GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 9 (366) Сентябрь 2025

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.

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Содержание:

GEORGIAN MEDICAL NEWS
No 9 (366) 2025

CYTOLOGICAL EXAMINATION OF THYROID NEOPLASMS IN INDIGENOUS RESIDENTS LIVING IN THE FORMER SEMIPALATINSK NUCLEAR TEST SITE AREA

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Abstract.

The Semipalatinsk Nuclear Test Site (SNTS) was a major source of radiation exposure for the population of East Kazakhstan between 1949 and 1989. Ionizing radiation is known to have significant mutagenic effects on thyroid tissue, increasing the incidence of benign and malignant thyroid neoplasms. This study analyzes the cytological features of thyroid nodules among native residents of radiation-affected areas and evaluates intergenerational differences in disease prevalence.

Objectives: To assess the diagnostic value of fine-needle aspiration biopsy (FNAB) in identifying benign and malignant thyroid lesions among populations exposed to chronic radiation and to investigate the cytomorphological patterns associated with each generation of residents.

Methods: A retrospective cross-sectional analysis was conducted on 134 native patients from high-radiation-risk areas of East Kazakhstan who underwent ultrasound-guided FNAB between 2013 and 2023. Clinical, ultrasound, and cytological data were evaluated, with generational stratification based on birth year in relation to periods of nuclear testing.

Results: A total of 134 patients were included in the study, with 92.5% females (n = 124) and 7.5% males (n = 10). The majority of patients were of Kazakh ethnicity (60.4%, n = 81), with the remainder belonging to other ethnic minorities, predominantly of Slavic origin (38.8%, n = 52). The mean age was 63.98 ± 12.6 years. Based on fine-needle aspiration biopsy (FNAB), the diagnoses were as follows: papillary thyroid carcinoma (PTC) – 42 cases (31.3%), suspicion of PTC – 40 cases (30.1%), follicular adenoma – 45 cases (33.8%), follicular variant of PTC (FVPTC) – 6 cases (4.5%), and medullary carcinoma – 1 case (0.8%). The highest incidence of malignant lesions was observed in the first generation (born 1949–1962), which correlates with higher radiation exposure during atmospheric nuclear testing. The second generation (born 1963–1983) showed a moderate decline in malignancy rates, though the risk remained elevated. The third generation (post-1983) exhibited minimal incidence of malignancy, but a notable increase in benign lesions, such as follicular adenomas, potentially due to residual radiation exposure.

Conclusion: The findings underscore the long-term impact of radiation exposure on thyroid pathology in affected populations. FNAB remains a highly effective diagnostic tool, especially when combined with ultrasound criteria. Intergenerational analysis supports a radiation dose-dependent relationship in the development of thyroid malignancies, with implications for screening and preventive strategies in high-risk regions.

Key words. Thyroid cancer, fine-needle aspiration biopsy, radiation exposure, cytology, papillary thyroid carcinoma, follicular adenoma, Bethesda classification.

Introduction.

Nodular thyroid disease is a prevalent condition, with a reported clinical incidence of 6% in women and 1% in men [1-7]. The majority of nodules detected through ultrasonography are benign; however, approximately 5% are malignant. Ultrasonography, in conjunction with fine-needle aspiration biopsy (FNAB), plays a pivotal role in the characterization of thyroid nodules and in guiding further clinical management. In recent decades, the incidence of thyroid cancer has been rising, particularly the papillary thyroid carcinoma (PTC), which now accounts for nearly 84% of all malignant thyroid tumors [1,8].

Papillary thyroid carcinoma is a malignant epithelial tumor characterized by the proliferation of follicular cells exhibiting distinctive nuclear features such as nuclear clearing, grooves, and pseudoinclusions [1]. Histologically, PTC encompasses several subtypes, including the classical papillary, follicular variant (FVPTC), and solid variants.

The growing recognition of the histological variants of PTC has led to refinements in pathological classifications. Notably, in 2016, Nikiforov et al. proposed renaming the "non-invasive encapsulated follicular variant of papillary thyroid carcinoma" (nEFVPTC) as "non-invasive follicular thyroid neoplasm with papillary-like nuclear features" (NIFTP), based on evidence indicating its indolent behavior and favorable prognosis [9-11]. Consequently, NIFTP was excluded from the carcinoma category, leading to significant changes in preoperative malignancy risk assessment [3,12-19] and influencing surgical and postoperative treatment strategies. The introduction of the NIFTP concept has impacted the cytological evaluation of thyroid nodules, particularly in diagnostic categories such as "Atypia of undetermined significance" or "Follicular lesion of undetermined significance" (AUS/FLUS), "Follicular neoplasm or suspicious for a follicular neoplasm" (FN), and "Suspicious for malignancy" (SusM). These adjustments were incorporated into the revised Bethesda System for Reporting Thyroid Cytopathology (BSRTC) in 2017 [9].

