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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.
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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.

Содержание:

DIFFERENTIAL ASSOCIATIONS BETWEEN PHYSICAL ACTIVITY AND GLYCEMIC CONTROL ACROSS BODY MASS INDEX IN TYPE 2 DIABETES: A COMPARATIVE ANALYSIS OF HBA1C AND FRUCTOSAMINE

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Abstract.

Background: Glycated hemoglobin (HbA1c) is the primary biomarker for assessing long-term glycemic control in type 2 diabetes (T2D). However, its wait time of 2-3 months, affects the timely intervention for the identification of acute metabolic enhancements resulting from lifestyle modifications. On the other hand, fructosamine reflects the glycemic regulation for over a period of 2-3 weeks and may provide supplementary short-term monitoring functions. Nevertheless, there is scant information comparing these markers across varying levels of physical activity and body mass index (BMI) strata in people with type 2 diabetes (T2D). **Objective:** To assess HbA1c and fructosamine as indicators of glycemic control in physically active and sedentary people with Type 2 Diabetes, and to investigate if BMI, sex, and glucose-lowering drugs influence the association between physical activity and these glycemic markers. **Methods:** This cross-sectional study was conducted at Thumbay Labs in the United Arab Emirates from January to October 2025, included 185 persons with Type 2 Diabetes (T2D), classified as physically active (n=98, engaging in ≥150 minutes of activity per week for over 3 months) or sedentary (n=87). HbA1c and fructosamine were assessed utilizing standardized laboratory techniques. Multivariable linear regression models evaluated the relationships between physical activity and glycemic indicators, controlling for age, sex, BMI, and primary glucose-lowering drug classes, while explicitly testing for interactions between Activity and BMI, as well as Activity and Sex. **Results:** Physically active participants exhibited lower HbA1c (6.84% vs. 8.07%, $p<0.0001$) and fructosamine levels (301.0 vs. 362.0 µmol/L, $p=0.0001$) compared to sedentary individuals. A significant Activity × BMI interaction for HbA1c ($\beta=0.156$, $p=0.0002$) was found, indicating decreased glycemic benefits of physical activity with higher BMI, persisting after controlling for diabetes medications. A similar but weaker effect for fructosamine ($\beta=7.481$, $p=0.0019$) was noted. No notable differences were observed between sexes regarding these markers when BMI was considered. **Conclusions:** Physical activity is associated with glycemic control, which is supported by HbA1c and fructosamine levels, even though obesity declines this effect, especially in long-term glycemic memory (HbA1c). Individuals who fall under the T2D and increased BMI category need stronger lifestyle interventions for similar glycemic benefits as those with lower BMI. HbA1c is a more reliable marker for activity-related metabolic benefits in stable T2D, while fructosamine is a useful short-term indicator but not interchangeable.

Key words. Body mass index, fructosamine, HbA1c, glycemic control Type 2 diabetes and physical activity.

Introduction.

Type 2 Diabetes (T2D) affects around 500 million adults worldwide and this statistic is said to rise with aging populations in unison with global obesity [1,2]. Tight glucose management minimizes the incidence of microvascular and, to a lesser extent, macrovascular problems [3,4]. Recent observational study demonstrated that higher HbA1c was associated with increased microvascular and macrovascular complications, reinforcing the link between chronic hyperglycemia and adverse outcomes [5]. Glycated hemoglobin (HbA1c) remains the cornerstone biomarker for long-term glycemic control and risk stratification, and its measurement is crucial for current treatment targets in international guidelines [3]. Although HbA1c is recognized as a marker of glycemic control for a period of 2-3 months, it is still influenced by factors that affect erythrocyte turnover, such as anemia, chronic renal illness, hemoglobinopathies, and recent transfusions, which may limit its trustworthiness in some clinical contexts [6].

An alternative to the conventional HbA1c, the short-term glycemic indicators, such as fructosamine and glycated albumin have sparked interest as supplementary techniques globally. These biomarkers detect glycation of circulating proteins with a half-life of 2-3 weeks and may respond faster to therapeutic modifications than that of HbA1c [6,7]. Several studies have found moderate to high relationships between fructosamine, glycated albumin, and HbA1c, implying that they predict microvascular and macrovascular outcomes in diabetic patients [6,7]. However, limited clinical data exists comparing HbA1c and fructosamine across obesity, physical activity, and pharmacologic therapy in T2D populations.

