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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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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.

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**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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# THE STUDY OF VDR FOKI rs2228570 SNP IN AUTOIMMUNE THYROIDITIS

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## Abstract.

**Aim:** Autoimmune thyroid disease (AITD) is a common organ-specific autoimmune disease. A strong influence of genetic and epigenetic modifications has been demonstrated to take part in the development and progression of autoimmune thyroid diseases. The linkage between the Vitamin D receptor (VDR) polymorphism and several autoimmune disorders, including the AITD. In this article, we aim to investigate the Frequency of VDR FokI (rs2228570) genotypes (CC, CT, TT) and alleles (C,T) in autoimmune thyroiditis.

**Materials and methods:** The investigation of VDR FokI (rs2228570) was conducted on 150 samples (control (75 healthy women) and diseased women (75 diseased with autoimmune thyroiditis)) patients from the Adjara (Georgia) Population. It also examined some clinical and laboratory characteristics of the study population. Autoimmune thyroiditis's disease was diagnosed by measuring blood antibodies, determining the level of thyroperoxidase, and conducting an ultrasound examination. Anti-TPO and TSH were studied using the ELISA method. The genomic DNA was extracted from the peripheral blood. The polymerase chain reaction was evaluated to examine the VDR FokI rs2228570 SNP polymorphism.

**Results:** According to VDR FokI (rs2228570) genotypes (CC; CT, TT) frequency, in the control group, the Frequency of CC-genotype is 48%, CT-heterozygous genotype is 29.33%, and TT-genotype is 22.67%; in the diseased population, the Frequency of CC-genotype is 57.33%, CT-genotype is 34.67%, and TT-genotype is 8%. According to VDR FokI (rs2228570) alleles (C, T), the Frequency of the C-allele is high, and the Frequency of the T-allele is low in both populations.

**Conclusion:** The Frequency of the CC and CT genotypes of VDR FokI (rs2228570) is high in the population with autoimmune thyroiditis compared to the control group; the TT genotype is relatively low in the population suffering from autoimmune thyroiditis; According to VDR FokI (rs2228570) alleles (C, T), the Frequency of C-allele is high both population.

**Key words.** Autoimmune thyroiditis, Vitamin D Receptor, single nucleotide polymorphism.

## Introduction.

Autoimmune thyroid disease (AITD) is a common organ-specific autoimmune disease. A strong influence of genetic and epigenetic modifications has been demonstrated to take part in the development and progression of autoimmune thyroid diseases. Environmental factors like drugs, iodine, hormone, multivitamin levels, radiation, and viral infections have been shown to have immunomodulatory and toxic effects. Some genes have been identified that contribute to the phenotype of the diseases. The genes involved can be classified as 1) Thyroid specific, e.g., the genes regulating the TSH receptor and Thyroglobulin, and 2) Immunomodulatory- the genes that regulate the immune system, e.g., HLA, CTLA4, IL2, Vitamin D Receptor (VDR- FOXP3) etc. Over centuries, it has been observed that first-degree relatives are more common to suffer from autoimmune diseases if someone in the family has one. The association between AITD and Human Leukocyte Antigens (HLAs) was the pioneer study that provided a mechanism for the genetic basis of AITD. These associations have been studied and demonstrated in twin studies [1]. The HLA genes form the major histocompatibility complex (MHC), which contains many genes related to immune system functions. These include a) HLA class I (A, B, and C), b) HLA class II (DP, DM, DOA, DOB, DQ, and DR), and c) HLA class III (coding for other immune proteins). The major GD-associated HLA is HLA-DR3 as a predisposing factor, while HLA DR7 was shown to have a protective role [2]. It plays a vital role in the normal immune response by binding peptide antigens in its pocket and presenting them to T-cell receptors. HLA genes aren't well established in the case of HT. A few studies have demonstrated HLA DR and DQ to be linked to Hashimoto's thyroiditis (HT) development and progression. The cytotoxic T-lymphocyte-associated protein 4 (CTLA4) gene is an immune regulatory molecule and negatively regulates Helper T cell activation. DeGroot and Colleagues first demonstrated the association between CTLA4 and autoimmunity. CTLA-4 was shown to confer susceptibility to producing thyroid antibodies (TAb) alone without the clinical disease [3]. Numerous research has been done, but the mechanisms by which the CTLA4 variant makes susceptibility to AITD have not been ascertained. The Protein Tyrosine Phosphatase-22 (PTPN22) produces a protein called LYP- lymphoid tyrosine phosphatase, which like CTLA4, negatively regulates T-cell activation. A tryptophan/arginine substitution at the codon 620 (R620W) of PTPN22 was found to be associated with AITD, including both Graves' disease (GD) [4] and HT [5] as well as with other autoimmune diseases. Genetic polymorphisms in the FOXP3 gene may promote autoimmune thyroid disease by weakening the inhibitory function of Tregs. Vitamin D receptor (VDR) polymorphisms have been receiving attention recently. VDR is an intranuclear receptor that has been shown to regulate immunoregulation by altering the expression of T-regulatory (Tregs) cells. Several SNPs have been known to be involved in VDR polymorphisms. Significant associations have been seen between SNP rs2228570 and AITD risk. The association is seen significantly more in HT than GD. Thyroglobulin is a homodimer protein that serves as a substrate and storehouse for the synthesis of thyroid hormones. It is one of the main targets of immune responses and the antibodies against it are also used as a marker for disease development and progression. HT