Accurate determination of the benign or malignant nature of a thyroid nodule remains the central diagnostic objective, as it directly influences treatment decisions. The most common thyroid neoplasms include follicular adenoma (FA), papillary carcinoma (PC), and its follicular variant (FVPTC). FA is a benign epithelial neoplasm with a generally favorable clinical course. However, due to its morphological resemblance

to FVPTC, it often presents diagnostic challenges during cytological evaluation [20,21]. PC is the most frequently diagnosed thyroid malignancy, constituting over 80% of all thyroid cancers. FVPTC shares cytological characteristics with both classical PTC and follicular tumors, further complicating diagnostic interpretation.

Nodular thyroid disease is a widespread endocrine disorder affecting a significant portion of the population. Although most nodules are benign, the increasing incidence of PTC over recent decades underscores the importance of reliable diagnostic methods. FNAB remains the gold standard for preoperative assessment, yet differentiating between FA, PC, and FVPTC—especially in the context of indeterminate categories such as AUS/FLUS and SusM—remains a clinical challenge. Recent publications in databases such as PubMed emphasize the need for refined diagnostic criteria and the identification of novel morphological and molecular markers to improve diagnostic accuracy.

The Semipalatinsk Nuclear Test Site (SNTS), active between 1949 and 1989, represents one of the world's most significant sources of environmental radioactive contamination [14,6]. During the period of atmospheric nuclear testing (1949–1962), local populations were exposed to considerable external and internal radiation, primarily due to radioactive iodine deposition from fallout, which entered the body through contaminated food and water sources. Following the site's closure in 1991, scientific attention has largely focused on evaluating the long-term health consequences of radiation exposure, particularly the elevated incidence of thyroid pathologies, including nodular and malignant conditions [2,18].

Epidemiological studies have established a strong correlation between radiation exposure and increased rates of thyroid nodular disease and differentiated thyroid carcinoma. Prior research has confirmed that individuals residing in areas of high radiation risk exhibit a significantly higher frequency of thyroid nodules compared to those in minimally exposed zones [4,5,13,20,21]. Of particular interest are individuals born during the atmospheric testing era (1949–1962), who received the highest radiation doses during childhood—a period of heightened thyroid sensitivity to radiation.

More than three decades have passed since the SNTS was decommissioned. As the number of first-generation individuals exposed during this period gradually declines, the cohort born between 1949 and 1962 remains a high-priority population for study due to their cumulative radiation exposure and the critical developmental timing of their exposure.

According to the Law of the Republic of Kazakhstan "On the social protection of citizens affected by nuclear tests at the Semipalatinsk nuclear test site" (№ 1787-XII, December 18, 1992), the studied territories are officially classified as zones of extreme radiation risk (>100 ber) and maximum radiation risk (35–100 ber). This legal classification served as the basis for defining the exposure categories of the included patients. Between 1949 and 1989, a total of 456 nuclear explosions were conducted at the Semipalatinsk Nuclear Test Site (SNTS), with the greatest radiation exposure occurring during the early atmospheric tests (1949, 1951, 1953) [5]. Ionizing radiation, particularly during childhood, is a well-recognized risk factor for thyroid cancer.

This study aims to analyze the cytological profiles of thyroid nodular lesions in individuals residing in extreme and maximum radiation risk areas, with the goal of identifying patterns indicative of increased susceptibility to thyroid pathologies.

Objective. The aim of this study is to analyze the cytological characteristics of benign and malignant thyroid neoplasms through ultrasound-guided fine-needle aspiration biopsy (FNAB) and to evaluate their diagnostic relevance for improving the accuracy and efficiency of differential diagnosis in patients residing in extreme and maximum radiation risk areas of the former Semipalatinsk Nuclear Test Site (SNTS). Particular attention is given to identifying potential patterns of radiogenic influence on thyroid tissue among individuals exposed to ionizing radiation during early life.

Materials and Methods.

This retrospective cross-sectional study included 134 indigenous patients who underwent FNAB of thyroid nodules between 2013–2023 years. All participants were permanent residents of extreme and maximum risk regions affected by SNTS nuclear fallout and were stratified by generation, with special focus on those presumed to have received the highest cumulative radiation doses during childhood—a developmental period of increased thyroid radiosensitivity.

Clinical data were collected from patient records and included demographic information (age and sex), family history of thyroid cancer, presence of clinical symptoms suggestive of local compression (e.g., dysphagia, hoarseness), and functional thyroid status (euthyroidism, hypothyroidism, or hyperthyroidism). Ultrasound characteristics of the nodules were also documented, including nodule size, echogenicity (hyperechoic, isoechoic, hypoechoic, markedly hypoechoic), vascular patterns assessed via Doppler ultrasound (perinodular, intranodular, or mixed), presence of microcalcifications, structural composition (solid or complex), definition of margins, and classification based on the American College of Radiology TI-RADS system [16].