Lifestyle modifications that are primarily focused on increasing physical activity, regular exercise training, along with proper medication, serve as a prime element for T2D management [3,8-9]. Regular aerobic and resistance exercise uplifts cardiorespiratory fitness, reduces body weight, and lowers HbA1c levels in T2D patients [8]. According to professional society standards, people with T2D should keep themselves occupied with at least 150 minutes pf moderate to vigorous aerobic activity, along with 2-3 days of resistance training every week [9]. On the other hand, the glycemic response to physical activity varies among different populations. Some people show significant decrease in their HbA1c levels corresponding to their physical activity, while others see minimal change despite identical exercise exposure. Emerging data suggests that obesity, gender, baseline fitness, and prescription regimes may influence the metabolic advantages of physical activity [8-10], but few research have systematically modeled these associations across both HbA1c and fructosamine.

Globally, obesity is recognized as primary contributing factor for insulin resistance and T2D [1,2]. A higher Body Mass Index (BMI) and central adiposity are responsible for poor glycemic profiles and higher cardiovascular risk. They may counteract with the insulin sensitivity improvements generally caused by exercise [10]. Corresponding to all this, the fat distributions, hormonal milieus and cardiometabolic risk varies between women and men, this may in turn influence their diabetes risk and treatment response [10]. To attain HbA1c targets, modern diabetes care increasingly relies on combination therapy, including Metformin, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, insulin, and other medications [3]. These medicines affect glycemia through distinct mechanisms, and patterns of drug use frequently correlate with BMI, disease duration, and comorbidity burden, making it necessary to account for pharmacotherapy when analyzing the independent effect of physical activity.

Against this backdrop, we sought to describe the connections between physical activity, BMI, sex, medicines, and glycemic control in persons with T2D, using both HbA1c and fructosamine as outcomes. We modeled the relationship between physical activity, HbA1c, and fructosamine across the BMI spectrum, testing for Activity × BMI and Activity × sex interactions while adjusting for major glucose-lowering medication classes.

Materials and Methods.

This cross-sectional study took place at Thumbay Labs in the United Arab Emirates from January to October 2025. A total of 185 patients with type 2 diabetes were categorized into sedentary (87) and active (98) groups according to their physical activity levels, defined as at least 150 minutes per week for over three months. Exclusion criteria encompassed type 1 diabetes, insulin therapy, suspected Latent Autoimmune Diabetes in Adults (LADA), prediabetes, other comorbidities, surgical disabilities, and thyroid disorders. Participants filled out a structured International Physical Activity questionnaire (IPAQ) that captured the type, frequency and duration of their physical activity to categorize them accordingly. Height and weight were assessed using standardized protocols, and body mass index (BMI) was computed (kg/m²). EDTA whole blood and serum samples were collected from participants. HbA1c levels were measured using the Beckman Coulter DXC 700 analyzer, employing enzymatic and latex agglutination inhibition methods. Fructosamine was quantified via a colorimetric method using the Cobas c 503 Roche instrument.

All procedures were validated in accordance with the guidelines established by the College of American Pathologists (CAP). Quality controls, both internal and external, were established, and calibration was conducted according to manufacturer specifications. The Institutional Review Board approved the study (Ref. No. IRB-COHS-STD-131-Dec-2024). All participants provided written informed consent; data were anonymized and securely stored.

Data analysis utilized IBM® SPSS® Statistics Version 30.0. Continuous variables were reported as median and interquartile range (IQR) because the data did not follow a normal distribution. The Mann-Whitney U test was utilized to compare cardiometabolic markers between active and sedentary groups. Multivariable linear regression models assessed associations between physical activity and glycemic markers, adjusting for age, sex, BMI, and major glucose-lowering medication classes, with explicit testing of Activity × BMI and Activity × Sex interactions. A p-value below 0.05 is deemed statistically significant, whereas a p-value below 0.001 is classified as highly significant.

