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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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ALLOPURINOL TREATMENT IMPROVES INSULIN RESISTANCE IN NON-DIABETIC PATIENTS WITH RENAL STONE

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Abstract.

Hyperuricemia is an objective risk factor of derangement of fasting serum glucose and type 2 diabetes (T2D), yet whether hyperuricemia has a causative influence on insulin resistance is still debatable. In this study, we tested the hypothesis that lowering uric acid in hyperuricemic nondiabetic subjects might improve insulin resistance. Patients with renal stone and hyperuricemia (n=15) were recruited from the private clinic of Ib-Sina Local Teaching Hospital in Mosul city and prospectively placed on allopurinol (300mg/day) for 6 months. Serum uric acid (SUA), fasting serum glucose (FSG), fasting insulin, and C-peptide were measured using commercial kits. Results confirmed that allopurinol has significantly ($P<0.05$) reduced c-peptide and insulin together with a non-significant ($p>0.05$) reduction of serum glucose levels. In conclusion, allopurinol has improved insulin level and glycemic control in a healthy individual, these findings could be used as a template for using allopurinol in diabetic patients to improve glycemic control or future studies could be directed toward structural modification of allopurinol which hopefully might lead to innovation of new antidiabetic drugs.

Key words. Uric acid, hyperuricemia, allopurinol, insulin, c-peptide, glucose.

Introduction.

The human body metabolizes food into various components to produce ATP at the end [1]. During this complicated processing, various byproducts were formed, some of which are harmful, such as uric acid, and need continuous removal from the body to avoid its toxicity [2,3]. As a part of our daily food, nucleic acids are metabolized to purines, and the latter were oxidized to uric acids which will continuously be removed through kidney excretion [1]. Failure of removal of uric acid might be associated with renal crystals or might proceed to a kidney stone. Accumulation in other body compartments might jeopardize tissue normal functionality or perturb cellular activity; the condition is known as hyperuricemia or gout [2].

Epidemiological studies have confirmed that hyperuricemia is common in the general population and accounts for up to 10-25% of the overall population; recent reports confirmed a higher prevalence rate in the general population due to inactive lifestyles. The seriousness of uric acid accumulation lay on the idea that hyperuricemia is a stand-alone menace factor for metabolic syndrome, diabetes, cardiovascular diseases, renal dysfunction, thyroid disorders, and hyperlipidemia [1,2,4]. Despite that, controversy exists in this study due to the lack of a clear mechanism of association together with the limitation of these reports because some of them has linked such correlation to the ethnicity/gender differences [5-9].

Various inconclusive studies have been piloted in this area to identify the link between diabetes and hyperuricemia. Some of these studies concluded that diabetes is inversely associated with hyperuricemia [10-14]. Conversely, some others confirmed that hyperuricemia positively conjoined with diabetes [15-18]. Alternatively, the third group of researchers reported no association between hyperuricemia and diabetes at all [19,20]. The justification become more complicated when the study was conducted in health or prediabetes patients because the outcome revealed a positive association between hyperuricemia and diabetes in such cases and conditions [13,18].

The discrepant results could be explained in the context of interindividual variations. A study accomplished on the Chinese [21] and British [2] population stated that the diabetic population revealed a lower menace for gout development. Similarly, some studies have reported an inverse correlation between serum glucose level and uric acid levels [10,13,14]. Conversely, some other studies reported no correlation between serum glycemic control and serum uric acid levels [19,20]. Hence, we hereby conducted this research to describe the relationship between glycemic control in apparently healthy patients with renal stones using allopurinol as a model for modulation of serum uric acid level.

Materials and Methods.

The sample enrolled in our study included fifteen patients (9 male; 6 females; 39.41±3.8 years old) with renal stones treated with allopurinol (300 mg/day) for 6 months. All patients were informed about their involvement in the study and the consent form was signed and recorded. Patients enrolled in the study were non-smokers, non-alcoholic, free from all chronic diseases, and they were not using any medication except allopurinol. No pregnant or lactating mothers have participated in the study. Blood withdrawn and serum separated before allopurinol and after 6 months of continuous therapy. Collected serum samples were frozen until ready for analysis.