Cytological evaluation was performed according to the Bethesda System for Reporting Thyroid Cytopathology (BSRTC), with each case classified into one of six categories: non-diagnostic (I), benign (II), atypia of undetermined significance or follicular lesion of undetermined significance (III: AUS/FLUS), follicular neoplasm or suspicious for follicular neoplasm (IV: FN/SFN), suspicious for malignancy (V: SusM), or malignant (VI). In addition to standard categorization, individual cytological features were analyzed in detail [1]. These included nuclear enlargement, irregular nuclear contours, chromatin clearing, presence of nuclear grooves and intranuclear pseudoinclusions, nuclear overlapping and crowding, and qualitative assessment of the cellular material (abundant, moderate, or scant). All cytological data were retrieved from documented pathology reports verified by licensed cytopathologists.

By examining morphological and cytological features of thyroid nodules in a population with documented radiation exposure, this study aims to assess the degree of radiogenic impact on thyroid tissue and to explore the potential

predisposition to malignant transformation. The results will be compared with existing literature to identify diagnostic trends and pathological markers that may assist in early detection, risk stratification, and the development of targeted preventive strategies in radiation-affected regions. The identification of specific cytological patterns in this unique population could offer valuable insights into radiation-induced thyroid pathology and help refine diagnostic criteria used in clinical practice.

Results.

A total of 134 patients with thyroid nodular formations residing in extreme and maximum radiation risk areas of the former Semipalatinsk Nuclear Test Site (SNTS) were included in the study. The majority of participants were female (92.5%, n = 124), while males accounted for only 7.5% (n = 10). Most patients were of Kazakh ethnicity (60.4%, n = 81), followed by individuals from other ethnic minorities, predominantly of Slavic origin (38.8%, n = 52). The mean age was 63.98 ± 12.6 years, ranging from 37 to 91 years (Figure 1).

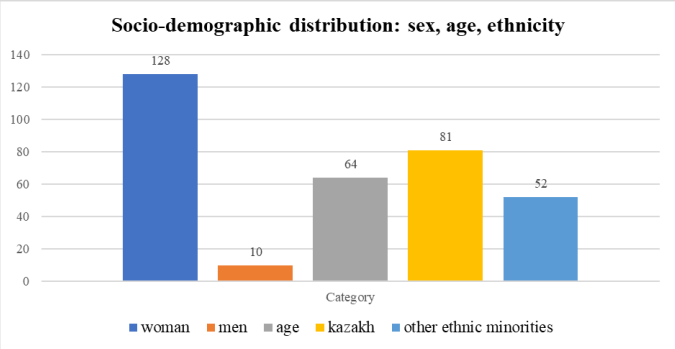

Figure 1. *Socio-demographic characteristics of the study population.*

According to the results of fine-needle aspiration byopsy (FNAB), the distribution of diagnoses was as follows: papillary thyroid carcinoma (PTC) – 42 cases (31.3%), suspicious for papillary carcinoma – 40 cases (30.1%), follicular adenoma – 45 cases (33.8%), follicular variant of papillary thyroid carcinoma (FVPTC) – 6 cases (4.5%), and medullary carcinoma – 1 case (0.8%) (Tab.1). According to the results of the Pearson χ^2 test, the differences in the distribution of tumor types across the three generations were statistically significant ($\chi^2 = 24.88$; $p = 0.0016$). Thus, malignant and suspicious lesions represented over 65% of the total sample. Among the 134 patients, thyroid function tests revealed that the majority were euthyroid, while a smaller percentage were diagnosed with hypothyroidism or hyperthyroidism. The functional status was correlated with the cytological findings, including an increased incidence of hypothyroidism in patients with follicular adenomas.

When analyzed across generations exposed to different levels of radiation, the highest number of malignant and suspicious cases was observed in the first generation (individuals born between 1949 and 1962 during active atmospheric nuclear testing), with 22 confirmed PTC cases and 23 suspicious nodules [2,6,13,18,21]. The second generation (born 1963–1983) demonstrated a moderate decline in malignancy rates (20 PTC, 15 suspicious), while the third generation (post-1983) had no confirmed PTC but exhibited cases of FVPTC and an increase in benign follicular adenomas [5,15,20].

The highest number of papillary thyroid carcinoma cases was recorded among individuals of the first generation, born during the period of active atmospheric nuclear testing. These findings support a strong link between high cumulative radiation doses in childhood and the development of malignant thyroid neoplasms, particularly papillary carcinoma. In addition, cases of the follicular variant of papillary carcinoma (FVPTC) were also noted, indicating the mutagenic impact of ionizing radiation on thyroid tissue. Among representatives of the second generation, whose childhood occurred during the period of underground testing, the incidence of thyroid cancer, including follicular tumors, remained high but was somewhat lower compared to the first generation. This may be attributed to the reduced intensity of radiation exposure, although environmental contamination with long-lived radionuclides persisted. In the third generation, the rate of malignant pathology was minimal (Figure 2). However, there was an increased frequency of benign tumors, such as follicular adenoma, likely linked to chronic exposure to residual radiation through contaminated soil, water, and food, as well as possible transgenerational genetic mutations inherited from parents.

