GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 2 (347) Февраль 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 2 (347) 2024

Содержание:

GEORGIAN MEDICAL NEWS
No 2 (347) 2024

ASSESSMENT OF OSTEOPONTIN, SCLEROSTIN, AND OSTEOCALCIN LEVELS IN PATIENTS WITH HYPOTHYROIDISM ON MEDICAL THERAPY

Zynab J. Jarjees[1], Entedhar R. Sarhat[2]*.

[1]*College of Medicine, Tikrit University, Tikrit, Iraq.*

[2]*College of Dentistry, Tikrit University, Tikrit, Iraq.*

Abstract.

Background: Thyroid hormones are critical regulators of bone maintenance in adulthood and play an important part in the development of bones. They also play a function in the formation of bones. Childhood hypothyroidism leads to delayed skeletal development, limited linear growth, and impaired bone mineral accumulation.

Aim of the study: This research aims to assess the serum concentration of sclerostin, osteocalcin, and osteopontin in women diagnosed with hypothyroidism. Additionally, it seeks to examine the impact of medical treatment on the levels of sclerostin, osteocalcin, and osteopontin in individuals with hypothyroidism.

Material and methods: This research examined a total of 180 women, divided into three groups: 70 women before treatment, 70 women after treatment, and 40 control subjects. The age range of the participants was between 15 and 54 years. The participants in this research are categorized into three distinct groups: The first cohort consisted of 70 women diagnosed with hypothyroidism, as confirmed by medical professionals. The second group consisted of 70 women who had undergone treatment for hypothyroidism. The research included a control group consisting of healthy women with no family history of thyroid illness. These women were in good health and their ages were similar to those of the women with hypothyroidism.

Results: According to the presented data show a decrease in the mean of the serum level of sclerostin, and osteocalcin in hypothyroidism women before and after treatment compared with the control group (13.4 ± 4.9 versus 19.8 ± 5.1 and 21.5 ± 5.0), (9.8±4.7 versus 14.35±12.63 and 15.20±14.73), respectively. The result was significant ($P < 0.01$), with no differences in osteopontin levels between study groups.

Conclusion: It was concluded that the sclerostin, and osteocalcin decreased in women with hypothyroidism before treatment in comparison with women after treatment and healthy women, while Furthermore no differences in Osteopontin levels between the three groups.

Key words. Thyroid hormones, thyroid peroxidase, osteopontin, sclerostin, osteocalcin.

Introduction.

Thyroid dysfunction is a prominent illness of the endocrine system that is widespread globally, affecting about 3-4% of the population [1]. Hypothyroidism, a disorder induced by several factors, leads to multiple pathophysiologic processes, some of which might have severe consequences if not treated [2]. Hypothyroidism may arise due to either primary gland failure or inadequate stimulation of the thyroid gland by the hypothalamus or pituitary gland [3]. Thyroid hormones have a significant impact on the control of metabolism and the growth of many organs, such as bones. They are essential for preserving bone structure and enhancing bone strength, as well as for attaining optimal bone mass [4]. Studies have shown that thyroid hormones may modify the length of the bone remodelling process and affect the balance between bone production and bone resorption [5]. The main indication for oral levothyroxine is to treat primary, secondary, and tertiary hypothyroidism. Primary hypothyroidism refers to the condition when the dysfunction originates specifically in the thyroid gland. Secondary hypothyroidism refers to a condition where the malfunction occurs in the pituitary gland, resulting in a reduction in the secretion of thyroid-stimulating hormone (TSH). Tertiary hypothyroidism occurs sporadically [6]. In addition, levothyroxine is approved by the FDA to suppress pituitary thyrotropin as a supplementary treatment to surgery and radioiodine therapy to control well-differentiated thyroid cancer that is reliant on thyrotropin. This activity provides comprehensive information on the prescription of levothyroxine, including its mechanism of action, pharmacology, adverse event profiles, eligible patient populations, and monitoring. It also emphasizes the role of the interprofessional team in managing different types of hypothyroidism using levothyroxine [7].

In hypothyroidism, bone remodelling is characterized by decreased turnover and a favourable equilibrium between resorption and production [8-10], which all contribute to a decrease in the likelihood of fractures. Prior research has shown that thyroid hormones govern the growth and specialization of osteoblasts, as well as the manifestation of bone remodelling factors such as osteocalcin [11,12]. Hyperthyroidism was seen to cause an elevation in serum osteocalcin levels in clinical investigations [13,14], whereas hypothyroidism was associated with a drop in these levels [15]. However, following therapy, the levels were found to return to normal [16,17].