Fasting serum glucose was quantified by colorimetric technique exploiting using a kit provided by Thermo-Fisher Scientific (EIAGLUC). The idea of the test is relied on the oxidation of glucose-by-glucose oxidase enzyme piloting to the production of equimolar concentration of colorless hydrogen peroxide which in the usage of horseradish peroxidase altered to an equimolar colored compound to be quantified spectrophotometrically at a wavelength of 560 nm.

Fasting serum glucose was quantified by a colorimetric technique, which exploits the use of a kit provided by Thermo-Fisher Scientific (EIAGLUC). This technique involves the oxidation of glucose-by-glucose oxidase enzyme, which leads to the production of equimolar concentrations of colorless hydrogen

peroxide. The hydrogen peroxide is then used in conjunction with horseradish peroxidase to create an equimolar colored compound, which can be quantified spectrophotometrically at a wavelength of 560 nm. This process is highly accurate and provides a precise measurement of fasting serum glucose levels, which is essential in the diagnosis and treatment of diabetes. The Thermo-Fisher Scientific kit is widely used in clinical settings and research laboratories due to its reliability and ease of use. Overall, this colorimetric technique is a valuable tool in the field of diabetes management and research, and the Thermo-Fisher Scientific kit has been instrumental in advancing our understanding of this disease.

The principle of measurement of insulin was based on Sandwich ELISA Technique using a kit supplied by COBAS (12017547, Roche) for insulin and (98126) for c-peptide, which includes two incubation periods and interaction with the reaction mixture, according to manufacturer instructions. Followed by aspiration of reaction mixture the chemiluminescent emission quantified by a photomultiplier.

The principle of measurement of insulin is based on the Sandwich ELISA Technique, which is a sensitive and specific method for detecting and quantifying proteins in biological samples. The kit supplied by COBAS (12017547, Roche) for insulin and (98126) for c-peptide. The Sandwich ELISA Technique involves two antibodies that recognize different epitopes on the insulin molecule. The first antibody is immobilized on a solid support, such as a microplate, and captures the insulin in the sample. The second antibody, which is conjugated to an enzyme, binds to a different epitope on the insulin molecule and forms a sandwich with the first antibody. The enzyme catalyzes a reaction that produces a detectable signal, such as chemiluminescence, fluorescence, or color change. The COBAS kit for insulin and c-peptide includes two incubation periods and interaction with the reaction mixture, according to the manufacturer's instructions. The first incubation is with the sample containing insulin, which allows the insulin to bind to the first antibody on the microplate. The second incubation is with the second antibody conjugated to the enzyme, which forms a sandwich with the insulin bound to the first antibody. The chemiluminescent emission produced by the enzyme is quantified by a photomultiplier, which converts the light signal to an electrical signal that can be measured and recorded.

The results were outlined and statistically analyzed using Prism (GraphPad USA V.6). Data expressed as mean and standard deviation. The differences were considered significant when $p<0.05$.

Results.

Following analysis of serum samples using specified kits. The results were analyzed and plotted together to show the difference. The outcome confirmed that serum uric acid has significantly ($p<0.05$) reduced after allopurinol therapy compared to before therapy (Figure 1A). To confirm that the renal system is functioning normal albumin was measured and the results substantiated non-significant ($p>0.05$) differences between before and after allopurinol therapy. Allopurinol has significantly ($p<0.05$) moderated both c-peptide and insulin rivalled to baseline concentration (Figure 1 B and D). Despite these changes fasting serum glucose showed a slight reduction ($p>0.05$) after allopurinol use contrasted to baseline concentration (Figure 1 C).

