, which used an independent t-test (male vs female) to see the Gender effect and used One-way ANOVA (4 groups: 30–45, 46–60, 61–75, 76–90 years) to see the Age effect. Parameter change was calculated as (Post – Pre) for each variable, and the significant value was> 0.05.

Discussion.

The current study examined how dapagliflozin affected vitamin D_3, HbA_{1c} levels, and thyroid function. The findings showed that while dapagliflozin had negligible effects on thyroxine (T_4) and thyroid-stimulating hormone (TSH), it significantly reduced serum triiodothyronine (T_3) and HbA_{1c}. Additionally, after taking dapagliflozin, there was a non-significant decrease in serum vitamin D_3.

This decrease in HbA_{1c} is consistent with other research showing that dapagliflozin inhibits sodium–glucose

Table 2. *The effect of Gender and Age group on the parameters under investigation.*

Parameter	Test Used	p-value (Gender)	Significant?	p-value (Age Group)	Significant?
D3 (ng/mL)	t-test/ ANOVA	0.396	No	0.072	No (trend)
T4 (nmol/L)	t-test/ ANOVA	0.795	No	0.409	No
T3 (nmol/L)	t-test / ANOVA	0.884	No	0.318	No
TSH (uIU/mL)	t-test / ANOVA	0.427	No	0.864	No
HbA1C (%)	t-test / ANOVA	0.102	No (borderline)	0.777	No

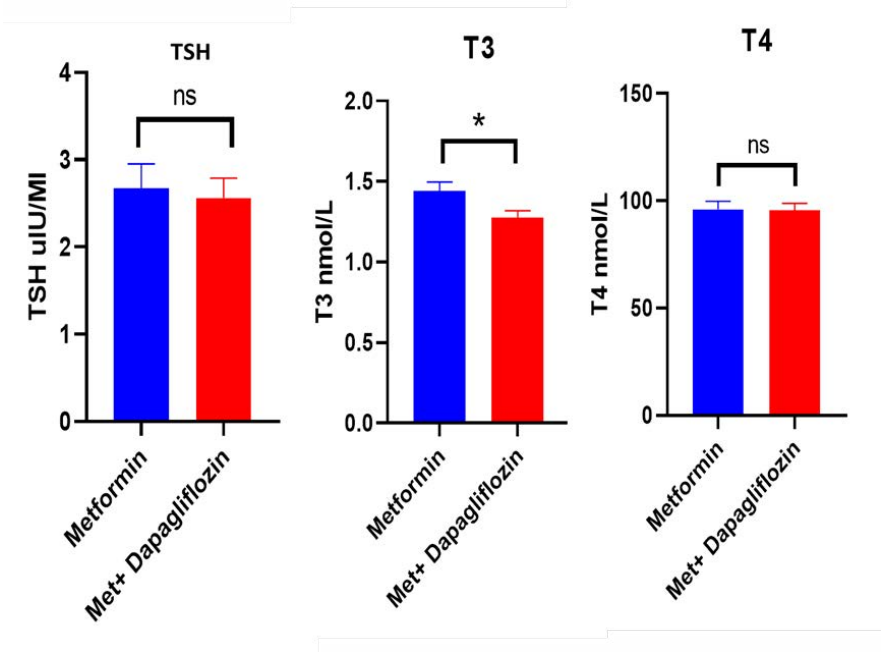

Figure 2. *Representative graph showing the effects of Dapagliflozin on TSH, T3, and T4. There is a significant reduction in T3 level, and there are no changes in serum levels of both T4 and TSH. Data were pooled from 30 participants (n=30) and presented as mean±SEM Statistical significance was determined by paired t-test, ns (non-significant) p value ≥0.05, while * p<0.01 is a significant value.*