Sclerostin is a protein that is produced by osteocytes and is coded by the SOST gene. This regulator of skeletal metabolism functions as a suppressor of bone production by promoting programmed cell death of osteocytes and osteoblasts [18]. Sclerostin decreases bone mineral content and cortical thickness, resulting in decreased bone resistance. Additionally, serum sclerostin has a negative correlation with parathormone and cortisol, but a positive correlation with calcitonin [19].

Osteopontin, a glycoprotein, is upregulated in hyperthyroid patients and downregulated in hypothyroid individuals. This suggests that it might serve as a novel biochemical marker for diagnosing thyroid dysfunctions [20]. The prefix "osteo" in the term denotes that the protein is specifically produced in bone, while the suffix "pontin" is derived from the Latin word "pons," meaning bridge, which suggests its function as a connecting protein [21].

Materials and Methods.

Subjects and study design: A cross-sectional study investigated 180 patients with hypothyroidism (70 patients and 40 control healthy subjects), Seventy patients were newly diagnosed with hypothyroidism, underwent treatment, for 3 months and completed the follow-up study Their ages ranged from 15 to 54 years. From September 2023 to December 2023, the patients were sent to two primary institutions, namely Azadi Hospital in Kirkuk City (Iraq) and Kirkuk General Hospital (Iraq). A brief questionnaire form (Appendix I) was used to gather clinical history data, including age, sex, weight, height, family history of thyroid illness, chronic conditions, and treatment history. Patients with diabetes and chronic diseases, as well as those using oral contraceptives, antiandrogenics, glucocorticoids, antihypertensive, antidiabetic, and antiobesity medicines, and those who smoke or have hypertension, were excluded.

Sample Collection: A sterile disposable syringe was used to collect about 5 ml of venous blood from each instance. The blood was then transferred into gel tubes and left to coagulate at room temperature for 20 minutes. The samples were subjected to centrifugation at a speed of 3000 revolutions per minute for 15 minutes. The resulting sera were then separated into three Eppendorf tubes, with each tube containing 500 µl of material. The tubes were thereafter maintained at a temperature of -20°C until they were used for the assay. The test involved the measurement of the following parameters: sclerostin, osteocalcin, and osteopontin.

Biochemical analysis: Sandwich-ELISA is utilized in this ELISA kit, namely the SunLong Biotech kit from China. An antibody that targets OPN, OC, and SOST is pre-coated on the Microelisa strip plate in this kit. Standards or samples are combined with the antibody in the Microelisa strip plate wells. Next, an HPP-conjugated antibody targeting OPN, OC, and SOST is added to each Microelisa stripplate well and incubated. Rinse away loose parts. The TMB substrate solution is injected into every well. Only wells containing OPN and HRP-conjugated OPN, OC, and SOST antibodies will be blue, which will become yellow upon stop solution injection. The optical density is measured at 450 nm using spectrophotometry. Osteopontin, osteocalcin, and sclerostin concentrations directly affect optical density.

Statistical Analysis: Microsoft EXCEL 2019 and SPSS 22 were used for data entry and analysis. Descriptive statistics were presented as frequencies and were applied to explain the characteristics of participants. The comparison between the study groups was done by t-test and Chi-Square test. A P-value of less than 0.05 will be considered statistically significant.

Results.

The result showed the serum level of osteocalcin in hypothyroidism women before and after treatment (P <0.01) compared with the control group (9.8±4.7 versus 14.35±12.63 and 15.20±14.73), respectively. The result showed the serum level of sclerostin in hypothyroidism women before and after treatment (P <0.01) compared with the control group (13.4 ± 4.9 versus 19.8 ± 5.1 and 21.5 ± 5.0), respectively. The result showed the serum level of OPN in hypothyroidism women before and after treatment (P>0.05) compared with the control group (6.55± 0.39versus 6.97 ± 1.45 and 7.12 ± 1.43), respectively. The result showed the serum level of human TPO in hypothyroidism women before and after treatment (P<0.01) compared with the control group (3498.2±503.75 versus 2756 ±1810.9 and 2629.47±289.5), respectively (Figure 1).