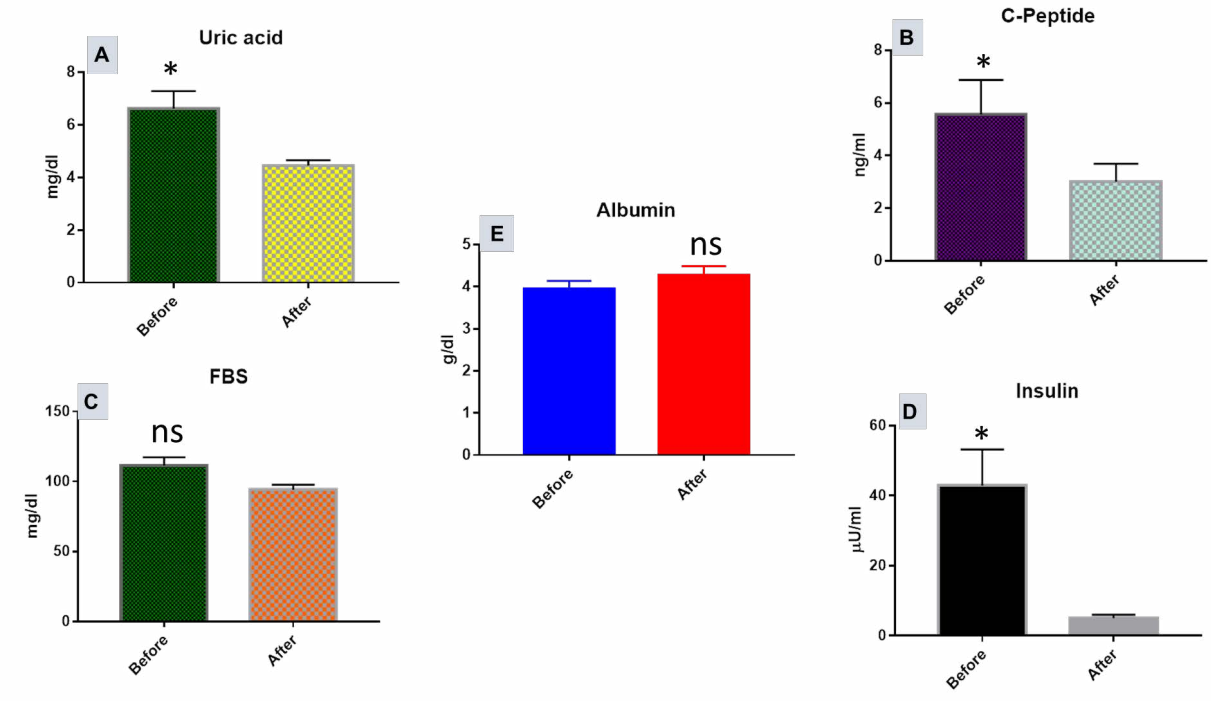

Figure 1. *Glycemic parameters in the allopurinol-treated patient before and after therapy. *p<0.05 as compared to after allopurinol therapy. Ns=non-significant.*

Discussion.

The current study was designed to look at the link across SUA and glycemic control parameters levels in non-diabetic subjects. The results confirmed that reduction of serum uric acids has been associated with a slight reduction of FBS and a significant reduction of insulin and c-peptide levels. However, albumin has slightly non-significantly elevated.

Certain investigations have identified a link between diabetes and SUA [15-18], however, in a 16-year follow-up study of Japanese people, uric acid was found to be unrelated to an increase in the chance of T2D [19]. New research in diabetic people in India reported no significant connection between SUA and FBG [20]. Other research has found an inverse association or a reduction in SUA levels in diabetics [21,22]. In different studies using male participants only, for example, a negative and significant relationship between SUA and FBG has been documented [23]. In another survey study, respondents found that SUA concentrations were inversely linked with T2D [10]. Other research [11-14], has testified no connotation between diabetes and SUA, which contrasts the current study findings.

Earlier research may have found some explanations for the reported affirmative link between diabetes and SUA. Preceding research, for example, related the connection of uric acid and diabetes mellitus to demographic groupings and gender, and the results were inconsistent. Additionally, these finding are of low impact and reliability due to their confounding insults of limited data, comprising either male or female participants, aged people, or subjects chosen from a subset of the overall population. We believe that, in addition to the recognized influencing factors, personal dietary choices, lifestyle parameters, genetic traits, and exogenous influences may have an impact on the context between diabetes and SUA in various demographic groups [5-9].