is characterized by chronic inflammation of the thyroid gland and the synthesis of thyroid peroxidase antibodies (TPO Ab) and/or thyroglobulin antibodies (TG Ab) [6]. Numerous VDR Single nucleotide polymorphisms (SNPs) have been identified, although the most studied is VDR SNP rs2228570 (FokI) in developing AITD. FokI is located in the start codon of the VDR gene, resulting in alternative splicing and production of two VDR isoforms, namely, VDR L and VDR S [7] Long isoform (VDR L) contains the functional domain of the receptor. In contrast, the short isoform (VDR S) has reduced transcriptional activity [8]. The T allele in rs2228570 results in VDR L isoform production while the C allele leads to VDR S isoform production. [9] It has been postulated that the mechanism that influences FokI polymorphism in the pathogenesis of AITD is due to VDR S reduced transcriptional activity, there is decreased expression of genes involved in inflammation, and various immunological functions. In addition, it is hypothesized that FokI polymorphism has altered interaction of various coactivators and corepressors with the VDR receptor leading to altered gene expression. The association between Vitamin D receptor (VDR) polymorphism and several autoimmune disorders, including but not limited to diabetes mellitus 1, Systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis, and tuberculosis, has been extensively studied. Autoimmune thyroiditis is one of the disorders where this association is observed. However, the impact of VDR SNPs on autoimmunity susceptibility varies across different populations and ethnicities. In this article, we aim to investigate the Frequency of VDR FokI (rs2228570) genotypes (CC, CT, TT) and alleles (C, T) in autoimmune thyroiditis.

## Materials and methods.

The investigation of VDR FokI (rs2228570) was conducted on 150 samples (control (75 healthy women) and diseased women (75 diseased with autoimmune thyroiditis)) patients from Adjara (Georgia) Population. The study also examined certain clinical and laboratory characteristics of the study population. The mean age of the control group was 43±16.84, and the mean age of the diseased group was 41.71±14.96 (p=0.5747). Autoimmune thyroiditis was diagnosed by measuring blood antibodies, determining the level of thyroperoxidase, and conducting an ultrasound examination. Anti-TPO, and TSH were studied using the ELISA method. The genomic DNA was extracted from the peripheral blood. The polymerase chain reaction (PCR) was performed to investigate the polymorphisms of the VDR rs2228570 gene. The PCR primers were: Forward, 5′- CTGGCACTGACTCTGGCTCT and Reverse, 5′- GGGCTCACCTGAAGAAGCCT. PCR was performed: 5 min at 94°C - the initial denaturation step; then 30 amplification cycles of: the denaturation: 95°C for 30 s; annealing: at 59°C for 30 s; the extension - at 72°C for 30 s; Final extension - 5 min at 72°C; FokI genotyping was evaluated by restriction fragment length polymorphism (RFLP). C allele was not cleaved and presented a unique 204 bp band, while the T allele yielded 156 and 48 bp products detected by electrophoresis on the 2% agarose gel. The statistical analyses were performed by Graphed Prism (Version 9.0).