Results.

The active group represented over 50% of the cohort, generally being younger and having a lower BMI compared to sedentary participants, who were predominantly middle-aged with more individuals aged 60 and older. Normally-weight and overweight categories were more common among active individuals, whereas higher obesity classes were found predominantly in the sedentary group. These patterns indicate significant demographic and anthropometric differences between activity groups that may influence glycemic outcomes (Figure1).

HbA1c and fructosamine levels were markedly elevated in sedentary participants relative to their active counterparts (Mann–Whitney U, $p < 0.001$), with rank-biserial correlations reflecting moderate to substantial effects (Table 1).

When categorized by gender, age group, and BMI category, people who were physically active usually had lower HbA1c and fructosamine levels than people who were not. The activity effect was strongest in men, adults aged 18 to 59, and people with a normal or overweight BMI. The rank biserial effect sizes were moderate to large. In older participants (60 years and older) and those with the highest BMI, differences by exercise were less and not statistically significant. This could be because these groups had less power and more advanced disease (Table 2).

Both HbA1c and fructosamine are significantly lower in active vs sedentary men. Effect sizes (rank-biserial r) are moderate-

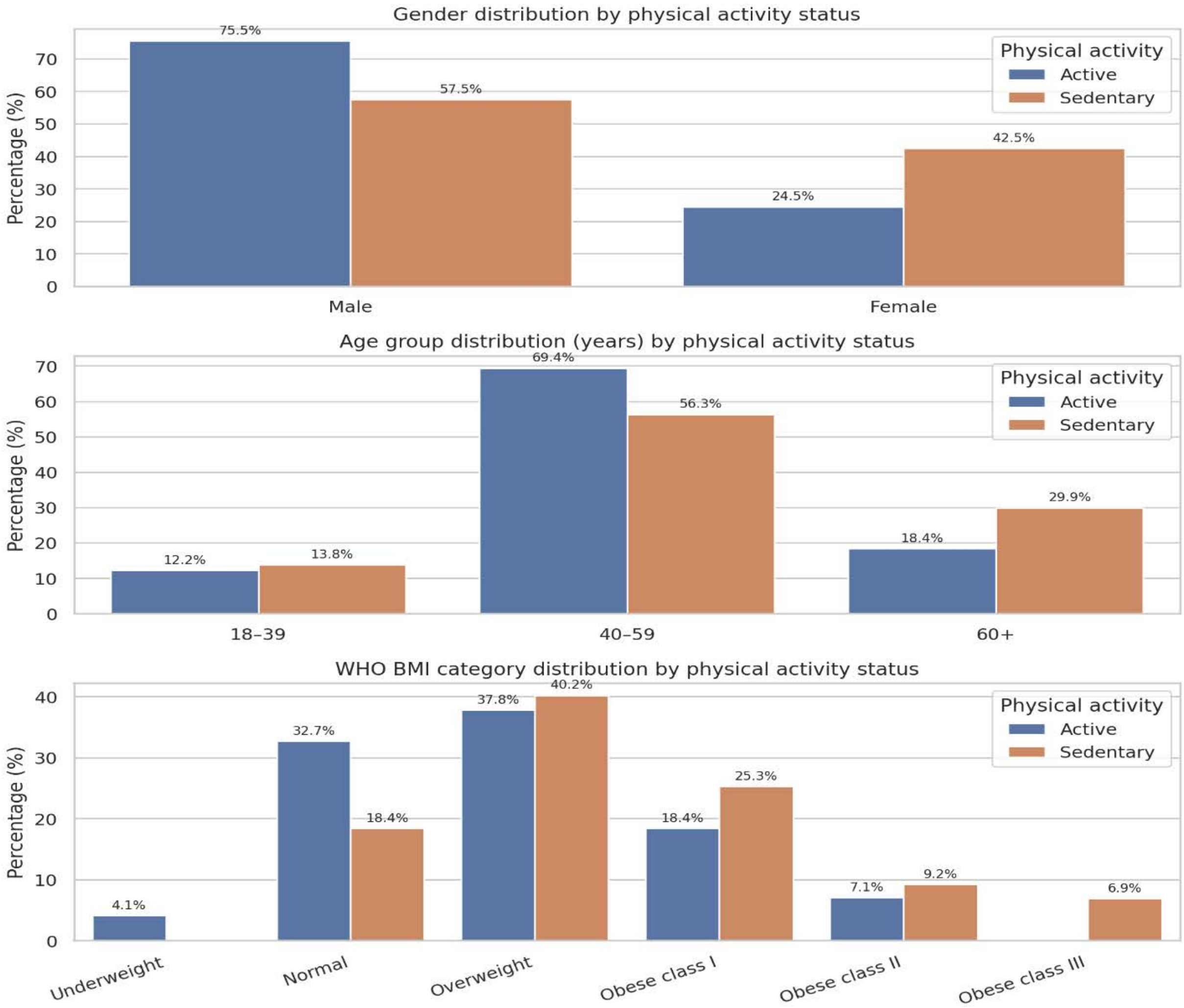

Figure 1. *The distribution of gender, age groups, and WHO BMI categories based on physical activity status among patients with type 2 diabetes (N = 185). The bars show the percentage of participants in each category who are considered physically active or sedentary. The percentages are shown above each bar.*

Table 1. *HbA1c and fructosamine by physical activity status (Active vs Sedentary).*

Marker	Active, median [IQR]	Sedentary, median [IQR]	p-value	Rank-biserial r
HbA1c	6.84 [6.49–8.04]	8.07 [7.14–9.61]	0.0000	0.422
fructosamine	301.0 [269.5–369.75]	362.0 [319.25–405.75]	0.0001	0.331

Median [IQR], (Mann–Whitney U), Rank-biserial r tests was used, P.value < 0.05 is considered significant, P.value < 0.001 is considered highly significant.

