GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 5 (350) Май 2024

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

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.

GEORGIAN MEDICAL NEWS
No 3 (348) 2024

Содержание:

GEORGIAN MEDICAL NEWS
No 5 (350) 2024

INVESTIGATING THE CORRELATIONS BETWEEN SUBSTANCE P, ANTIOXIDANT LEVELS, AND METABOLIC MARKERS IN NON-OBESE TYPE 2 DIABETIC PATIENTS

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Abstract.

Background: Hyperglycemia and hyperinsulinemia in type 2 diabetes result in complications exacerbated by oxidative stress, leading to cardiovascular, nephropathic, neuropathic, and retinopathic problems. Substance P(SP), a natural neuropeptide, inhibits cell death and enhances cell growth during oxidative or inflammatory stress, suggesting a potential role in reducing diabetic complications.

Objective: Investigate serum levels of SP, total antioxidant status (TAS), glycemic measures, and lipid profiles in non-obese type 2 diabetic patients and evaluate the relationships involving these biomarkers.

Method: A case-control study involved 85 adult subjects (46males & 39females), aged (30-60) year, included two groups; diabetic group:53(males & females) non-obese type 2 diabetic patients, healthy group: Apparently healthy subjects of 32 individuals chosen from the general population and matched with patients age, sex and BMI.

Results: The results showed that patients' glucose levels increased as percentage increase of(>141%),mild elevated insulin levels (>50%), higher insulin resistance (>250%), the lipid parameters exhibited disruption in comparison to the control group, in diabetic group, the serum levels of TAS, SP decreased considerably in comparison to the control group.

Conclusion: As evidenced by the outcomes; the TAS showed significant negative correlations with fasting serum glucose and low-density lipoprotein, and positive correlations with high-density lipoprotein. Neither the glycemic indices nor the lipid profiles or TAS demonstrated any notable associations with SP levels. This suggests that while SP levels are reduced in type 2 diabetes, they do not appear to be directly linked with the measured biomarkers.

Key words. Lipid profile, Oxidative stress, Substance P, Total Antioxidant Status.

Introduction.

Diabetes mellitus is a metabolic condition that involves a continuous rise in blood glucose levels and various degree of disruption in the metabolizing process of proteins, lipids, and carbohydrate [1-3]. Prolonged hyperglycemia causes serious consequences to several organs, such as peripheral neuropathy, nephropathy, which results in kidney failure, cardiovascular conditions, and retinal degeneration that impairs vision [4,5]. After a long period of uncontrolled hyperglycemia, complications of diabetes developed, cardiovascular disease is more common in those who have type 2 diabetes (T2DM). as a result of a condition known as atherogenic dyslipidemia. Coronary artery disease, specifically myocardial infarction, is the main contributor to morbidity and mortality among individuals with diabetes worldwide [6].

Elevated glucose levels result in the generation of reactive oxygen species (ROS) and the occurrence of oxidative stress inside mitochondria; however, their strong chemical reactivity makes them susceptible to cause destruction of large molecules such as lipids, proteins, and nucleic acids. Therefore, cells initiate protective mechanisms that control the generation of these ROS and prevent oxidative damage [7].

SP which interacts with neurokinin receptor 1 (NK-1R), it has been demonstrated that SP inhibits cellular alterations and promotes cell proliferation while preventing apoptosis in response to oxidative or inflammatory stress [8]. SP has been shown to enhance the inflammatory response by increasing the population of M2 macrophages and regulatory T cells in both the bloodstream and lymphoid organs, resulting in a reduction in the severity of the disease [9].

Antioxidants are compounds that can alleviate the consequences of oxidative stress. Endogenous antioxidants comprise of reduced glutathione and antioxidant enzymes, including catalase, superoxide dismutase, glutathione peroxidase, and reductase; while exogenous antioxidants are antioxidant vitamins such as vitamins A, C, and E. Both types can help prevent the production of free radicals by either removing them or speeding up their breakdown [10]. Due to the impracticality of individually measuring various antioxidant molecules, the total antioxidant status (TAS), considered as a measurement of a sample's overall antioxidant activity. Another name for TAS are total antioxidant activity (TAA) and total antioxidant capacity (TAC) [11].

Materials and Methods.