## Results.

The pituitary thyrotrophic TSH hormone concentration in a healthy population was elevated about ~1.39 times within autoimmune thyroiditis compared to the control group (Figure 1).

Compared to the healthy population, the high concentrations of antibodies against thyroperoxidase (Anti-TPO) were revealed in autoimmune thyroiditis. In particular, the level of Anti-TPO antibodies was increased ~48 times (Figure 2).

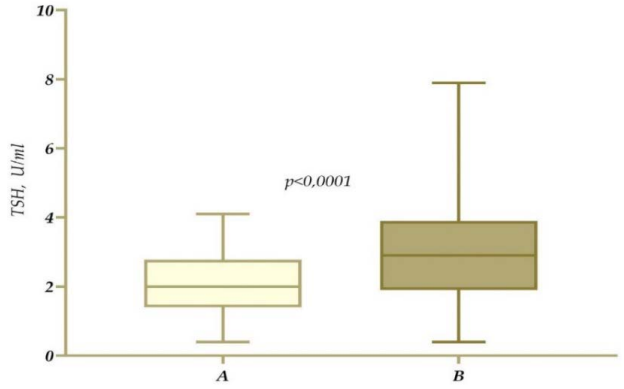


***Figure 1.*** *Study of TSH's Levels in autoimmune thyroiditis. A - control group; B - autoimmune thyroiditis group.*

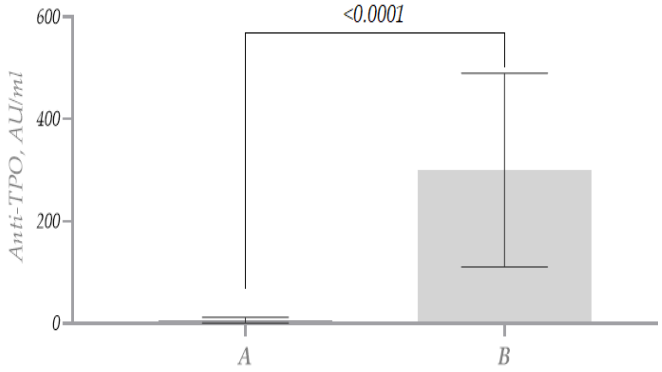


***Figure 2****. Anti-TPO's levels in autoimmune thyroiditis. A - the control group; B - The autoimmune thyroiditis group.*

According to frequencies of VDR FokI (rs2228570) CC, CT, and TT genotypes (Table 1) and alleles (C,T) have revealed differences between the healthy and diseased populations. As already well known, the rs2228570 polymorphism produces two different protein lengths by the vitamin D receptor, depending on whether t is in the second exon of the start codon (contains ATG or ACG. Specifically, if the second nucleotide in the start codon of the second exon is cytosine instead of thymine, a protein containing 423 amino acids is produced instead of the normal protein containing 427 amino acids. The literature suggests that the short (423 amino acid length) and long (427 amino acid length) vitamin D protein molecules have different activity levels.

The study population was analysed for the CC-dominant homozygous (which represents the wild type), CT-heterozygous,

***Table 1.*** *Study of the FokI (rs2228570) genotypes's frequency in autoimmune thyroiditis.*

| Study object | Number of samples (n) | Age | CC Genotype n (%) | CT Genotype n (%) | TT Genotype n (%) |
|---|---|---|---|---|---|
| **Total** | n=150 | 42.8±25.7 | 79 (52,67%) | 48 (32.%) | 23 (15%) |
| **Control group** | n=75 | 43 ±16,84 | 36 (48%) | 22 (29,33%) | 17 (22,67%) |
| **Autoimmune thyroiditis's group** | n=75 | 41,71±14,96 | 43 (57,33%) | 26 (34,67%) | 6 (8%) |