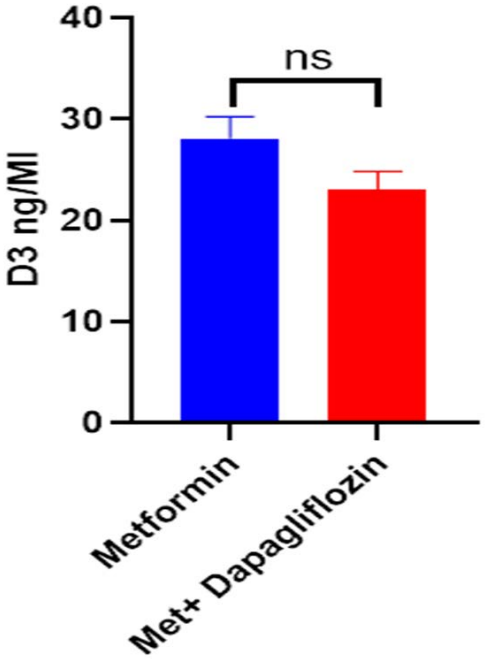

Figure 3. *Representative graph showing the effects of Dapagliflozin on Vitamin D3. There are no significant changes in the vitamin D3 level. Data were pooled from 30 participants (n=30) and presented as mean±SEM Statistical significance was determined by an paired t-test, ns (non-significant) p value ≥0.05.*

cotransporter-2 (SGLT2) in the proximal renal tubules, thereby lowering plasma glucose and glycated hemoglobin [13,14]. Regardless of insulin secretion or sensitivity, dapagliflozin enhances glycemic control by encouraging urine glucose excretion [15]. Depending on baseline glycemia, renal function, and treatment duration, reported decreases in HbA_1c usually fall between 0.5% and 1.0% [13]. The study's substantial reduction in HbA_1c thus validates dapagliflozin's ability to lower blood sugar and supports its therapeutic role in enhancing metabolic control in diabetic patients.

Dapagliflozin significantly decreased serum T_3 without changing T_4 or TSH, according to our findings. This implies a selective impact on the metabolism of peripheral thyroid hormones as opposed to the regulation of the pituitary-thyroid axis. The decrease in T_3 might be due to modifications in peripheral deiodinase activity rather than a direct suppression of thyroid hormone synthesis, as T_4 and TSH stayed constant. There is little information on the connection between thyroid hormones and SGLT2 inhibition. According to some studies, SGLT2 inhibitors may indirectly regulate thyroid homeostasis by enhancing systemic metabolism and oxidative stress [16,17]. Although there is conflicting and inconclusive evidence, a brief clinical observation indicated changes in thyroid hormone profiles following dapagliflozin therapy [18].

This decrease in T_3 may be the result of improved glycemic and metabolic status, which lowers the conversion of $T_4 \rightarrow T_3$. It is well known that insulin resistance and hyperglycemia can increase type 1 deiodinase activity, which in turn promotes the formation of T_3. Consequently, T_3 synthesis may be decreased by glucose normalization after dapagliflozin treatment [19]. Mild calorie loss through glycosuria, which simulates a fasting-like state and physiologically reduces T_3 through decreased deiodinase activity, may be another explanation [20]. Crucially, unaltered TSH and T_4 show that dapagliflozin does not directly affect thyroid or pituitary gland function, which is in line with previous experimental results [17].

Moreover, Divergent physiological processes could be the cause of the observed decrease in circulating T3 in the absence of notable changes in TSH and T4. On the one hand, this pattern, which is marked by decreased peripheral T4-to-T3 conversion and a brief decrease in energy expenditure, may be an adaptive reaction to a fasting-like or calorie-restricted state, possibly conferring metabolic efficiency. However, low T3 syndrome, a non-thyroidal illness that has been linked to poor metabolic outcomes, also exhibits a similar hormonal profile. It is still unclear whether the T3 decrease seen in this study is pathological or beneficial in the absence of functional or clinical endpoints. These results should therefore be interpreted with caution, and more research involving metabolic and clinical outcomes is necessary to elucidate their significance [21,22].