to-large, meaning activity is meaningfully associated with better glycemic control in men, not just statistically different. For women, sample sizes or differences were not strong enough to reach p < 0.05 in this stratified test. The beneficial effect of being active on both HbA1c and fructosamine is especially clear in men.

For those aged 18 to 39, HbA1c was much lower in active people than in sedentary people. fructosamine showed a similar tendency, although it wasn't statistically significant at 0.05. The effect size for HbA1c is big, which means that activity has a strong influence on younger adults.

In the 40–59 years age range, both HbA1c and fructosamine levels are significantly lower in active participants, with effect sizes ranging from moderate to large, indicating a strong activity effect in middle-aged adults.

In the 60+ years cohort, neither HbA1c nor fructosamine variations by exercise achieved statistical significance (p < 0.05). The sample size is probably smaller and/or the effect is weaker at older ages. There is a clear link between physical exercise and better HbA1c (and often fructosamine) levels in younger and middle-aged people. The link is not as clear in people over 60.

In the Normal BMI group, both HbA1c and fructosamine levels are considerably lower in those who are active compared to those who are sedentary. The impact sizes are quite big, which means that activity has a strong influence when BMI is in the normal range.

In the overweight group, active participants have considerably lower levels of both HbA1c and fructosamine. Effect sizes are modest to big, and it's evident that being active helps overweight people with their glycemic indicators.

In Obese class I, HbA1c is much lower in people who are active than in people who are sedentary (moderate effect size). The variations in fructosamine go in the same direction, although they don't quite reach $p < 0.05$.

In Obese class II / III, there are no statistically significant changes by exercise (and small n), thus we can't claim for sure that there is an effect in this dataset. The most significant and consistent advantage of physical activity on both HbA1c and fructosamine is observed in individuals with normal and overweight BMI, with a moderate benefit noted for those classified as obese class I. The evidence is less strong in this sample for higher obesity classes (because the numbers are modest) (Table 3).