Study design: A case-control study design conducted at The National Center of Diabetes/ College of Medicine / University of Al- Mustansryia, from October/ 2023 to January/ 2024, using. The study included fifty-three T2DM, from 35 to 60 years of age, under the supervision of a specialized endocrinologist. Of these patients, 33 were males and 20 were females. The control subjects matched the corresponding patients (age & sex), consisting of a total number of thirty-two healthy individuals (13 male and 19 female), selected from the general community, with ages ranging from 30 to 51 years.

Inclusion criteria: All diabetic patients ≥18 years have diagnosed with T2DM for a minimum duration of one year and with BMI (18.6-29.9 Kg\m2), on oral hypoglycemic medicines, never received insulin therapy and were fasting overnight.

Exclusion criteria: Alcoholic patients, those with autoimmune disease, chronic inflammation, chronic kidney, and liver diseases, malignant diseases, pregnant or lactating women, or having other endocrinopathies.

Ethical consideration: The research protocol was granted approval from the College of Pharmacy Scientific

and Ethical Committee at the University of Baghdad (No. RECAUBCP6102023K). Additionally, informed agreement was obtained from each participant in the study.

Materials: Five milliliters of fasting venous blood were collected from all participants and collected in a gel tube, the samples were subjected to centrifugation at 4000 rpm for a duration of 15 minutes. The serum was stored in a 1.5 milliliter Eppendorf tube and stored in a refrigerator at a temperature of -20°C for later measurement of the study biomarkers. Serum insulin, SP and TAS were measured by ELISA kits provided by Cloud-clone Corp. (CCC, USA), Glycated hemoglobin (HbA1c) was measured by boronate affinity assay using the Nyco-Card Reader II(Sweden). The colorimetric test was used to evaluate fasting serum glucose (FSG), total cholesterol (TC), triglyceride(TG), high-density lipoprotein cholesterol (HDL) levels were provided by Linear chemicals (Spain), Low-density lipoprotein (LDL), as estimated by the Friedewald formula in (mg/dl) which is TC minus HDL minus TG divided by 5, Insulin resistance can be predicted using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), which is a simplified by the formula of multiplying the fasting insulin (μU/ml) by the fasting glucose (mg/dl) and dividing the result by 405 [12].

Statistical analysis: The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) (Windows version 26). The Shapiro-Wilk test was used to evaluate the normality of the data distribution, The obtained P-values for the measured data were found to be less than 0.05, indicating that the data did not follow a normal distribution. Consequently, non-parametric tests were employed for data analysis. Using the Mann -Whitney U test, we compared the patient and control groups' outcomes; the median and interquartile range are the descriptive data presented. Categorical variables were expressed as number and percents and differences were expressed using Chi-Squared test. Parameter correlations were examined using Spearman's correlation test.

Results.

The study compared the selected group of T2DM patients and a control group of healthy individuals, taking into account their demographic characteristics such as age, sex, and BMI. The comparison is presented in Table (1).

Table 1. *Characteristics of participants' demographics.*

Variables		Diabetes Patients	Control	P Value
		n=53	n=32	
Age(year)		52(13)	40(7)	0.062
Gender	Male	33(62%)	13(41%)	0.073
	Female	20(38%)	19(59%)	
BMI (kg/m²)		26.2(4)	25.53(3)	0.068

The study enrolled participants within the age range of 35 to 60 years in the patients' group, with a median (IQR) of [52 (13)]. While in the control group, the age range was 30 to 51 years, with a median (IQR) of [40 (7)]. Therefore, there is no considerable difference in age between the group of patients with diabetes and the control groups (P = 0.062); Table (1).

Of the 53 diabetic patients surveyed, 33 were men and 20 were women, making up 62% and 38%, respectively. Alternatively, of the 32 participants in the control group, 13 were men (41% of the total) and 19 were females (59% of the total). There was no statistically significant difference between the sexes in the two groups, as shown in Table (1).

Table (2) shows that individuals with diabetes have elevated FSG levels in comparison to the control group. The diabetes patients group exhibits a higher median (IQR) compared to other groups. There are substantial differences between the groups (P = 0.001). In addition, the studied groups were showed a significant difference in their fasting serum insulin levels. The glycated hemoglobin also demonstrates a statistically significant variation in the measured value between patients with diabetes and the control group (P =0.001). According to the HOMA-IR analysis, there are notable distinctions between the diabetic and control groups. Individuals with diabetes exhibit higher values (p = 0.001).