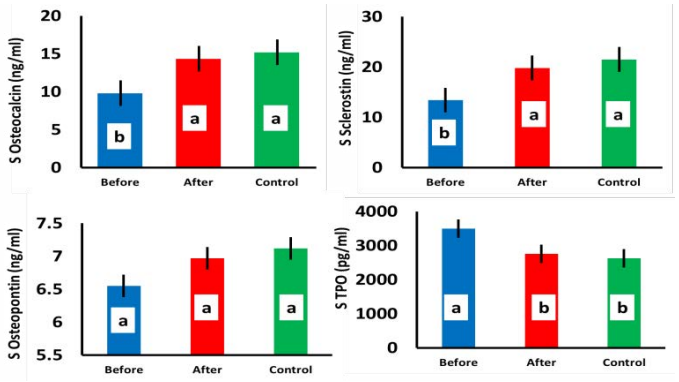

Figure 1. *Comparison between hypothyroidism patients and healthy individuals of some bone-related parameters [Serum osteocalcin, sclerostin, osteopontin, and TPO] before and after treatment with thyroid medicaments. Data expressed as mean±SD, Different letters express significant differences at p-value less than 0.05.*

Discussion.

This result shows a decreased level of osteocalcin in hypothyroidism patients compared with control at (P <0.01), while no differences between osteocalcin levels after treatment with levothyroxine and the control group. An abrupt rise in blood OC levels was found after the commencement of supplementary L-T4 therapy in individuals with hypothyroidism. This indicates a direct impact of thyroid hormone on osteoblasts in hypothyroid patients. This result agrees with previous studies that showed a decrease in osteocalcin in hypothyroid patients which suggested Osteoblastic activity is increased in persons with hyperthyroidism and decreased in those with hypothyroidism [17,22-24], which shows a decrease of osteocalcin level in hypothyroidism patients.

Osteocalcin, a protein produced by osteoblasts, serves as a valuable indicator of bone remodelling, and likely indicates the metabolic function of osteoblastic bone cells [25]. Hyperthyroidism leads to an increase in bone turnover, whereas hypothyroidism causes a reduction in bone turnover [26]. Moreover, there is a notable and favourable association between the concentration of serum osteocalcin (OC) and the levels of serum triiodothyronine (T3), thyroxine (T4), free triiodothyronine (FT3), or free thyroxine (FT4) in blood samples collected from untreated individuals with hypothyroidism. This connection might be attributed to the direct influence of thyroid hormones on bone metabolism, as shown by previous research [17]. Consistent with a prior study [27], the blood levels of osteocalcin (OC) in six individuals with hypothyroidism showed a concurrent rise with the increase in serum thyroxine (T4) levels, occurring within 1-2 months following therapy. This research contradicts the findings that indicate no substantial difference in osteocalcin levels before and after LT4 therapy [28]. Another

research demonstrates that there is no notable disparity in osteocalcin levels between individuals with hypothyroidism and those without the condition [29].

This result shows decreased level of Sclerostin in hypothyroidism patients in compared with control at (p-value≤ 0.001), while no differences between Sclerostin levels after treatment with levothyroxine and control groups at (p-value 0.06), This result agrees with Mihaljević et al. The study revealed that blood sclerostin levels were significantly lower in the hypothyroidism group compared to the control groups [18]. Additionally, sclerostin exhibited variations in circulation across individuals with three distinct forms of thyroid dysfunction: hypothyroidism, hyperthyroidism, and subclinical hyperthyroidism [19]. These findings are consistent with the data acquired by Tsourdi et al. [29].

Sclerostin hurts bone mineralization by diminishing bone mineral content, thereby attracting considerable attention in several research investigations [30]. Patients with hyperthyroidism had elevated levels of serum sclerostin. Therefore, it was shown that thyroid hormones may enhance the quantity of osteocytes that express sclerostin in individuals with hyperthyroidism [31,32]. Thyroid hormones play a crucial role in regulating bone metabolism. Any insufficiency or excess of these hormones might disrupt the process of bone turnover. Thyroid hormones have the potential to alter the pace at which bones are replaced, which in turn affects the strength of the skeletal system. In cases of hyperthyroidism, bone turnover may be accelerated, whereas in cases of hypothyroidism, it may be slowed down. This may also impact bone density [33]. Conversely, it is well acknowledged that TSH can inhibit the creation of osteoclasts and promote the development of osteoblasts [34]. Abe and colleagues [35] proposed that thyroid-stimulating hormone (TSH), rather than thyroxine and triiodothyronine, directly inhibits skeletal development.