Table 2. *Stratified comparison of HbA1c and fructosamine by physical activity status.*

Subgroup type	Subgroup	Marker	Active median [IQR]	Sedentary median [IQR]	p-value
Age groups	18–39	fructosamine	320.5 [250.0–384.25]	352.0 [298.75–399.0]	0.2722
		HbA1c	7.52 [6.69–8.5]	10.0 [8.22–10.5]	0.0158
	40–59	fructosamine	290.5 [263.5–353.0]	361.5 [321.5–434.25]	0.0006
		HbA1c	6.71 [6.41–7.74]	8.07 [7.14–10.4]	0.0
	60+	fructosamine	328.5 [281.75–390.75]	363.0 [321.5–390.25]	0.2568
		HbA1c	6.84 [6.71–8.43]	7.57 [6.98–8.56]	0.1553
BMI groups	Normal	fructosamine	333.5 [282.75–369.0]	389.0 [339.75–492.75]	0.0049
	Normal	HbA1c	6.71 [6.41–8.04]	8.56 [8.06–9.92]	0.0004
	Obese class I	fructosamine	260.5 [243.25–328.5]	336.0 [296.0–398.5]	0.0665
	Obese class I	HbA1c	6.71 [6.52–7.35]	7.77 [6.98–8.8]	0.0426
	Obese class II	fructosamine	509.0 [362.0–539.0]	359.0 [344.5–393.75]	0.2022
	Obese class II	HbA1c	9.34 [7.54–12.05]	7.78 [7.29–7.98]	0.1176
	Overweight	fructosamine	288.0 [274.0–367.0]	363.0 [326.75–419.0]	0.0009
	Overweight	HbA1c	7.07 [6.56–7.6]	8.5 [7.38–10.5]	0.0002
Gender	Female	fructosamine	305.5 [274.75–363.5]	349.0 [309.0–402.0]	0.1302
		HbA1c	7.07 [6.64–8.32]	7.55 [7.1–9.5]	0.2287
	Male	fructosamine	297.5 [259.0–369.75]	364.0 [329.0–423.0]	0.0002
	Male	HbA1c	6.75 [6.49–7.7]	8.17 [7.57–9.51]	0.0

Median [IQR], (Mann–Whitney U) test was used, P.value < 0.05 is considered significant, P.value < 0.001 is considered highly significant.

Table 3. *Multivariable linear regression with interaction terms for HbA1c and fructosamine.*

Outcome	Predictor	Beta	SE	t	p-value
HbA1c	Intercept	8.82	0.284	31.06	< 0.001
	Active vs. Sedentary	-0.963	0.43	-2.24	0.0263
	Male vs. Female	-0.274	0.357	-0.77	0.4433
	Age (centered)	-0.033	0.015	-2.23	0.0269
	BMI (centered)	-0.085	0.029	-2.99	0.0032
	Activity × Gender	-0.017	0.536	-0.03	0.9744
	Activity ×_Age	0.036	0.023	1.52	0.1296
	Activity ×_BMI	0.156	0.042	3.76	0.0002
	Model R^2	0.186			
fructosamine	Intercept	379.591	16.252	23.36	< 0.001
	Active vs. Sedentary	-35.354	24.596	-1.44	0.1524
	Male vs. Female	-3.24	20.419	-0.16	0.8741
	Age (centered)	-0.27	0.841	-0.32	0.7488
	BMI (centered)	-4.673	1.631	-2.86	0.0047
	Activity × Gender	-9.129	30.681	-0.3	0.7664
	Activity ×_Age	1.361	1.337	1.02	0.3098
	Activity ×_BMI	7.481	2.376	3.15	0.0019
	Model R^2	0.124			

Beta = regression coefficient (predicted change in outcome per unit increase in predictor) - SE = standard error (precision of the beta estimate) - t = t-statistic (Beta/SE), used to calculate p-value. Age (centered) and BMI (centered) were calculated by subtracting the sample mean from each individual value. This centering allows the intercept to represent the predicted outcome for an average participant and facilitates interpretation of interaction terms.