Table 2. *Serum levels of studied biochemical markers among Groups.*

Variables	Diabetes Patients	Control	P -Value
	n=53	n=32	
FSG (mg/ dL)	219.13(31.18)	90.94(13.57)	0.001*
Insulin(μU/ml)	3.03(1.27)	1.99 (0.381)	0.001*
HOMA-IR	1.687(0.704)	0.446(0.60)	0.001*
HbA1c (%)	8.10(1.70)	5.00 (0.70)	0.001*
TG (mg/ dL)	209.48(13.20)	139.49(14.54)	0.001*
TC (mg/ dL)	176.50(17.80)	138.31(17.93)	0.001*
LDL (mg/ dL)	76.62(19.473)	51.85(16.59)	0.001*
HDL (mg/ dL)	52.64(2.23)	59.14(5.07)	0.001*
VLDL (mg/ dL)	41.89(2.64)	27.89(2.91)	0.001*
SP (p g/ml)	181.49(79.93)	445.40(136.25)	0.001*

Where n=number, FSG =Fasting Serum Insulin, HOMA-IR= Homeostatic Model Assessment-Insulin Resistance, HbA1c= Glycated hemoglobin, Where n=number. TC=Total Cholesterol, TG= Triglycerides, LDL=Low Density Lipoprotein, VLDL=Very Low Density Lipoprotein, HDL=High Density Lipoprotein, SP=substance p
** Significant when p<0.05*

Lipids profile shows statistically significant difference in the measured values of TC, TG, Low LDL, and HDL between the diabetes patients and the control groups (P =0.001); Table (2).

Total antioxidant status shows significant variances between the groups. The diabetic group had been subjected to the lowered values, with median (IQR) of 71.363mmol/L (12.589) Vs. 137.844 (66.985) for the controls, as illustrated in Figure (1).

The present investigation identified a statistically significant disparity in the measured serum level of SP between the groups. The diabetes patients' group had lower median value of 181.49 p g/ml in comparison with the control group of 445.37 p g/ml, Figure (2).

Results of correlation analysis regarding TAS and SP for diabetes patients (n=53) is displayed in Table (3).

The serum TAS showed significant negative correlations with fasting FSG and LDL, while it showed significant positive correlations with HDL; (P<0.05). There were no significant correlations involving SP and the other variables.

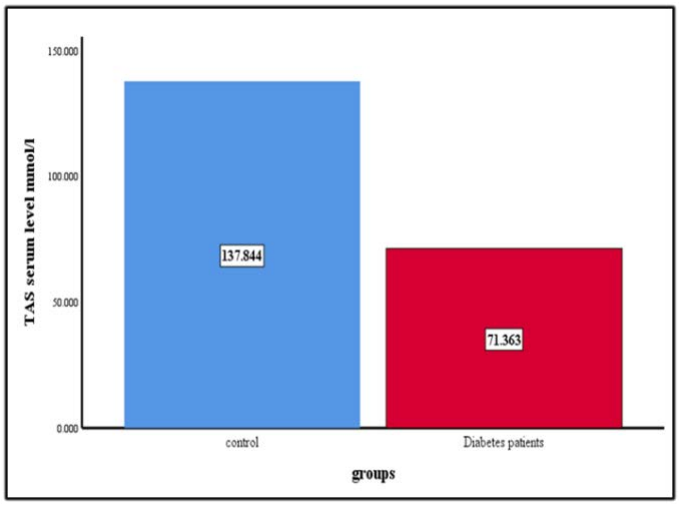

Figure 1. *Serum Level of Total Antioxidant Status in Studied Groups. TAS= Total antioxidant status.*

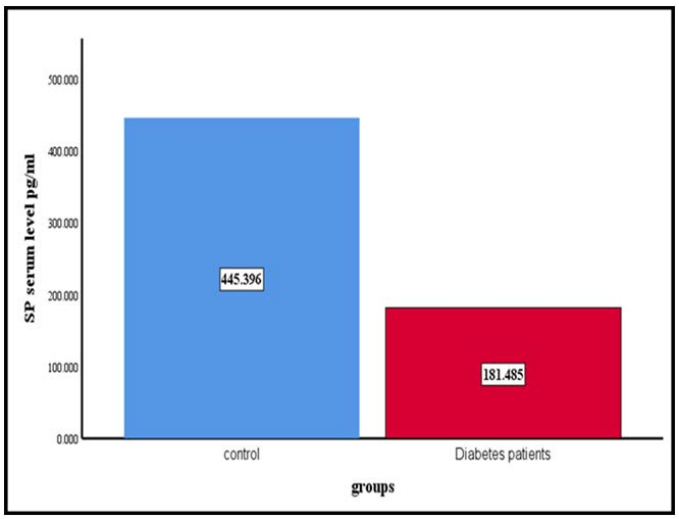

Figure 2. *Serum Level of Substance P in Studied Groups. SP = Substance P.*

Discussion.