This result shows no significant differences in osteopontin between the three groups. This study agrees with DUMAN et al. show no differences in OPN between hypothyroid women and control while decreasing its level when administrated thyroxin for 2 months [35], that suggested may be due to only premenopausal women involved in their study [36] according to an investigation conducted by Cho et al., there is a positive correlation between serum osteopontin (OPN) levels and bone mineral density (BMD) in postmenopausal women compared to premenopausal women [37].

Another research conducted by REZA et al. examined the adult population of Pakistan and found that hypothyroidism was associated with a drop in osteopontin (OPN) [19], while hyperthyroidism was associated with an increase in OPN. This suggests that the levels of OPN may be influenced by the cellular processes occurring in the thyroid gland [20]. Our findings align with the research conducted by Liou YM et al. [37]. There is a notable disparity in the levels of osteopontin in the blood serum of patients with hypothyroidism and hyperthyroidism. This discrepancy may be attributed to the role of osteopontin in promoting the development of autoimmune illnesses by stimulating the activation and movement of immune cells, as well as the generation of inflammatory cytokines [38].

TPO-Ab is one of the known factors that cause an autoimmune thyroid disease that results in hypothyroidism; levels of TPO-Ab titer could be positively associated with a low level of thyroid function. Moreover, a previous cross-sectional study reported that hypothyroidism showed significantly higher serum levels of human TPO (Thyroid Peroxidase) in women before treatment of levothyroxine than normal control subjects [39]. These studies indicate that the presence of low levels of thyroid function, rather than the presence of TPO-Ab, could be associated with hypothyroidism disorder [40]. However, in the present study, we found a significant positive association between TPO-Ab titer and hypothyroidism disorder in women before treatment of levothyroxine compared with women after treatment of levothyroxine and control groups.

On the other hand, Kachouei et al., studied reported that thyroid hormone levels before and after the intervention showed a significant reduction in the levels of the anti-TPO receiving group but in the control group no significant difference before and after treatment was observed. On the other hand, FT3 and FT4 levels in both groups fell to the same level. In other words, it can be concluded that the increase in serum levels of Thyroid Peroxidase has significantly reduced the levels of anti-thyroid hormone antibodies [41]. Moreover, the presence of other diseases could further complicate bone mineralization such as diabetes [42,43], thalassemia [44], polycystic ovarian syndrome [45], hyperlipidemia [46], and electrolyte disturbances [47].

Conclusion.

The study concluded Thyroid hormones are critical regulators of bone maintenance and play an important part in the development of bones sclerostin, and osteocalcin decreased in women with hypothyroidism before treatment in comparison with women after treatment and healthy women, while Furthermore no differences in Osteopontin levels between three groups. Furthermore, the treatment with levothyroxine increases the level of both sclerostin and osteocalcin.

REFERENCES

1. Garmendia Madariaga A, Santos Palacios S, Guillén-Grima F, et al. The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 2014;99:923-31.

2. Das D, Banerjee A, Jena AB, et al. Essentiality, relevance, and efficacy of adjuvant/combinational therapy in the management of thyroid dysfunctions. Biomedicine & Pharmacotherapy. 2022;146:112613.

3. Sarhat ER, Abbas MQ, Ali NH, et al. Evaluation of ceruloplasmin, sialic acid and liver function for women with breast cancer. InAIP Conference Proceedings. 2022;2394:1.

4. Hart NH, Newton RU, Tan J, et al. Biological basis of bone strength: anatomy, physiology and measurement. Journal of musculoskeletal & neuronal interactions. 2020;20:347.

5. Abid IM, Khalaf SJ, Zbaar SA, et al. Dental caries and hormonal changes in postmenopausal women. Archivos Venezolanos de Farmacologia y Terapeutica. 2022;41.

6. Sarhat KG, Jabir TH. Assessment of melatonin and oxidant-antioxidant markers in infertile men in Thi-Qar Province. Indian J. Forensic Med. Toxicol. 2019;13:1500-4.