The low uric acid content in plasma may be due to the uricosuria impact of glucose on uric acid, which may alter uric acid excretion and reabsorption from the renal system. In other words, glucose may interfere with the process of eliminating uric acid from the body [24,25]. The actual mechanism by which uric acid is eliminated from the body is unknown [26,27]. However, researchers have theorized that 100% of uric acid is filtered in the glomerulus to the renal tubules, with approximately 80% of the filtration burden recycled back [28]. This means that a significant portion of uric acid is recycled back by the proximal tubules via urate or anion exchangers and voltage-sensitive urate channels. The process of recycling uric acid helps to maintain the normal levels of uric acid in the body [29-32].

The association at the molecular level could be explained in the kinetic context. To explain that there might be a competition between uric acid and glucose in the proximal renal tubules for reabsorption, because blood glucose and uric acid are both reabsorbed at the same location in the kidney, blood sugar levels may influence uric acid reabsorption [14,33]. Additionally, renal handling of uric acid can be impacted by numerous inorganic and organic ions, as well as glucose, resulting in decreased reabsorption and increased excretion of uric acid [34,35].

The limitation of our study is based on the small sample size, patient diets cannot be controlled, their prediabetes history is unclear, nevertheless, this study could give a clear idea about the future direction of allopurinol indication in subjects with impaired glucose tolerance tests.

Conclusion.

Allopurinol imparts a reduced insulin level in a participant without robust glucose level modulation. These effects could highlight the effect of allopurinol and structurally could be used as a template for the discovery of new antidiabetic drugs.

REFERENCES

1. Miolski J, Ješić M, Kovačević S, et al. Diabetic ketoacidosis: Our experiences. Medicinski časopis. 2021;55:71-4.
2. Remedios C, Shah M, Bhasker AG, et al. Hyperuricemia: a reality in the Indian obese. Obesity surgery. 2012;22:945-8.
3. Glantzounis GK, Tsimoyiannis EC, Kappas AM, et al. Uric acid and oxidative stress. Current pharmaceutical design. 2005;11:4145-51.
4. Faisal IM, Merkhan MM, Almukhtar HM. Effect of chronic Allopurinol therapy on Thyroid function in patients with urate stones. Journal of Advanced Pharmacy Education & Research. 2020;10:5.
5. Ali N, Rahman S, Islam S, et al. The relationship between serum uric acid and lipid profile in Bangladeshi adults. BMC cardiovascular disorders. 2019;19:1-7.
6. Wang S, Shu Z, Tao Q, et al. Uric acid and incident chronic kidney disease in a large health check-up population in Taiwan. Nephrology. 2011;16:767-76.
7. Shankar A, Klein R, Klein BE, et al. The association between serum uric acid level and long-term incidence of hypertension: population-based cohort study. Journal of human hypertension. 2006;20:937-45.
8. Chang CC, Wu CH, Liu LK, et al. Association between serum uric acid and cardiovascular risk in nonhypertensive and nondiabetic individuals: The Taiwan I-Lan Longitudinal Aging Study. Scientific Reports. 2018;8:1-6.
9. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. New England Journal of Medicine. 2008;359:1811-21.
10. Bandaru P, Shankar A. Association between serum uric acid levels and diabetes mellitus. International journal of endocrinology. 2011;2011.
11. Bonakdaran S, Kharaqani B. Association of serum uric acid and metabolic syndrome in type 2 diabetes. Current diabetes reviews. 2014;10:113-7.
12. Oda E, Kawai R, Sukumaran V, et al. Uric acid is positively associated with metabolic syndrome but negatively associated with diabetes in Japanese men. Internal medicine. 2009;48:1785-91.
13. Rabari K, Samadhiya A, Saha S, et al. A study to assess serum uric acid level and its association with glycemic parameters in individuals with prediabetes and diabetes mellitus in a North Indian tertiary care hospital. Yuva J Med Sci. 2018;4:12-8.
14. Nan H, Dong Y, Gao W, et al. Diabetes associated with a low serum uric acid level in a general Chinese population. Diabetes research and clinical practice. 2007;76:68-74.
15. Dehghan A, Van Hoek M, Sijbrands EJ, et al. High serum uric acid as a novel risk factor for type 2 diabetes. Diabetes care. 2008;31:361-2.