***Table 2.*** *To study of VDR Fokl (rs2228570) alleles' frequency (C, T) in autoimmune Thyroiditis.*

| Study object | Number of samples (n) | Age | The Frequency of the C-allele | The Frequency of the T-allele | P Value |
|---|---|---|---|---|---|
| **Total** | n=150 | | 0,6867 | 0,3133 | |
| **Control group** | n=75 | 43±17,74 | 0,62667 | 0,37333 | 0,00541 |
| **Autoimmune thyroiditis's group** | n=75 | 41,77±1,45 | 0,74667 | 0,25333 | 0,76922 |

and TT-genotypes. As previously mentioned, our research showed a difference in the Frequency of genotypes between the health and diseased groups. In the control group, the CC genotype's Frequency is 48%, the CT genotype is 29.33%, and the TT genotype is 22.67% (Table 1). In the autoimmune thyreoditis's population, the distribution of the CC genotype was 57.33%, the CT genotype - 34.67%, and the TT genotype - 8% (Table 1). The distribution of the CC- homozygous and CT-heterozygous genotypes was relatively higher in the autoimmune thyroiditis population compared to the control group. It should be noted that the frequency distribution of the CC and CT genotypes was higher in the control (health population) group than the TT genotype. Overall, the TT genotype was relatively low in both populations compared to the CC and CT genotypes. However, its percentage was relatively higher in the healthy population than in the diseased population. Our study shows that the CC and CT genotypes may represent relatively more disease-susceptible than the TT genotype.

The study revealed a high percentage of CC genotype in both study populations. However, a relatively higher prevalence of the CT genotype was observed in the diseased population (29.33% in the control group and 34.67% in the diseased population). In the entire population, the genotype distribution was as follows: CC-52.67%, CT-32%, and TT-15%. Based on these results, a relatively high frequency of the CC genotype was observed, suggesting that the CC genotype may be associated with susceptibility or propensity to autoimmune thyroiditis in the population of Adjara.

According to the alleles, the C allele frequency is higher than the T allele in both populations. Notably, the Frequency of the C allele was 0.74667 (q=0.74667) in Autoimmune thyroiditis compared to the control group, where there is 0.62667 (q=0.62667). On the other hand, the T allele frequency was high ~ 1.5 times in the healthy population than in the diseased population. The prevalence of the C allele was ~ 1.7-times higher than the T allele in the control group (p=0.00541). In contrast, in the population with autoimmune thyroiditis, the frequency of C allele was ~ 2.9 -times higher than the T allele. Although the Frequency of the T allele was slightly higher in the diseased population compared to the control group (p=0.2533), OR=1.450; (95%CI (0.8185-2.608)), it was still lower than the prevalence of the C allele in both study populations (Table 2).

## Discussion.

Zarrin et al.'s research in northwest Iran compared 121 adult patients with autoimmune Thyroiditis and Graves' disease (GD) and 117 healthy controls. The results indicated that individuals with Fokl CC and CT genotype had a higher risk of AITDs; specifically, the CC genotype showed a higher likelihood of developing Hashimoto thyroiditis (p= 0.04; OR= 3.38). The study also concluded not much difference was noticed between Fokl and Apal polymorphism in AITD patients and healthy controls [10]. In a study conducted by Hanna et al. in 2021, the focus was on the prevalence of the FokI polymorphism in the Egyptian population, specifically in patients with Hashimoto's Thyroiditis (HT) and hypothyroidism as controls. The study analyzed a sample size of 112 HT patients and 48 hypothyroid patients as controls. The study's results consistently showed a higher occurrence of the FokI polymorphism in HT patients (11.4%) as compared to controls, where there were zero occurrences. The findings indicate a potential correlation between the FokI polymorphism and the occurrence of Hashimoto's Thyroiditis in the Egyptian population. Moreover, the study also explored the Frequency of the FF genotype in the general Egyptian population, which was found to be relatively low in non-HT individuals (2.6%) and hypothyroid control patients (6%). Also found that BsmI polymorphism had no significant association compared to Fokl. This suggests that the FokI polymorphism is more likely associated with autoimmunity in the Egyptian population, specifically in patients with Hashimoto's Thyroiditis [11].