7. Mahmood DA, Sarhat ER, Sulaiman YA, et al. Relationship between Paraoxonase and Malondialdehyde as a marker of oxidative stress in patients with psoriasis. Revista Latinoamericana de Hipertension. 2022;17.
8. Charles P, Mosekilde L, Risteli L, et al. Assessment of bone remodeling using biochemical indicators of type I collagen synthesis and degradation: relation to calcium kinetics. Bone and mineral. 1994;24:81-94.
9. Szulc P. Biochemical bone turnover markers in hormonal disorders in adults: a narrative review. Journal of endocrinological investigation. 2020;43:1409-27.
10. Eriksen EF, Mosekilde L, Melsen F. Kinetics of trabecular bone resorption and formation in hypothyroidism: evidence for a positive balance per remodeling cycle. Bone. 1986;7:101-8.
11. Khalaf SJ, Aljader GH, Sarhat ER, et al. Antidiabetic effect of Aqueous Extract of Medicago Sativa with Enhanced Histopathology of Pancreas in Alloxan Induced Diabetic Rats. PJMH S. 2021;15:492-6.
12. Akalin A, Colak Ö, Alatas Ö, et al. Bone remodelling markers and serum cytokines in patients with hyperthyroidism. Clinical endocrinology. 2002;57:125-9.
13. Shinkov AD, Borissova AM, Kovatcheva RD, et al. Age and menopausal status affect osteoprotegerin and osteocalcin levels in women differently, irrespective of thyroid function. Clinical Medicine Insights: Endocrinology and Diabetes. 2014;7:CMED-S15466.
14. Botella-Carretero JI, Alvarez-Blasco F, San Millán JL, et al. Thyroid hormone deficiency and postmenopausal status independently increase serum osteoprotegerin concentrations in women. European journal of endocrinology. 2007;156:539-45.
15. Garnero P, Vassy V, Bertholin A, et al. Markers of bone turnover in hyperthyroidism and the effects of treatment. The Journal of Clinical Endocrinology & Metabolism. 1994;78:955-9.
16. Saleh SS, Sarhat ER. Effects of ethanolic Moringa oleifera extract on melatonin, liver, and kidney function tests in alloxan-induced diabetic rats. Indian Journal of Forensic Medicine & Toxicology. 2019;13:1015-9.
17. van Bezooijen RL, ten Dijke P, Papapoulos SE, et al. SOST/sclerostin, an osteocyte-derived negative regulator of bone formation. Cytokine & growth factor reviews. 2005;16:319-27.
18. Mihaljević O, Živančević-Simonović S, Lučić-Tomić A, et al. The association of circulating sclerostin level with markers of bone metabolism in patients with thyroid dysfunction. Journal of Medical Biochemistry. 2020;39:436.
19. Reza S, Shaukat A, Arain TM, et al. Expression of osteopontin in patients with thyroid dysfunction. PLoS One. 2013;8:e56533.
20. Alwakeel MA, Tawfeek HM, El Hamid SM. Osteopontin as a new biomarker for diagnosis of patients with thyroid dysfunctions. AAMJ. 2012;10:280-95.
21. Barsal G, Taneli F, Atay A, et al. Serum osteocalcin levels in hyperthyroidism before and after antithyroid therapy. The Tohoku Journal of Experimental Medicine. 2004;203:183-8.
22. Kim CO, Park KS, Park KC, et al. The Relationship of Subclinical Hypothyroidism with Bone Mineral Density and Biochemical Bone Markers in Postmenopausal Women. Journal of the Korean Academy of Family Medicine. 2008;29:41-7.
23. Rija FF, Hussein SZ, Abdalla MA. Osteoprotegerin, sclerostin, and osteocalcin serum levels in thyroid disorder patients. Ukr Biochem J. 2021;93:117-21.
24. Martinez ME, Herranz L, De Pedro C, et al. Osteocalcin levels in patients with hyper-and hypothyroidism. Hormone and metabolic research. 1986;18:212-4.
25. Zoch ML, Clemens TL, Riddle RC. New insights into the biology of osteocalcin. Bone. 2016;82:42-9.
26. Bergmann P, Dediste A, Demeester-Mirkine N, et al. Serum bone Gla protein (BGP) in primary hypothyroidism before and during treatment with thyroid hormones. Hormone and metabolic research. 1989;21:47-8.
27. Rezaee R, Mohebbi M, Afkhamizadeh M, et al. The Effect of Levothyroxine in Comparison with Placebo on Serum Osteocalcin Levels in Patients with Subclinical Hypothyroidism. Current Drug Safety. 2022;17:64-9.
28. Martinez ME, Herranz L, De Pedro C, et al. Osteocalcin levels in patients with hyper-and hypothyroidism. Hormone and metabolic research. 1986;18:212-4.
29. Tsourdi E, Rijntjes E, Köhrle J, et al. Hyperthyroidism and hypothyroidism in male mice and their effects on bone mass, bone turnover, and the Wnt inhibitors sclerostin and dickkopf-1. Endocrinology. 2015;156:3517.
30. Mustafa B, Shareef A, Mahmood M. Comparison of bone maturation response to treatment with short and long-term growth hormone therapy in short-stature pediatric patients. Georgian Medical News. 2022;331:27-30.
31. 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.
32. Tuchendler D, Bolanowski M. The influence of thyroid dysfunction on bone metabolism. Thyroid Res. 2014;7:12.
33. Sampath TK, Simic P, Sendak R, et al. Thyroid-stimulating hormone restores bone volume, microarchitecture, and strength in aged ovariectomized rats. Journal of Bone and Mineral Research. 2007;22:849-59.
34. Abe E, Marians R C, Yu W, et al. TSH is a negative regulator of skeletal remodeling. Cell. 2003;115:151.
35. Duman G, Ertorer EM, Mete T, et al. Association between Serum Osteopontin Levels and Cardiovascular Risk in Hypothyrodism. Turk J Endocrinol Metab. 2016;20:36-42.
36. Cho EH, Cho KH, Lee HA, et al. High serum osteopontin levels are associated with low bone mineral density in postmenopausal women. Journal of Korean Medical Science. 2013;28:1496-9.
37. Liou YM, Chang LY, Liaw JM, et al. Osteopontin gene expression in the aorta and the heart of propylthiouracil-induced hypothyroid mice. Journal of biomedical science. 2005;12:869-80.
38. Sarhat ER. Altered Serum Marker Of Thyroid Profile And Antioxidant Enzymes In Individuals With Alzheimer's Disease. JK Practitioner. 2019;24.
39. Shimizu Y, Kawashiri SY, Noguchi Y, et al. Normal range of anti–thyroid peroxidase antibody (TPO-Ab) and atherosclerosis among eu-thyroid population: a cross-sectional study. Medicine. 2020;99.

