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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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ASSOCIATION BETWEEN THYROID HORMONE LEVELS AND ADVANCED LIVER FIBROSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Abstract.

Background: The degree of hepatic fibrosis is a significant predictor of mortality in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetic mellitus (T2DM). This study aims to evaluate the relationship between blood thyroid hormone levels and advanced liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus.

Method: A cross-sectional study involving 350 patients with Type 2 Diabetes Mellitus (T2DM) was carried out at the Ibn-Khaldon Diabetic Medical Center in Port-Sudan City, Red Sea State, Sudan, between December 2024 and February 2025. Of these, 140 patients had T2DM without NAFLD, and 210 patients had NAFLD, of whom 114 had progressive liver fibrosis and 96 did not. Following a 12-hour fast, laboratory tests were conducted. A Mindray A88 biochemical analyzer was used to examine blood samples for lipid profiles (total cholesterol, triglycerides, HDL, and LDL) and liver function indicators (AST, ALT, and albumin). FT3, FT4, TT3, TT4, and TSH levels were measured using a Finecare Plus 114 chemical analyzer to evaluate thyroid function. Non-alcoholic fatty liver disease (NAFLD) was diagnosed by abdominal ultrasound imaging; an NFS of more than 0.676 denoted growing hepatic fibrosis.

Result: BMI, ALT, AST, TG, TC, and TT3 were significantly greater in T2DM with NAFLD, while HDL-C, FT3, FT4, and TT4 were significantly decreased ($P < 0.05$). relative to T2DM in the absence of NAFLD. Levels of FT3, FT4, TT3 ALT, TC, TG, PLT, ALB, TT4, and BMI were considerably lower in T2DM patients with increasing liver fibrosis than in those without the condition ($p < 0.05$). There was no significant difference in HDL-C, LDL-, AST, or TSH levels between the two groups ($P > 0.05$). TT3, TT4, and TSH levels did not positively correlate with NAFLD (p=0.409, 0.352, 0.081). Model 3 included adjustments for age, BMI, TG, and HDL. It was evident from the study's results that FT3 and NAFLD were negatively correlated (p=0.004).

Conclusion: Significant association between liver fibrosis in those with type 2 diabetes and abnormal thyroid hormone levels. There is a negative correlation between the prevalence of advanced fibrosis and cases of T2DM and NAFLD, and a low FT3 level is an independent risk factor for advanced fibrosis.

Key words. Non-alcoholic fatty liver disease, liver fibrosis, Type 2 diabetes mellitus, thyroid hormones, NAFLD fibrosis score, Free triiodothyronine (FT3), insulin resistance, metabolic syndrome.

Introduction.

Non-alcoholic fatty liver disease (NAFLD), which includes steatosis, non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma, is a rapidly growing health concern with a current global prevalence of over 25% [1]. Patients with type 2 diabetes mellitus (T2DM) and obesity are at the highest risk, with 60% to 80% of them also having NAFLD [2-4]. Moreover, hepatic ATP production decreases while liver fat content increases rapidly during the early stages of type 2 diabetes [5,6].

Thyroid hormones, being the primary regulators of energy and lipid homeostasis, may play a crucial role in the development of NAFLD. Hypothyroidism may favor the accumulation of hepatic triglycerides, increase the flux of free fatty acids (FFA), and elevate pro-inflammatory adipokines in the blood [7]. T2DM, a major risk factor for NAFLD, is also closely linked to the risk of advanced fibrosis [8]. Reports suggest that the prevalence of advanced fibrosis is 17.02% higher in cases of NAFLD and T2DM [9]. Therefore, monitoring the progression of NAFLD in patients with T2DM is crucial.

Liver biopsy, the gold standard for diagnosing hepatic fibrosis, is an invasive test that may result in complications such as bleeding or infection. In recent years, various non-invasive scoring systems, such as the NAFLD fibrosis score (NFS), FIB-4 (fibrosis 4 score), ELF (European Liver Fibrosis), and APRI (aspartate aminotransferase-to-platelet ratio Index), have been developed to detect advanced fibrosis associated with NAFLD. NFS > 0.676 for advanced fibrosis has a high accuracy, with the most commonly used positive predictive value (PPV) in clinical practice being 90% [10].