Following dapagliflozin treatment, there was a non-significant decrease in serum vitamin D_3 (25-hydroxyvitamin D). This finding partially supports previous research showing that SGLT2 inhibitors may change the homeostasis of phosphate and parathyroid hormone (PTH) without appreciably altering the amount of 25(OH)D in the blood [23,24]. Dapagliflozin raises serum phosphate by increasing renal phosphate reabsorption, which in turn triggers the release of PTH and fibroblast growth factor-23 (FGF23). By decreasing renal 1-α-hydroxylase activity, these hormonal changes may have a secondary effect on vitamin D metabolism, resulting in slight drops in active $1,25(OH)_2D$ levels [23].

In line with the Islek et al. (2024) short-term biomarker study, our analysis revealed a declining trend in vitamin D_3, but the change did not reach statistical significance. Therefore, dapagliflozin seems to have little clinical effect on vitamin D_3 concentration during the studied period, even though it may have a slight effect on mineral regulatory hormones [24]. Besides that, previous study conducted using different medication showed that serum 25-hydroxyvitamin D levels changed after six weeks of carbamazepine or oxcarbazepine treatment. Given the 2-3-week half-life of 25-hydroxyvitamin D and the enzyme-inducing characteristics of these antiepileptic medications, this relatively short duration is adequate to identify changes in vitamin D status. These results support the need for early monitoring after treatment initiation by showing that even brief exposure can affect vitamin D metabolism [25].

Thus, rather than directly affecting thyroid gland function or vitamin D synthesis, these results imply that dapagliflozin mainly influences metabolic and peripheral hormonal conversion processes. An adaptive metabolic response associated with better glycemic control and mild energy loss from glucosuria may be the cause of the observed drop in T_3.

To determine whether dapagliflozin has clinically significant effects on thyroid hormone metabolism and vitamin D status, as well as to clarify the underlying mechanisms linking glucose regulation, deiodinase activity, and mineral homeostasis, more research with larger cohorts and longer treatment durations is necessary.

Regarding the effect of gender and age group on HbA1C, although the change in HbA1C approached borderline significance ($p \approx 0.10$), the analysis of gender and age group effects on the biochemical parameters in the current study did not reveal any statistically significant differences between males and females for any of the measured variables. This finding is consistent with other research showing that there aren't many gender-related variations in glycemic response after taking sodium-glucose cotransporter-2 (SGLT2) inhibitors like dapagliflozin [26,27]. The hormonal environment, insulin sensitivity, and fat distribution may vary between males and females, but these variables don't seem to have a significant impact on the glycemic response to dapagliflozin28. However, the study's nearly significant change in HbA1c may indicate minor physiological differences, perhaps as a result of sex-specific differences in body composition or drug pharmacokinetics [29].

Regarding the thyroid function test, there were no discernible gender-dependent differences in thyroid function metrics (TSH, T3, and T4). This aligns with data indicating that dapagliflozin primarily affects metabolism by inhibiting renal glucose reabsorption instead of directly modifying thyroid hormones [30]. Additionally, the hypothalamic-pituitary-thyroid axis feedback mechanisms tightly regulate thyroid hormone homeostasis, potentially mitigating the small metabolic effects of SGLT2 inhibition [31].

About the effect of age and while the change in serum vitamin D3 showed a trend toward significance ($p \approx 0.07$), the results showed that none of the biochemical parameters were significantly impacted by age group. Given that older people typically have decreased cutaneous synthesis, altered renal hydroxylation, and variations in drug metabolism, this pattern may represent age-related physiological variation in vitamin D metabolism [32,33]. Additionally, prior studies have demonstrated that age has a greater impact on vitamin D levels when metabolic disorders or medication are present [34]. Therefore, the data may suggest an age-related susceptibility to changes in vitamin D metabolism during dapagliflozin therapy, even though the trend did not reach statistical significance.

Overall, it appears that dapagliflozin has generally consistent biochemical effects on adult patients, as evidenced by the lack of significant differences across gender and age groups. The sample size was small overall (N = 30), despite exploratory subgroup analyses by age and sex. Additional stratification, such as grouping people into different age groups, led to significantly lower statistical power, which limited these analyses' dependability and interpretability. Therefore, it is not appropriate to interpret the lack of statistically significant differences in subgroup comparisons as proof of equivalency or the absence of an effect. Larger, sufficiently powered studies are needed to reach firm conclusions, and these analyses should be viewed as hypothesis-generating. Accordingly, the near-significant trends for vitamin D3 (age) and HbA1C (gender) that have been found call for more investigation with bigger sample sizes because inaddition to what mentioned earlier, they might be biological variability rather than chance variation.