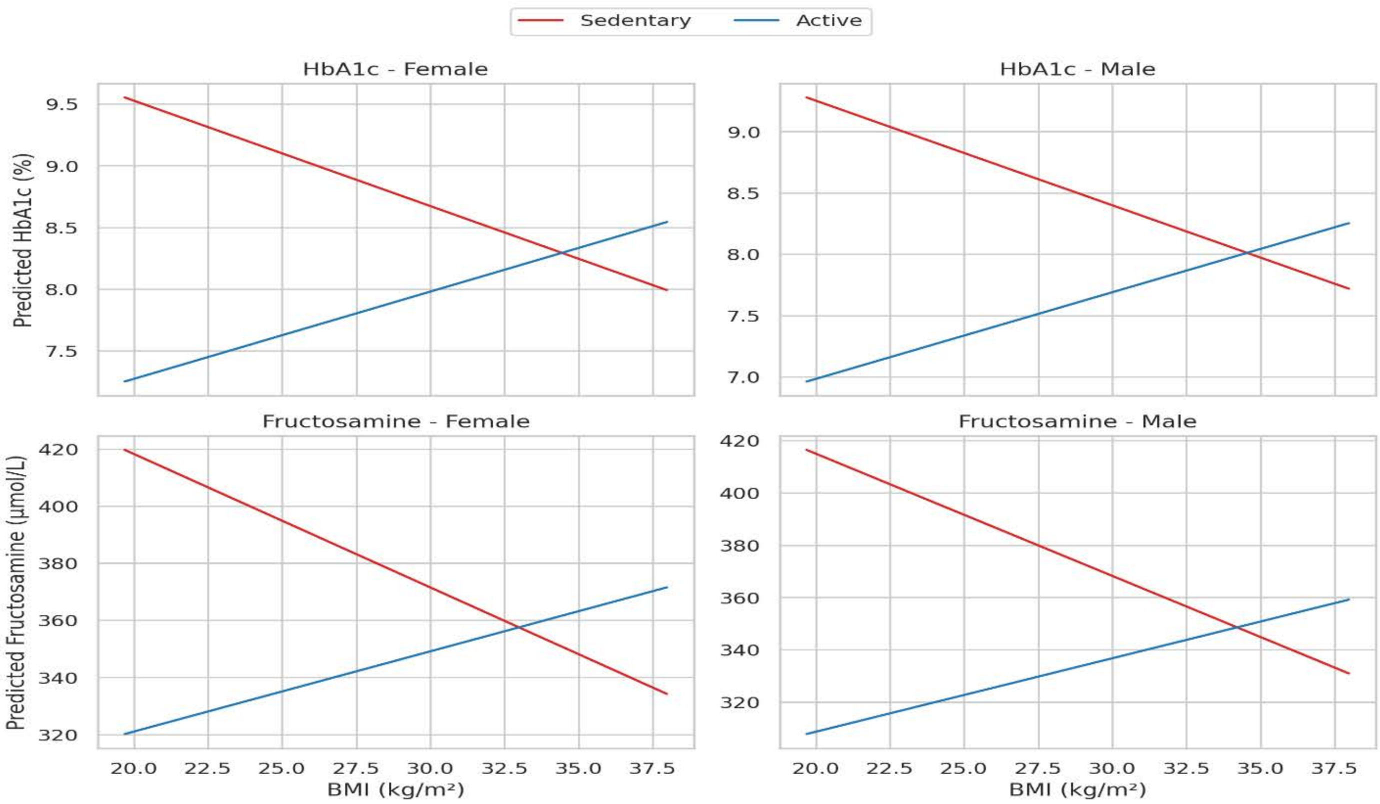

Figure 2. Predicted HbA1c and fructosamine across BMI by physical activity and sex. *Panels illustrate predicted levels of HbA1c (%) (top) and fructosamine (µmol/L) (bottom) across BMI for women (left) and men (right). Curves distinguish between sedentary (red) and physically active (blue) individuals, based on multivariable linear regression models that account for physical activity, gender, age, and BMI interactions. Models center age and BMI at the cohort mean for plotting purposes.*