Recent studies have shown an inverse correlation between serum thyroid hormone levels and the incidence of NAFLD [11], and a Mendelian randomization study demonstrated the causal relationship between hypothyroidism and NAFLD [12]. Furthermore, decreased thyroid hormone levels were found to accelerate the development and progression of liver fibrosis [13,14]. However, studies investigating the relationship between thyroid hormone levels and advanced liver fibrosis in patients with both NAFLD and T2DM are limited.

To address this research gap, the present study aims to:

1. Evaluate the association between thyroid hormone levels and advanced liver fibrosis in patients with NAFLD and T2DM.
2. Compare the levels of thyroid hormones (FT3, FT4, TT3, TT4, and TSH) and other metabolic parameters between T2DM patients with and without NAFLD.

3. Assess the relationship between thyroid hormone levels and the risk of advanced liver fibrosis in T2DM patients with NAFLD.

By providing insights into the role of thyroid hormones in the progression of liver fibrosis in patients with NAFLD and T2DM, this study aimed to contribute to the development of better screening and management strategies for this high-risk population.

Materials and Methods.

Study design, subject and area:

From December 2024 to February 2025, a cross-sectional study was carried out at the Ibn-Khaldon Diabetic Medical Center in Port-Sudan City, Red Sea State, Sudan. The study population consisted of three groups: patients with T2DM and NAFLD, patients with T2DM without NAFLD, and early T2DM patients with NAFLD. A consecutive sampling method was employed, whereby all eligible patients presenting at the centre during the study period were sequentially enrolled.

The inclusion criteria for the study were as follows:

1. Adults aged 18 years or older.
2. Confirmed diagnosis of T2DM based on the American Diabetes Association (ADA) criteria [reference].
3. Presence or absence of NAFLD confirmed by abdominal ultrasound imaging.
4. Availability of sufficient information to assess the degree of liver fibrosis and thyroid function.

The exclusion criteria were:

1. History of excessive alcohol consumption (>30 g/day for men and >20 g/day for women).
2. Liver diseases caused by viruses, alcohol, drugs, autoimmunity, and/or total parenteral nutrition.
3. Incomplete information on thyroid function.
4. Overt thyroid diseases or abnormal thyroid function.
5. Pregnancy or breastfeeding.

The diagnosis of NAFLD was based on the presence of hepatic steatosis on abdominal ultrasound imaging, in the absence of secondary causes of liver fat accumulation, such as significant alcohol consumption or other liver diseases. Advanced liver fibrosis was defined as an NFS score > 0.676, which has been shown to have a high accuracy for detecting advanced fibrosis in patients with NAFLD [15].

All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board of the participating medical center. The study was conducted in accordance with the Declaration of Helsinki's ethical principles.

Sample size:

The sample size for this study was determined based on the available patient population and resources. A total of 350 T2DM patients with normal thyroid function were included in the study, with 140 patients in the T2DM without NAFLD group and 210 patients in the T2DM with NAFLD group.

Laboratory test markers and general clinical data:

The general data collected from participants included age (years), gender (male/female), height (cm), weight (kg), and duration of diabetes (years). After a 12-hour fasting period, venous blood samples were obtained from each patient. Platelet count was measured using a Mindray BC-700 haematology analyser, and whole blood was centrifuged at 3,000 rpm for 10 minutes to separate serum. A mindrayA88 biochemical analyser was used to assess the lipid profile, including total cholesterol (TC, mg/dL), triglycerides (TG, mg/dL), high-density lipoprotein cholesterol (HDL, mg/dL), and low-density lipoprotein cholesterol (LDL, mg/dL), as well as liver function markers, including aspartate aminotransferase (AST, IU/L), alanine aminotransferase (ALT, IU/L), and albumin (ALB, g/dL). Thyroid hormones, including free triiodothyronine (FT3, pg/mL), free thyroxine (FT4, ng/dL), total triiodothyronine (TT3, ng/mL), total thyroxine (TT4, μg/dL), and thyroid-stimulating hormone (TSH, μIU/mL), were measured using a Fine care Plus 114 chemistry analyser with the following assays: FT3 (ELISA, CatLog No. E-EL-H0781), FT4 (ELISA, CatLog No. E-EL-H0782), TT3 (ELISA, CatLog No. E-EL-H0779), TT4 (ELISA, CatLog No. E-EL-H0780), and TSH (ELISA, CatLog No. E-EL-H0778). All procedures were carried out in compliance with the applicable laboratory guidelines and regulations. Internal quality control samples were run daily to ensure the reliability of the test results, and the laboratory participated in an external quality assessment scheme for thyroid function tests.