Conclusion.

This study assessed the effects of dapagliflozin on vitamin D_3 levels, thyroid function, and glycemic control while looking into potential age and gender-related variations. Without influencing the levels of thyroxine (T_4), thyroid-stimulating hormone (TSH), or vitamin D_3, dapagliflozin markedly decreased HbA_1c and serum triiodothyronine (T_3). These results imply that rather than directly affecting thyroid or vitamin D synthesis, dapagliflozin mainly affects peripheral metabolic processes like glucose regulation and T_4-to-T_3 conversion. The modest, non-significant drop in vitamin D_3 could be the result of minor changes in the balance of minerals and hormones. While HbA_1c showed a near-borderline difference between sexes and vitamin D_3 showed a mild age-related trend, no significant gender- or age-related differences were found. Dapagliflozin's role in enhancing glycemic control was supported by its overall consistent metabolic effects across demographic groups.

REFERENCES

1. Mauvais FX, van Endert PM. Type 1 diabetes: A guide to autoimmune mechanisms for clinicians. Diabetes, Obesity and Metabolism. 2025;27:40-56.
2. Khursheed R, Singh SK, Wadhwa S, et al. Treatment strategies against diabetes: Success so far and challenges ahead. European Journal of Pharmacology. 2019;862:172625.
3. Ong KL, Stafford LK, McLaughlin SA, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 2023;402:203-34.
4. Yapislar H, Gurler EB. Management of microcomplications of diabetes mellitus: Challenges, current trends, and future perspectives in treatment. Biomedicines. 2024;12:1958.
5. Saarti M, Khalaf MM, Althanoon ZA. Non-Nutritive sweeteners modulated creatinine and urea levels in white albino rats. Pharmacognosy Journal. 2024;16.
6. Akalu Y, Birhan A. Peripheral arterial disease and its associated factors among type 2 diabetes mellitus patients at Debre Tabor general hospital, Northwest Ethiopia. Journal of Diabetes Research. 2020;2020:9419413.
7. Hsia DS, Grove O, Cefalu WT. An update on sodium-glucose co-transporter-2 inhibitors for the treatment of diabetes mellitus. Current Opinion in Endocrinology, Diabetes and Obesity. 2017;24:73-9.
8. Bhatt DL, Szarek M, Steg PG, et al. Sotagliflozin in patients with diabetes and recent worsening heart failure. New England Journal of Medicine. 2021;384:117-28.
9. Hierro-Bujalance C, Infante-Garcia C, Del Marco A, et al. Empagliflozin reduces vascular damage and cognitive impairment in a mixed murine model of Alzheimer's disease and type 2 diabetes. Alzheimer's Research & Therapy. 2020;12:40.
10. Nair A, Jayakumari C, Jabbar PK, et al. Prevalence and associations of hypothyroidism in Indian patients with type 2 diabetes mellitus. Journal of Thyroid Research. 2018;2018:5386129.
11. O'Callaghan KM, Funk C, Fariha F, et al. Serum 25-hydroxyvitamin D and intact parathyroid hormone as functional biomarkers of bone mass in early childhood. The Journal of Nutrition. 2025.
12. Rodríguez-Ortiz ME, Rodríguez M. Recent advances in understanding and managing secondary hyperparathyroidism in chronic kidney disease. F1000Research. 2020;9:F1000.
13. Rosenstock J, Vico M, Wei LI, et al. Effects of dapagliflozin, an SGLT2 inhibitor, on HbA1c, body weight, and hypoglycemia risk in patients with type 2 diabetes inadequately controlled on pioglitazone monotherapy. Diabetes Care. 2012;35:1473-8.
14. Wang DD, Zhang C, Hu K, et al. Therapeutic effect and rebound evaluation of dapagliflozin on glycated hemoglobin (HbA1c) in type 1 diabetes mellitus patients. Frontiers in Pharmacology. 2023;13:972878.
15. Wu Q, Zhang J, Zhang F, et al. SGLT2 inhibitors as metabolic modulators: beyond glycemic control in type 2 diabetes. Frontiers in Endocrinology. 2025;16:1601633.
16. Buczyńska A, Kościuszko M, Krętowski AJ, et al. Exploring the clinical utility of DPP-IV and SGLT2 inhibitors in papillary thyroid cancer: a literature review. Frontiers in Pharmacology. 2024;15:1323083.
17. Bastawy N, El-Mosallamy AE, Aljuaydi SH, et al. SGLT2 inhibitor as a potential therapeutic approach in hyperthyroidism-induced cardiopulmonary injury in rats. Pflügers Archiv-European Journal of Physiology. 2024;476:1125-43.