In this study, the groups were carefully selected to ensure that there were no differences in age, sex, or BMI among the participants. This was done to avoid any potential influence of these factors on the biomarkers being investigated in the current study. Individuals diagnosed with diabetes exhibited elevated FSG levels compared to healthy control subjects [13-15]. In addition, the individuals with diabetes showed higher levels of fasting insulin of percentage increase of (>50%) and HOMA-IR (>250%), indicating inadequate management of the disease [16,17]. the insulin levels and HOMA-IR values in non-obese T2DM patients were not as high as expected (Table 2). These findings are consistent with the results drawn in earlier studies [18]. This is likely due to a combination of reduced insulin secretion and minimal or no insulin resistance. It has been observed that circulating insulin levels in non-obese diabetic patients are lower compared to their obese counterparts, these findings suggest a more severe beta-cell failure in the non-obese group, Importantly, this failure appears to be functional rather than structural [19].

The HbA1c that used as an indicator to determine the average blood glucose level in an individual's bloodstream, as the hemoglobin becomes glycated. There is a clear association between the HbA1c values, and the blood glucose levels [20]. The study revealed that the HbA1c values were significantly higher (>60%) compared to the control group. These elevated values primarily will contribute to the development of various complications associated with diabetes [21,22].

Patients with T2DM had higher lipolysis and lower glucose absorption, which led to an increase in TG production by adipose tissue [23]. This study showed that patients with diabetes had elevated serum TG levels and decreased HDL levels, reflecting the presence of dyslipidemia. An increase in insulin resistance would lead to an increase in the amount of free fatty acids (FFAs) that are delivered to the liver because the uptake of FFAs by skeletal muscle and adipose tissue is mediated by insulin. This results in elevated VLDL-cholesterol concentrations and overproduction of VLDL, which is clinically characterized as hypertriglyceridemia, also reduced lipoprotein lipase activity may also lead to an accumulation of TG-rich lipoproteins in circulation [24]. Our data indicated that the diabetic group exhibited higher levels of TC, TG, and LDL, while also showing lower levels of HDL compared to healthy individuals. Variations in lipid metabolism are regarded as risk factors for an increased incidence of cardiovascular complications related to diabetes [25,26].

Antioxidant defenses in the body continuously counteract the natural production of oxidants, ensuring a stable redox balance and protecting against damage. Insufficient antioxidant defenses or disruptions in redox signalling can lead to cellular membrane damage and the inhibition of essential enzymes and pathways [27]. The current study in line with Rani et al. [28] and Picchi et al. [29] that there is significant decrease in the TAS among diabetic patients in comparison to controls. Several studies have demonstrated an increase in antioxidant activity in diabetes, which is likely a result of a compensatory response to the oxidant environment associated with the diabetes [30,31].

The SP/NK1R system and diabetes are related as well. Significantly, deregulated expression of SP has been reported in diabetes and diabetes-associated chronic complications [32]. This study confirmed findings by Guo et al. [33], Yan et al. [34] and Wang et al. [35], that serum SP content was significantly lowered in non-obese T2DM patients as compared to healthy individuals. However, a study by fu j. et al. refuted this evidence in obese diabetes patients [36].

The study findings indicate that there was no significant correlation between SP levels and the variables that were examined. However, the statistical analysis showed a negative association between SP levels and fasting insulin levels, HOMA-IR, and lipid profile (except for HDL) and had a positive association with BMI, HbA1c, and HDL, as shown in Table (3). This finding is consistent with a previous study conducted by Kunt et al. [37].

Oxidative stress is typically associated with tissue damage and inflammation, in diabetic individuals, where oxidative stress levels are often elevated, SP can exert beneficial effects by promoting neuroprotection, modulation of oxidative stress, wound healing, and regulation of inflammation as mentioned by studies [9,38].