Definition, calculation and group:

Ultrasound imaging of the abdomen was used to identify non-alcoholic fatty liver disease (NAFLD). The diagnosis of NAFLD was based on the presence of hepatic steatosis on ultrasound, in the absence of excessive alcohol consumption (>30 g/day for men and >20 g/day for women) and other chronic liver diseases such as viral hepatitis, autoimmune hepatitis, drug-induced liver injury, or total parenteral nutrition. The presence of NAFLD was determined by experienced radiologists blinded to the participants' clinical and laboratory data.

Body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared. The NAFLD fibrosis score (NFS) was calculated using the following formula: NFS = -1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m2) + 1.13 × impaired fasting glucose/diabetes (yes = 1, no = 0) + 0.99 × aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio - 0.013 × platelet count (×109/L) - 0.66 × albumin (g/dL). Advanced liver fibrosis was defined as an NFS > 0.676, which has been previously validated as a reliable cut-off for identifying advanced fibrosis in patients with NAFLD [16].

Based on the presence of NAFLD and the NFS results, participants were divided into three groups:

1. T2DM without NAFLD (control group).
2. T2DM with NAFLD.
3. T2DM with NAFLD and advanced liver fibrosis (defined as NFS > 0.676).

The characteristics and laboratory findings of these three groups were compared to investigate the association between thyroid hormone levels and the presence and severity of NAFLD in patients with T2DM.

Statistical Analysis:

SPSS version 26.0 was used for data analysis. The normality of continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and median (interquartile range) for non-normally distributed variables. Categorical variables were expressed as frequencies and percentages.

Independent t-tests were used to compare the means of normally distributed variables between T2DM patients with and without NAFLD. The Mann-Whitney U test was employed to compare the means of non-normally distributed variables between T2DM patients with and without advanced liver fibrosis (defined as NFS > 0.676).

Logistic regression analyses were performed to evaluate the associations between thyroid hormone levels and the presence of NAFLD. Three models were constructed: Model 1 (unadjusted), Model 2 (adjusted for sex), and Model 3 (adjusted for age, sex, BMI, triglycerides, and HDL cholesterol). Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs) and p-values.

The chi-square test was used to assess the association between categorical variables, such as the presence of advanced liver fibrosis and thyroid hormone status (e.g., low FT3 and FT4 levels).

A p-value < 0.05 was considered statistically significant for all analyses.

Results.

There were 350 T2DM patients with normal thyroid function who took part in the study. They were split into two groups:

Table 1. *Compare the average metabolic test results between T2DM with and without NAFLD. n=350.*

	Mean ± SD		
Variable	**T2DM with NAFLD**	**T2DM without NAFLD**	
Age /years	66.7±29.04	61.9±27.6	0.003
Gender (male/female) Ratio	128\82	82/58	0.076
BMI /kg/M2	27.2±2.9	25.2±2.1	0.000
Duration /Year	8.5±5.01	7.4±3.17	0.103
AST (IU/L)	25.3±8.3	21.8±9.0	0.000
ALT (IU/L)	33.3±9.5	24.6±7.6	0.000
ALB (g/dL)	4.2±0.76	4.0±1.08	0.216
PLT × 10⁹/L)	222±60.5	225±54.5	0.157
TSH (uIU/ml)	1.5±0.34	1.4±0.71	0.123
TT4 (µg/ml)	7.3±4.12	8.2±4.65	0.002
TT3 (ng/mL)	1.89±0.96	1.24±0.89	0.004
fT4 (pg/ml)	0.99±0.32	1.26±0.54	0.002
fT3 (pg/ml)	3.14±2.09	3.94±2.06	0.000
TC (mg/dl)	172.08±48.3	165.1±43.3	0.011
TG (mg/dl)	226.5±135.6	150.4±120.3	0.000
HDL-C(mg/dl)	35.9±13.1	39.8± 13.1	0.000
LDL-C(mg/dl)	101.3±35.5	98.6±34.4	0.104