16. Chien KL, Chen MF, Hsu HC, et al. Plasma uric acid and the risk of type 2 diabetes in a Chinese community. Clinical chemistry. 2008;54:310-6.
17. Kramer CK, Von Mühlen D, Jassal SK, et al. Serum uric acid levels improve prediction of incident type 2 diabetes in individuals with impaired fasting glucose: the Rancho Bernardo Study. Diabetes care. 2009;32:1272-3.
18. Kodama S, Saito K, Yachi Y, et al. Association between serum uric acid and development of type 2 diabetes. Diabetes care. 2009;32:1737-42.
19. Taniguchi Y, Hayashi T, Tsumura K, et al. Serum uric acid and the risk for hypertension and Type 2 diabetes in Japanese men: The Osaka Health Survey. Journal of hypertension. 2001;19:1209-15.
20. Modi AS, Sahi N. Serum uric acid levels in type 2 diabetes mellitus. Indian J Basic Appl Med Res. 2018;7:459-63.
21. Pan A, Teng GG, Yuan JM, et al. Bidirectional association between diabetes and gout: the Singapore Chinese Health Study. Scientific reports. 2016;6:1-8.
22. Rodríguez G, Soriano LC, Choi HK. Impact of diabetes against the future risk of developing gout. Annals of the rheumatic diseases. 2010;69:2090-4.
23. Strasak A, Ruttmann E, Brant L, et al. Serum uric acid and risk of cardiovascular mortality: a prospective long-term study of 83 683 Austrian men. Clinical chemistry. 2008;54:273-84.
24. Tuomilehto J, Zimmet P, Wolf E, et al. Plasma uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of Fiji. American journal of epidemiology. 1988;127:321-36.
25. Herman JB, Medalie JH, Goldbourt U. Diabetes, prediabetes and uricaemia. Diabetologia. 1976;12:47-52.
26. Xu L, Shi Y, Zhuang S, et al. Recent advances on uric acid transporters. Oncotarget. 2017;8:100852.
27. Mount DB, Kwon CY, Zandi-Nejad K. Renal urate transport. Rheumatic Disease Clinics. 2006;32:313-31.
28. Pavani CH, Mohanty S, Dharwadkar AA. Hypouricemia in type 2 diabetes mellitus without nephropathy: a case control study. Int J Clin Biochem Res. 2018;5:201-5.
29. Maesaka JK, Fishbane S. Regulation of renal urate excretion: a critical review. American journal of kidney diseases. 1998;32:917-33.
30. Levinson DJ, Sorensen LB. Renal handling of uric acid in normal and gouty subject: evidence for a 4-component system. Annals of the rheumatic diseases. 1980;39:173-9.
31. Lipkowitz MS. Regulation of uric acid excretion by the kidney. Current rheumatology reports. 2012;14:179-88.
32. Anzai N, Kanai Y, Endou H. New insights into renal transport of urate. Current opinion in rheumatology. 2007;19:151-7.
33. Mather A, Pollock C. Glucose handling by the kidney. Kidney international. 2011;79:S1-6.
34. Augustin R, Carayannopoulos MO, Dowd LO, et al. Identification and characterization of human glucose transporter-like protein-9 (GLUT9): alternative splicing alters trafficking. Journal of Biological Chemistry. 2004;279:16229-36.
35. Schembri B, Falzon ML, Casingena L, et al. Adequacy of clinical surveillance of diabetic patients requiring minor foot amputations. Malta Medical Journal. 2022;34:76-86.