18. Sarode A, Deshmukh A, Chaudhari SR. Effect of antidiabetic drugs on thyroid function and vascular biomarkers. International Journal of Innovative Research in Technology. 2022;9:15253.
19. Bianco AC, da Conceição RR. The deiodinase trio and thyroid hormone signaling. Thyroid Hormone Nuclear Receptor: Methods and Protocols. 2018:67-83.
20. Sinha RA, Singh BK, Yen PM. Thyroid hormone regulation of hepatic lipid and carbohydrate metabolism. Trends in Endocrinology & Metabolism. 2014;25:538-45.
21. Savvidis C, Ragia D, Kallistrou E, et al. Critical illness-implications of non-thyroidal illness syndrome and thyroxine therapy. World Journal of Critical Care Medicine. 2025;14:102577.
22. Partsalaki I, Markantes GK, Michalaki MA. Low-glycemic load diets and thyroid function: A narrative review and future perspectives. Nutrients. 2024;16:347.
23. de Jong MA, Petrykiv SI, Laverman GD, et al. Effects of dapagliflozin on circulating markers of phosphate homeostasis. Clinical Journal of the American Society of Nephrology. 2019;14:66-73.
24. Islek T, Mirioglu S, Gursu M, et al. Short-term effects of dapagliflozin on biomarkers of bone and mineral metabolism in patients with diabetic kidney disease: A prospective observational study. Nefrologia (Engl Ed). 2024;44:868-876.
25. Mintzer S, Boppana P, Toguri J, et al. Vitamin D levels and bone turnover in epilepsy patients taking carbamazepine or oxcarbazepine. Epilepsia. 2006;47:510-5.
26. Vallon V. State-of-the-Art-Review: Mechanisms of Action of SGLT2 Inhibitors and Clinical Implications. Am J Hypertens. 2024;37:841-852.
27. O'Donoghue ML, Kato ET, Mosenzon O, et al. The efficacy and safety of dapagliflozin in women and men with type 2 diabetes mellitus. Diabetologia. 2021;64:1226-1234.
28. Maric C, Sullivan S. Estrogens and the diabetic kidney. Gender medicine. 2008;5:S103-13.
29. Abdul-Ghani MA, DeFronzo RA. Inhibition of renal glucose reabsorption: a novel strategy for achieving glucose control in type 2 diabetes mellitus. Endocr Pract. 2008;14:782-90.
30. Matsumoto S, Yoshino S, Okada S, et al. Thyroid Hormones Regulate Postprandial Glucose Metabolism by Regulating SGLT1 Expression in the Small Intestine in Rats and Mice. International Journal of Molecular Sciences. 2025;26:8854.
31. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiological Reviews. 2014;94:355-82.
32. Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Reviews in endocrine and metabolic disorders. 2017;18:153-65.
33. Boucher BJ. The problems of vitamin d insufficiency in older people. Aging and Disease. 2012;3:313.
34. Christakos S, Dhawan P, Verstuyf A, et al. Vitamin D: metabolism, molecular mechanism of action, and pleiotropic effects. Physiological Reviews. 2016;96:365-408.