Abbreviations: *T2DM: Type 2 Diabetes Mellitus; NAFLD: Non-Alcoholic Fatty Liver Disease; BMI: Body Mass Index; PLT: Platelet; ALB: Albumin; TC: Total Cholesterol; TG: Triglycerides; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TSH: Thyroid Stimulating Hormone; T4: Total Thyroxin; T3: Total Triiodothyronine.*

Table 2. *Compare the average metabolic test results between T2DM with PLF and without PLF. n=210*

	Mean ± SD		
Variable	**T2DM without PLF NFS<0.676**	**T2DM with PLF NFS>0.676**	**P. value**
BMI (kg/M2)	25.3±4.08	28.3±3.8	0.001
Serum AST (IU/L)	21.3±8.7	20.8±9.9	0.206
Serum ALT (IU/L)	24.2±11.0	20.4±4.4	0.004
ALB (g/dL)	4.2±1.36	3.6±1.04	0.003
PLT × 10⁹/L	256±86	178±53	0.003
TSH (uIU/ml)	1.43±0.48	1.72±0.79	0.205
TT4 (µg/ml)	7.02±3.39	6.44±3.12	0.000
TT3 (ng/mL)	1.53±1.00	1.22±0.94	0.008
fT4 (pg/ml)	0.86±0.37	0.48±0.29	0.040
fT3 (pg/ml)	3.09±1.93	2.68±1.82	0.000
TC(mg/dl)	187.5±37.5	168.6±56.4	0.005
TG(mg/dl)	274.6±235.6	174.5±114.2	0.001
HDL-C(mg/dl)	34.4±8.12	35.9±13.1	0.211
LDL-C(mg/dl)	111.3±41.7	103.2±34.4	0.084

Abbreviations: *T2DM: Type 2 Diabetes Mellitus; NAFLD: Non-Alcoholic Fatty Liver Disease; BMI: Body Mass Index; PLT: Platelet; ALB: Albumin; TC: Total Cholesterol; TG: Triglycerides; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TSH: Thyroid Stimulating Hormone; T4: Total Thyroxin; T3: Total Triiodothyronine.*

Table 3. *Multiple factors logistic regression analysis of thyroid hormones and risk of NAFLD and progressive liver fibrosis.*

	Thyroid hormones and the risk of NAFLD			
TFT		**OR**	**95% CI**	**P. value**
FT3	Model 1	2.432	(1.115-5.304)	0.021
	Model 2	3.684	(1.593-8.520)	0.002
	Model 3	2.696	(1.058-6.868)	0.004
FT4	Model 1	4.571	(1.027-20.347)	0.045
	Model 2	5.467	(1.434-20.836)	0.012
	Model 3	1.040	(0.997, 1.085)	0.216
TT3	Model 1	0.386	(0.196-0.759)	0.468
	Model 2	1.238	(0.500-3.061)	0.409
	Model 3	0.804	(0.280-2.307)	0.446
TT4	Model 1	2.563	(0.222-29.534)	0.621
	Model 2	0.535	(0.151-1.888)	0.352
	Model 3	1.133	(0.489-2.625)	0.057
TSH	Model 1	1.324	(0.894-1.962)	0.092
	Model 2	0.990	(0.972-1.008)	0.081
	Model 3	0.535	(0.151-1.888)	0.225