An individual's genetic makeup determines their risk of developing certain diseases. In the case of Hashimoto's Thyroiditis, dominant or recessive genes have been found to impact the risk assessment. A study conducted in the Iraqi population found that the presence of the homozygous genotype (FF) was higher in patients with Hashimoto's Thyroiditis, with a p-value of 0.0002 and an odds ratio (OR) of 2.22. This indicates that individuals carrying the dominant genotype have a two-fold higher risk of developing Hashimoto's Thyroiditis. On the other hand, the study also found that individuals with the heterozygous

genotype (Ff) and homozygous recessive genotype (ff) had a lower risk of developing the disease, with an OR of 0.63 and 0.40, respectively. The p-values for these genotypes were 0.029 and 0.017, respectively. This suggests that individuals carrying the heterozygous or recessive genotype have a lower risk of developing Hashimoto's Thyroiditis. In summary, dominant, or recessive genes play a crucial role in the risk assessment of Hashimoto's Thyroiditis. While the homozygous genotype (FF) increases the risk of the disease, the heterozygous (Ff) and homozygous recessive (ff) genotypes offer protection against the condition in the Iraqi population [12]. Despite the observed association between VDR polymorphisms and autoimmune thyroid disease (AITD), some populations have failed to show consistent results [13]. For instance, a study was conducted on 223 adult Caucasian Polish patients with AIT and 130 unrelated controls of the same origin. The study found no significant association between the rs2228570 FokI polymorphism and the risk of disease occurrence in the studied population [14]. These findings suggest that the association between VDR polymorphisms and AITD may be influenced by factors such as ethnicity, geographical region, and lifestyle factors like diet and sunlight exposure, leading to inconsistencies in the results. SNPs such as VDR rs1544410 (BsmI), rs7975232(ApaI), and rs731236 (TaqI) polymorphisms have shown susceptibility to AITD development. An association in the Apa I gene has been identified in the Southwest Chinese Han population. A case-control cohort study was conducted to investigate this association, comprising 650 Chinese individuals with Graves' disease (GD) and 1209 healthy controls. The study aimed to examine the role of various genetic polymorphisms, including VDR/Apa I, FokI, TaqI, and BsmI, in developing GD. The study results showed that the AA genotype and A allele of VDR/Apa I were significantly associated with the risk of developing GD. In contrast, no significant correlation was found between GD and other polymorphisms, such as FokI, TaqI, and BsmI. These findings suggest that VDR mRNA expression and levels of secreted cytokines may play a role in the development of GD [15].

After conducting a meta-analysis that looked at the relationship between ethnicity and VDR polymorphisms found that the rs1544410 polymorphism is associated with an increased risk of autoimmune thyroid disease (AITD) in Asian populations. In contrast, African and European populations showed a decreased risk of AITD. Additionally, the rs731236 polymorphism in both Asian and African populations is associated with an increased risk of AITD, including Hashimoto's thyroiditis and Graves. At the same time, no significant relationship was found in European populations. These findings suggest that the effect of VDR polymorphisms on AITD risk varies by ethnicity, highlighting the importance of considering genetic variations in different populations [16]. Although association varies among the population, VDR SNP rs2228570 (FokI) is proposed as a potential risk for AITD susceptibility. However, this association's pathogenesis is unclear and requires further studies to determine the significant clinical significance of such genetic variations among populations.

## Conclusion.

According to VDR Fokl (rs2228570) genotypes (CC; CT, TT) frequency, in the control group, the Frequency of the CC-genotype is 48%, CT-heterozygous genotype is 29.33%, and TT-genotype is 22.67%; in the diseased population, the Frequency of CC-genotype is 57.33%, CT-genotype is 34.67%, and TT-genotype is 8%. The CC and CT genotypes of VDR Fokl (rs2228570) are high in the population with autoimmune thyroiditis compared to the control group; TT genotype is relatively low in the population suffering from autoimmune thyroiditis; According to VDR Fokl (rs2228570) alleles (C, T ), the Frequency of C-allele is high both population; And the Frequency of T-allele is low in both populations; The high Frequency of the C-allele (1.2-fold) was revealed in the autoimmune thyroiditis's population compared to the control group. The Frequency of the T allele is low (1.5 times) in the autoimmune thyroiditis population.

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