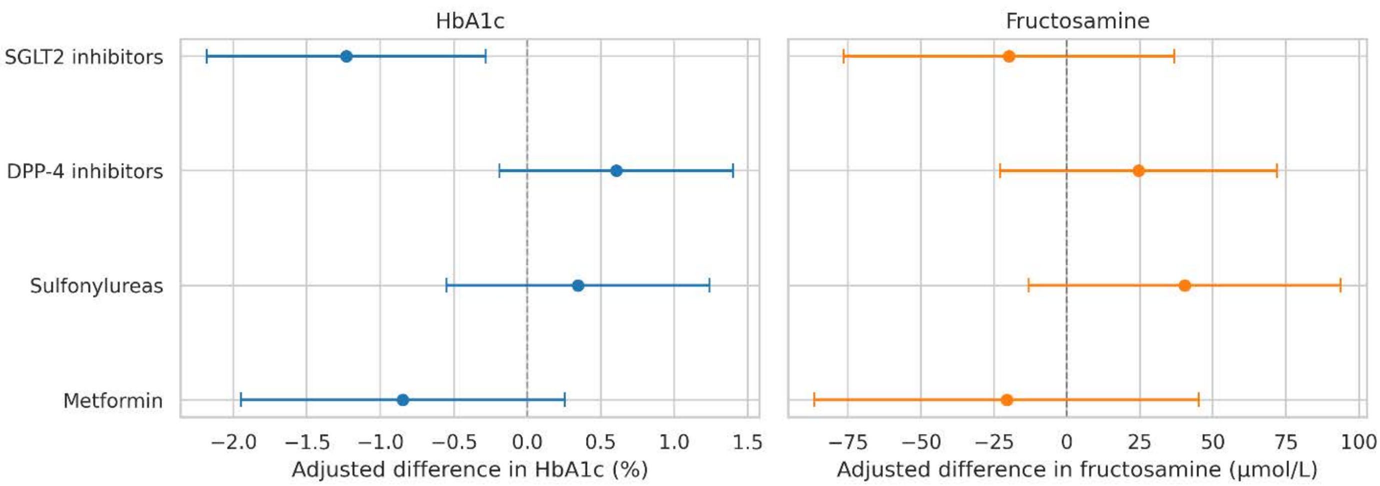

Figure 3. Adjusted associations between glucose lowering medication classes and HbA1c and fructosamine.
Forest plots show adjusted differences in HbA1c (left, %) and fructosamine (right, µmol/L) associated with current use of Metformin, sulfonylureas, DPP 4 inhibitors and SGLT2 inhibitors, compared with nonuse of each class. Estimates and 95% confidence intervals are from multivariable linear regression models adjusted for age, sex, BMI, physical activity, and their interaction. Participants treated with insulin were excluded from these analyses.

In multivariable models controlled for age, sex, and BMI, physical activity correlated with reduced projected HbA1c and fructosamine levels across the BMI spectrum. The top row of Figure 3 shows model-based prediction curves for HbA1c, and the bottom row shows model-based prediction curves for fructosamine. The curves are separated by sex, with women on the left and men on the right.

For HbA1c, both physically active women and men exhibited lower projected values compared to their sedentary counterparts across nearly all BMI categories. The gap between the active and sedentary curves was biggest at lower BMI and got smaller as BMI went up. This shows the strong Activity× BMI interaction that was seen in the HbA1c model. This pattern was consistent across both women and men, showing no definitive evidence of a sex-specific variation in the shape or amount of the exercise effect.

For fructosamine, physically active individuals exhibited lower projected values compared to sedentary individuals of both sexes; however, the curves were more closely aligned and parallel across the BMI range. In line with this visual impression, the Activity × BMI interaction for fructosamine did not achieve statistical significance, suggesting that the short-term glycemic fluctuation measured by fructosamine exhibited a weaker and less consistent alteration by BMI compared to HbA1c (Figure 2).

Metformin and SGLT2 inhibitors were linked to reduced adjusted HbA1c levels, while sulfonylureas and DPP-4 inhibitors were generally associated with increased HbA1c levels. The associations for fructosamine exhibited a similar direction; however, the confidence intervals were broader and frequently encompassed the null value. Adjustment for these medication classes did not significantly change the observed relationships between physical activity, BMI, and glycemic markers (Figure 3).

Discussion.

This cross-sectional study of patients with type 2 diabetes revealed that frequent physical activity was associated with lower levels of HbA1c and fructosamine, even after accounting for age, gender, BMI, and major classes of glucose-lowering medicines. Prediction plots from interaction models demonstrated that physically active adults had lower projected HbA1c levels than sedentary participants over the majority of the BMI range, in both men and women.