Abbreviations: *TFT: Thyroid Function Test; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TT4: Total Thyroxin; TT3: Total Triiodothyronine; TSH: Thyroid Stimulating Hormone.*

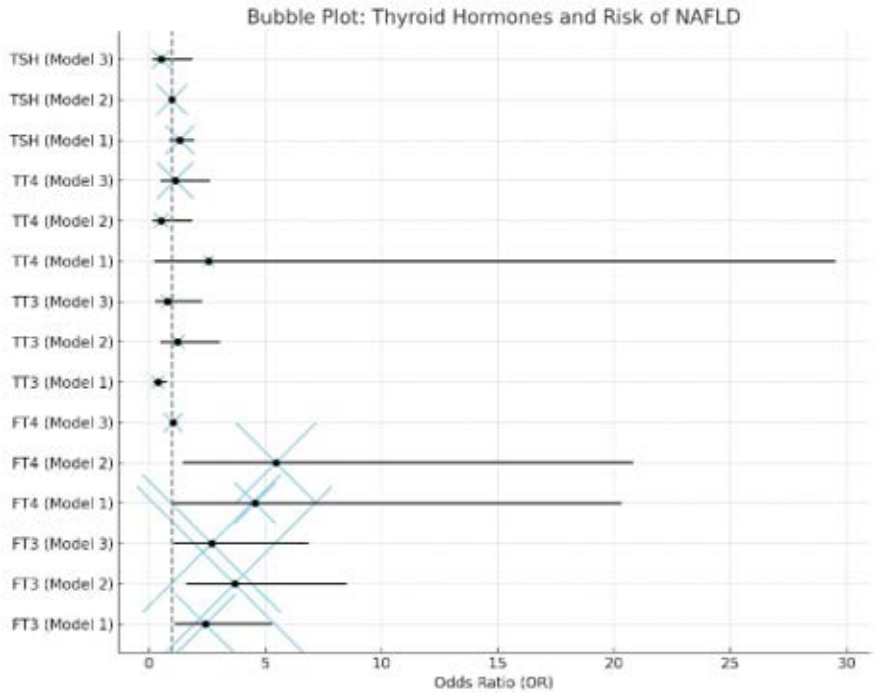

Figure 1. *Relationship between odd ratio and thyroid hormone.*

T2DM without NAFLD (140 cases) had an average age of 61.9±27.6 years and a duration of diabetes of 7.4±3.17 years, and T2DM with NAFLD (210) had an average age of 66.7±29.04 years and a duration of DM of 8.5±5.01 years. In comparison to T2DM cases without NAFLD, the T2DM cases with NAFLD had significantly lower levels of HDL-C, FT3, FT4, and TT4 ($P < 0.05$) and significantly higher levels of BMI, ALT, AST, TG, TC, and TT3. When compared to T2DM without NAFLD, there was no discernible difference in the percentage of males or the levels of PLT, ALB, HDL-C, and TSH between the two groups ($P > 0.05$) (Table 1).

DM type 2 patients with NAFLD Based on the NAFLD fibrosis score (NFS) > 0.676, which was deemed to be progressive liver fibrosis, patients were split into two groups: T2DM with progressive liver fibrosis (114 cases) and T2DM without progressive liver fibrosis (96 cases). Individuals with increasing liver fibrosis had significantly lower levels of FT3, FT4, TT3 ALT, TC, TG, PLT, ALB, TT4 and BMI than those without the condition ($p < 0.05$). The values of HDL-C, LDL-, AST, and TSH did not differ significantly between the two categories ($P > 0.05$) (Table 2).

Regression models 1, 2, and 3 were built with NAFLD as the dependent variable, while levels of FT3, FT4, TT3, TT4, and TSH were designated as independent variables with various regression models, respectively. The results indicated that the association between FT3, FT4, and NAFLD was regarded as

negative (p=0.021, p=0.045), however the correlation between TT4, TT3, and TSH level and NAFLD was the opposite (p=0.468, 0.621, 0.092). Model 1 did not correct any parameters. After adjusting for gender, Model 2 found a negative correlation (p=0.002) between FT3 and NAFLD. In the meantime, there was a negative correlation (p=0.012) between the FT4 level and NAFLD. There was no positive link between NAFLD and TT3, TT4, or TSH levels (p=0.409, 0.352, 0.081). Age, BMI, TG, and HDL were adjusted for in Model 3. The study's findings made it clear that FT3 had a negative relationship with NAFLD (p=0.004) (Table 3 and Figure 1).