Table 3. *Spearman's Correlation Coefficient of Serum TAS and SP levels with the Studied Variables in Diabetics.*

Variable		SP	TAS
Age(years)	P-value	0.068	0.263
	rho	-0.253	-0.156
BMI	P-value	0.769	0.985
	rho	0.041	0.003
HbA1c	P-value	0.959	0.165
	rho	0.007	0.193
Insulin	P-value	0.165	0.636
	rho	-0.194	-0.066
FSG	P-value	0.439	0.001
	rho	-0.109	-0.457**
HOMA-IR	P-value	0.176	0.161
	rho	-1.898	-0.195
TG	P-value	0.247	0.765
	rho	-0.162	0.042
TC	P-value	0.166	0.006
	rho	-0.193	0.371**
HDL	P-value	0.632	0.007
	rho	0.067	0.365**
LDL	P-value	0.257	0.006
	rho	-0.159	-0.371**
VLDL	P-value	0.247	0.765
	rho	-0.162	0.042

Where FSG =Fasting Serum Glucose, HOMA-IR= Homeostatic Model Assessment-Insulin Resistance, HbA1c= Glycated hemoglobin TC=Total Cholesterol, TG= Triglycerides, LDL=Low Density Lipoprotein, VLDL=Very Low Density Lipoprotein, HDL=High Density Lipoprotein, rho=Spearman's correlation coefficient.
**Correlation is significant when P-value ≤ 0.05.*

Hyperglycemia initiates metabolic disorders by activating abnormal pathways that results in intracellular oxidative tissue stress. Oxidation of glucose and the generation of advanced glycation products are the consequence. Therefore, the rising oxidative stress is the main cause for the use of antioxidants as they are the substances which reduce the level of damage [39], in this study the serum TAS displayed significant negative correlations with FSG as confirmed with Baharirad et al [40]. Serum TAS displayed no significant correlations with HbA1c as agreed with Piechota study [41], and no correlation observed with HOMA-IR [42].

A positive correlation exists between HDL and TAS in diabetics group, as in an environment of oxidative stress brought on by hyperglycemia, insulin resistance, and increased plasma TGs may trigger a mechanism initiated by cholesteryl ester transfer protein that results in a generation of cholesteryl ester depleted, then renal catabolization of small HDL occurs rapidly [43], as well negative correlation with LDL, Nour Eldin et al. [44].

Conclusion.

The amount of circulating TAS may have gone down over the period since it was consumed in more quantities to defeat the high levels of the free radicals, which were coming up as a result of increased oxidative stress. Diabetes management techniques focus on glucose uptake and lack antioxidant activity. Early intervention, such as consuming antioxidant-rich foods and taking vitamins and trace minerals, is the key. Research in the future will address the question about molecular pathways of SP that provide the antioxidant effect, taking into account the complicate connection between SP, oxidative stress, and diabetic pathology. The precise mechanisms underlying the indirect correlation between SP and glycemic indices remain incompletely understood and require additional investigations. However, the evident reduction in SP levels raises significant inquiries regarding its role in the pathophysiology of diabetes, complications, and especially its potential influence on cardiovascular well-being.

Funding.

None.

Conflict of interest.

None.

Author contribution.

S W. A: Methodology, draft writing, visualization, writing, and editing; Sh H. A: formal analysis, supervision.