The disparity between active and sedentary curves was most pronounced at lower BMI and gradually diminished with rising BMI, signifying a notable Activity × BMI interaction. This pattern continued even after adjusting for treatment with Metformin, sulfonylureas, DPP-4 inhibitors, and SGLT2 inhibitors, indicating that adiposity itself, rather than varying intensification of pharmacotherapy, may diminish the glycemic advantages of physical activity. The association between fructosamine and activity was analogous; however, the Activity × BMI interaction did not achieve statistical significance, and the curves were more closely aligned, suggesting that short-term glycemic fluctuations may exhibit reduced responsiveness—or greater variability—in relation to habitual physical activity within this real-world T2D cohort.

Our results align with previous meta-analyses and guidelines indicating that consistent aerobic and resistance training yield moderate although clinically significant decreases in HbA1c levels among individuals with T2D [8–9]. By explicitly modeling Activity × BMI interactions, we enhance the existing evidence by illustrating that the relative HbA1c advantage of physical activity is most pronounced in persons with lower BMI and diminished in those with higher BMI. This conclusion is biologically plausible: increased adiposity correlates with heightened insulin resistance, ectopic fat deposition, and chronic low-grade inflammation [10], all of which may attenuate the enhancement in insulin sensitivity attained by typical physical activity levels. Our findings thus advocate a more nuanced perspective than the simplistic assertion that "exercise is beneficial for all." While both lean and obese individuals with T2D derive advantages from physical activity, those with obesity may necessitate either an increased exercise regimen or a combination of approaches—such as organized exercise alongside dietary weight reduction or supplementary pharmacotherapy—to attain glycemic enhancements akin to those observed in individuals with a lower BMI.

Sex-stratified predictions indicated comparable patterns between women and men, revealing no significant sex-specific divergence in the Activity × BMI effect on HbA1c. This is consistent with certain aspects of existing literature regarding sex differences in the pathophysiology and treatment response of Type 2 Diabetes (T2D). Women with type 2 diabetes frequently exhibit elevated obesity rates and may receive a diagnosis later in the progression of the disease, resulting in an increased relative cardiovascular risk in comparison to men [10]. Our data indicate that, after adjusting for BMI and medications, the additional glycemic benefit of physical activity is similar for both sexes. This observation aligns with existing guideline recommendations advocating for equal promotion of physical activity for both women and men with T2D [3,9]. It underscores the necessity of customizing interventions based on individual BMI and comorbidity profiles, rather than focusing solely on sex.

The discrepancy observed between HbA1c and fructosamine responses to physical activity is significant. Physically active participants exhibited lower fructosamine levels compared to sedentary participants; however, the observed effects were minimal, and a significant Activity × BMI interaction was not identified. Previous studies indicate that fructosamine and glycated albumin are correlated with HbA1c and reflect short-term glycemic changes; however, their accuracy may be affected by variables including serum albumin levels, nephrotic-range protein loss, and acute illness [6,7].

Medication classes exhibit specific patterns of glycemic control that align with their anticipated clinical applications. Metformin and SGLT2 inhibitors demonstrate superior glycemic profiles, while sulfonylureas and DPP-4 inhibitors are more prevalent in individuals with suboptimal control, indicating a trend towards treatment intensification. Nevertheless, the broad confidence intervals, especially for fructosamine, suggest a constrained ability to accurately quantify these effects. The primary relationship among physical activity, adiposity, and glycemia persisted significantly after controlling for medication class, indicating the lifestyle factor's independence from pharmacological interventions.

In this clinical cohort, day-to-day variability in diet, medication adherence, and acute health events may have introduced noise into fructosamine measurements, thereby obscuring more subtle patterns related to activity and BMI. Alternatively, the adaptation to habitual activity, particularly resistance training, may be more accurately reflected by long-term markers like HbA1c rather than a brief two-to-three-week assessment of glycation. Our findings support the ongoing use of HbA1c as the primary metric for assessing lifestyle interventions in stable T2D, while fructosamine functions as a complementary, albeit non-interchangeable, marker.

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Conflict of interest.

The authors declare that there is no conflict of interest.

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