Discussion.

Obesity and diabetes mellitus are closely associated with nonalcoholic fatty liver disease (NAFLD). Among other histological abnormalities, it encompasses cirrhosis, liver cancer, non-alcoholic steatosis, and NASH (non-alcoholic steatohepatitis) [17]. Type 2 diabetes is a major risk factor for NAFLD, and those with T2DM who also have NAFLD are more likely to have additional metabolic syndrome components such obesity, hypertension, and hyperlipidemia [18]. In our study, 210 (60.0%) of the T2DM cases had NAFLD. Our findings indicated that T2DM patients with NAFLD had higher levels of BMI, ALT, AST, TG, TC, and TT3 than T2DM patients without NAFLD. This suggests that patients with NAFLD were more likely to be obese, have metabolic issues, and have liver damage. There was also a decrease in HDL-C, FT3, FT4, and TT4. Thyroid hormone is involved in human lipid metabolism, produces lipolysis in the liver, and aids in the storage and degradation of lipid droplets in the liver lysosome [19]. individuals with advanced liver fibrosis have lower levels of AST, ALT, TT3, TT4, FT3, and FT4 than individuals without advanced liver fibrosis, according to the NFS score. Low thyroid function decreases the liver's lipase activity and triglyceride clearance, which results in intrahepatic triglyceride accumulation and the development of non-alcoholic fatty liver disease (NAFLD). and this outcome was consistent with the findings of Manka et al. (2019) [20]. Therefore, as FT3's serum level drops, its protective actions in the liver are lessened, which may accelerate the onset and progression of hepatic fibrosis [21]. In individuals with non-alcoholic fatty liver disease (NAFLD), FT3 and FT4 levels independently are strongly correlated with the development of hepatic fibrosis. When BMI, TG, HDL, and NAFLD were taken into account, this study showed a significant negative connection between FT3 and FT4. This finding is in line with that of Loria P et al. [22], who showed that low levels of FT4 raised triglyceride levels in T2DM patients as the risk of NAFLD increased. This study included 232 patients with normal thyroid function in T2DM, and the current finding that there was a clear trend of an increase in the incidence of NAFLD and a decline in FT4 levels suggests that FT3 and FT4 levels independently have a close relationship with the risk of hepatic fibrosis that occurs in patients with NAFLD. Furthermore, our research revealed no association between NAFLD and the risk factors TT4, TT3, and TSH. On the other hand, Kim et al. (2019) [23] and Bano et al. (2016) [24] observed that a higher risk of liver fibrosis was linked to higher TSH levels and lower FT4 levels. The different study populations and advanced fibrosis diagnosis criteria for NAFLD may be the source of the discrepancies. Additionally, the serum level of FT3 was not examined in any of these two studies. The current investigation found that FT3 levels were lower in patients with severe fibrosis than in those without the condition. Even after adjusting for sex, WC, SBP, TC, TG, HOMA-IR, and Scr, there was still a link between FT3 levels and advanced fibrosis. Even though FT3 is not used as much in everyday treatment, a low FT3 level seems to be an independent risk factor for progressive fibrosis in people with NAFLD and T2DM.

Conclusion and Recommendations.

The study's findings suggest a strong correlation between aberrant thyroid hormone levels and liver fibrosis in individuals with type 2 diabetes. a low FT3 level is an independent risk factor for advanced fibrosis, and cases of NAFLD and T2DM are also observed to be negatively correlated with the prevalence of advanced fibrosis. indicated that thyroid hormone levels in T2DM patients should be routinely assessed for evaluating the patient's condition and predicting the prognosis, and that blood FT3 and FT4 levels may be crucial for the prediction of advanced fibrosis.

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