REFERENCES

1. Faris Raheem M, H Ali S, M. A. AL-Nuaimi A, et al. Impact of Serum Vitamin D Level on Selected Bone-Related Markers in Obese- Type 2 Diabetes Patients. F1000Res. 2023;12:56.
2. Yaas A.A, Al-Shakour A.A, Mansour A.A. Assessment of Serum Level of Protein Carbonyl as a Marker of Protein Oxidation in Patients with Type 2 Diabetes Mellitus. AL-Kindy College Medical Journal. 2022;18:190-195.
3. Abed B.A, Farhan L.O, Dawood A.S. Relationship between Serum Nesfatin-1, Adiponectin, Resistin Concentration, and Obesity with Type 2 Diabetes Mellitus. Baghdad Science Journal. 2024;21:0117.
4. Jaid H.K, Khaleel F.M, Salman I.N, et al. Estimation of Apelin Levels in Iraqi Patients with Type II Diabetic Peripheral Neuropathy. Baghdad Science Journal. 2023;20.
5. J. Abdulrahman A, Jabarah M.A.-H, A. Najjar S. Effects of Liraglutide on Weight Control and Blood Pressure in Type 2 Diabetes Mellitus Iraqi Patients. J Fac Med Baghdad. 2023;64:227-232.
6. Bhambhani G, Bhambhani R, Thakor N. Lipid Profile of Patients with Diabetes Mellitus: A Cross Sectional Study. Int J Res Med Sci. 2015:3292-3295.
7. Burgos-Morón, Abad-Jiménez, Marañón, et al. Relationship Between Oxidative Stress, ER Stress, and Inflammation in Type 2 Diabetes: The Battle Continues. J Clin Med. 2019;8:1385.
8. Park J.S, Piao J, Park G, et al. Substance-P Restores Cellular Activity of ADSC Impaired by Oxidative Stress. Antioxidants (Basel). 2020:9.
9. Kim D.Y, Piao J, Hong H.S. Substance-P Inhibits Cardiac Microvascular Endothelial Dysfunction Caused by High Glucose-Induced Oxidative Stress. Antioxidants. 2021;10:1084.
10. Pasupuleti V.R, Arigela C.S, Gan S.H, et al. A Review on Oxidative Stress, Diabetic Complications, and the Roles of Honey Polyphenols. Oxid Med Cell Longev. 2020;2020:1-16.
11. Silvestrini A, Meucci E, Ricerca B.M, et al. Total Antioxidant Capacity: Biochemical Aspects and Clinical Significance. Int J Mol Sci. 2023;24:10978.