40. Wells BJ, Hueston WJ. Are thyroid peroxidase antibodies associated with cardiovascular disease risk in patients with subclinical hypothyroidism?. Clinical Endocrinology. 2005;62:580-4.
41. Kachouei A, Rezvanian H, Amini M, et al. The effect of levothyroxine and selenium versus levothyroxine alone on reducing the level of anti-thyroid peroxidase antibody in autoimmune hypothyroid patients. Advanced Biomedical Research. 2018;7.
42. Mohammad S, Fadhil N, Mahmood M. Effects of metformin and cinnamon on 1, 5 anhydroglucitol, adiponectin and ghrelin on newly diagnosed type 2 diabetes mellitus patients. Jordan Medical Journal. 2021;55.
43. Media AH, Al Abachi SZ. Impact of diabetes mellitus on serum irisin level and other biochemical parameters. Medicinski časopis. 2023;57:21-6.
44. Althanoon ZA, Merkhan MM. The assessment of the incidences of ocular toxicity and ocular findings caused by iron-chelating compound. Archivos Venezolanos de Farmacologia y Terapéutica. 2022;41:514-9.
45. Mahmood MD, Merkhan MM. Role of Spironolactone in the Treatment of Female Patterns Hair Loss With Polycystic Ovarian Syndrome. On Research In. 2023.
46. Mohammad JA, Fathi FH, Almulathanon AA, et al. Hyperlipidemia connoted vitiation of serum adipokines and redox imbalances. Military Medical Science Letters. Vojenské Zdravotnické Listy. 2023;92.
47. Mahmood MD, Younes MA, Saarti M. Pathophysiological Electrolyte Changes Connoted via Antagonism of Serotonin Receptor in Experimental Animals. Pharmacognosy Journal. 2022;14.