12. Blackburn H, Jacobs D. Commentary: Origins and Evolution of Body Mass Index (BMI): Continuing Saga. Int J Epidemiol. 2014;43:665-669.
13. Prasad PS. Hyperglycaemia and Inflammation Are Prime Factors to Persuade Endothelial Dysfunction in Patients with Type 2 Diabetes Mellitus. Indian J Public Health Res Dev. 2020;11:288-293.
14. Patel B.J, Dave B, Dave D, et al. Comparison and Correlation of Glucose Levels in Serum and Saliva of Both Diabetic and Non-Diabetic Patients. J Int Oral Health. 2015;7:70-76.
15. Kadhim SA, Saleh ES, Jaafer AD. Assessment of Serum Levels of Advanced Oxidation Protein Products in Type 2 Diabetic Patients with and without Retinopathy Taking Different Antidiabetic Treatments. Iraqi Journal of Pharmaceutical Sciences. 2023;32:74-82.
16. Lee J, Kim M, Jang J.-Y, et al. Assessment HOMA as a Predictor for New Onset Diabetes Mellitus and Diabetic Complications in Non-Diabetic Adults: A KoGES Prospective Cohort Study. Clin Diabetes Endocrinol. 2023;9:7.
17. A. Ali I, H. Ali S. Impact of Osteocalcin Level on Vascular Calcification in Type 2 Diabetics in Relation to Fibroblast Growth Factor-23(FGF-23). Iraqi Journal of Pharmaceutical Sciences. 2018:42-54.
18. Marita A.R, Sarkar J.A, Rane S. Type 2 Diabetes in Non-Obese Indian Subjects Is Associated with Reduced Leptin Levels: Study from Mumbai, Western India; Springer. 2005;275.
19. Olaogun I, Farag M, Hamid P. The Pathophysiology of Type 2 Diabetes Mellitus in Non-Obese Individuals: An Overview of the Current Understanding. Cureus. 2020.
20. Sherwani S.I, Khan H.A, Ekhzaimy A, et al. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomark Insights. 2016;11:95-104.
21. Valizadeh R, Moosazadeh M, Bahaadini K, et al. Determining the Prevalence of Retinopathy and Its Related Factors among Patients with Type 2 Diabetes in Kerman, Iran. Osong Public Health Res Perspect. 2016;7:296-300.
22. Faris Raheem M, H. Ali S, G. Shareef L. Impact of Serum Levels of Vitamin D on Lipid Profiles, Glycemic Indices, and Insulin Resistance in Obese Type 2 Diabetes Patients: An Observational Study. F1000Res. 2022;11:1002.
23. Alaaraji S.F, Alrawi K.F, Allah P.H.S, et al. Evaluation of Serum Malondialdehyde, Glutathione and Lipid Profile Levels in Iraqi Females with Type 2 Diabetes Mellitus. Baghdad Science Journal. 2016;13:0383.
24. Chen S, Tseng C.-H. Dyslipidemia, Kidney Disease, and Cardiovascular Disease in Diabetic Patients. Rev Diabet Stud. 2013;10:88.
25. Biadgo B, Abebe S.M, Baynes H.W, et al. Correlation between Serum Lipid Profile with Anthropometric and Clinical Variables in Patients with Type 2 Diabetes Mellitus. Ethiop J Health Sci. 2017;27:215-226.
26. Boussekine S, Menaceur F, Gasmi S, et al. Oxidative Stress Assessment and Its Relationship with the Prevalence of Atherogenic Risk in Patients with Type 2 Diabetes. J Diabetes Metab Disord. 2021;20:583-590.
27. Sies H, Belousov V. V, Chandel N.S, et al. Defining Roles of Specific Reactive Oxygen Species (ROS) in Cell Biology and Physiology. Nat Rev Mol Cell Biol. 2022;23:499-515.
28. Rani A.J. Study on Total Antioxidant Status in Relation to Oxidative Stress in Type 2 Diabetes Mellitus. Journal of clinical and diagnostic research. 2014.
29. Picchi A, Capobianco S, Qiu T, et al. Coronary Microvascular Dysfunction in Diabetes Mellitus: A Review. World J Cardiol. 2010;2:377.
30. Akbari H. Ar Ch Ar Ch. J Clin Psychol. 2009;2:205-211.
31. Srivatsan R, Das S, Gadde R, et al. Antioxidants and Lipid Peroxidation Status in Diabetic Patients with and without Complications. 2009.
32. Kokabi F, Ebrahimi S, Mirzavi F, et al. The Neuropeptide Substance P/Neurokinin-1 Receptor System and Diabetes: From Mechanism to Therapy. BioFactors. 2023;49:534-559.
33. Guo Z. Plasma Substance P Concentration in Patients with Diabetes Mellitus during Perioperative Period. The Journal of Clinical Anesthesiology. 2013.
34. Yan L, Zhang R, Guo Z. Relationship between Plasma Substance P and Calcitonin Gene-Related Peptide Concentrations and Intraoperative Cardiovascular Events in Diabetic Patients. Chinese Journal of Anesthesiology. 2017:649-652.
35. Wang L, Zhou S, Li R, et al. Serum Levels of Calcitonin Gene-Related Peptide and Substance P Are Decreased in Patients with Diabetes Mellitus and Coronary Artery Disease. Journal of International Medical Research. 2012;40:134-140.
36. Fu J, Liu B, Liu P, et al. Substance P Is Associated with the Development of Obesity, Chronic Inflammation and Type 2 Diabetes Mellitus. Experimental and Clinical Endocrinology & Diabetes. 2010;119:177-181.
37. Kunt T, Forst T, Schmidt S, et al. Serum Levels of Substance P Are Decreased in Patients with Type 1 Diabetes. Experimental and Clinical Endocrinology & Diabetes. 2000;108:164-167.
38. Leal E.C, Carvalho E, Tellechea A, et al. Substance P Promotes Wound Healing in Diabetes by Modulating Inflammation and Macrophage Phenotype. Am J Pathol. 2015;185:1638-1648.
39. Yaribeygi H, Atkin S.L, Sahebkar A. A Review of the Molecular Mechanisms of Hyperglycemia-induced Free Radical Generation Leading to Oxidative Stress. J Cell Physiol. 2019;234:1300-1312.
40. Baharirad N, Pasdar Y, Nachvak M, et al. The Relationship of Dietary Total Antioxidant Capacity with Sarcopenia and Cardiometabolic Biomarkers in Type 2 Diabetes Patients. Physiol Rep. 2022;10.
41. Piechota W. Lipid Peroxidation, Total Antioxidant Status, and Glycemic Control in Patients with Type 2 Diabetes Mellitus. Military Physician. 2018;96:14-18.
42. Najafi A, Pourfarzam M, Zadhoush F. Oxidant/Antioxidant Status in Type-2 Diabetes Mellitus Patients with Metabolic Syndrome. J Res Med Sci. 2021;26:6.
43. Bonilha I, Zimetti F, Zanotti I, et al. Dysfunctional High-Density Lipoproteins in Type 2 Diabetes Mellitus: Molecular Mechanisms and Therapeutic Implications. J Clin Med. 2021:10.
44. Nour Eldin E.E.M, Almarzouki A, Assiri A.M, et al. Oxidized Low Density Lipoprotein and Total Antioxidant Capacity in Type-2 Diabetic and Impaired Glucose Tolerance Saudi Men. Diabetol Metab Syndr. 2014;6:94.