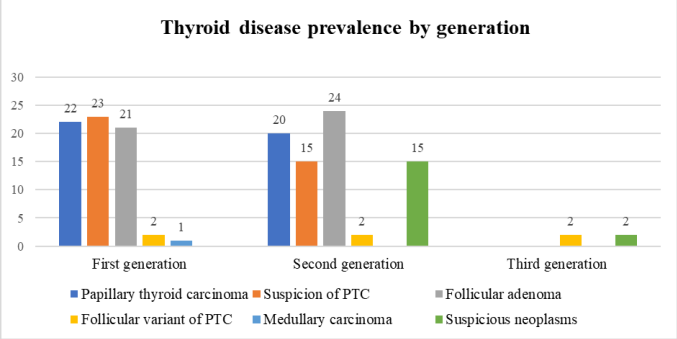

Figure 2. *Thyroid disease prevalence by generation.*

Cytological evaluation revealed distinct patterns correlating with the type of lesion. PTC was characterized by large oval nuclei with irregular membranes, chromatin clearing, nuclear grooves, and pseudoinclusions. Suspicious lesions presented similar features but to a lesser degree. FVPTC cases combined follicular architecture with nuclear atypia typical of papillary carcinoma. Follicular adenomas exhibited monolayered follicular cells with round, clearly contoured nuclei and no signs of vascular invasion or nuclear atypia.

Ultrasound analysis indicated that hypoechoic nodules with irregular margins, microcalcifications, and mixed vascularization were more commonly associated with high Bethesda categories (V–VI). Isoechoic nodules with well-defined borders and peripheral flow patterns were predominantly benign. These findings emphasize the diagnostic value of combining ultrasound and cytological features in populations exposed to chronic radiation.

Cytological diagnosis of papillary thyroid carcinoma (PTC) is primarily based on a set of nuclear features that include nuclear enlargement, chromatin clearing, irregular nuclear contours, nuclear grooves, molding, intranuclear pseudoinclusions,

and papillary architectural formations with clearly defined anatomical boundaries. In cases where these features are only focally present, a definitive malignant diagnosis cannot be established, and such samples are generally classified as "suspicious for malignancy".

Among the morphological variants, the follicular variant of papillary thyroid carcinoma (FVPTC) is the most commonly reported and accounts for up to 30% of all PTCs in some series [14]. In our study, cases of FVPTC demonstrated moderate nuclear hyperplasia, a follicular growth pattern with the presence of colloid, and occasionally subtle nuclear grooves and pseudoinclusions—features which require careful differentiation from benign follicular neoplasms. The presence of dense or viscous colloid and uniform follicular architecture further complicates cytological distinction. In doubtful cases, molecular testing may be required.

Follicular adenoma, a benign epithelial tumor, was frequently encountered in our radiation-exposed cohort. Cytologically, these lesions were characterized by monolayered follicular cells with round, smooth nuclear contours and an absence of pseudoinclusions. The orderly architecture and presence of dense, homogeneous colloid further supported their benign nature.

Discussion.

The analysis of thyroid nodular lesions among residents of eastern Kazakhstan, who were exposed to radiation from the Semipalatinsk Nuclear Test Site (SNTS), remains a highly relevant field of scientific inquiry. Given the pronounced radiosensitivity of thyroid tissue, early detection of precancerous conditions and consistent monitoring of morphofunctional changes are critical for minimizing oncological risks in this population. The results of this study may serve as a foundation for the development of targeted screening programs and ongoing medical support for individuals living in radiation-affected areas.

A comparative generational analysis revealed that individuals from the first generation (born 1949–1962, during active atmospheric nuclear testing) showed the highest incidence of malignant thyroid lesions. The second generation (1963–1983) continued to demonstrate elevated risk, albeit to a lesser extent. The third generation (post-1983), who experienced lower radiation exposure, exhibited the lowest incidence of malignancy, which may be attributed to the gradual reduction in environmental radiation levels [2,18].

Cytological examination confirmed that the majority of papillary thyroid carcinoma (PTC) cases were diagnosed in the first generation, highlighting the role of ionizing radiation as a key etiological factor. Follicular tumors, including benign follicular adenomas, were also frequently observed in this cohort, warranting further investigation into their radiation-induced pathogenesis.

The introduction of the NIFTP (non-invasive follicular thyroid neoplasm with papillary-like nuclear features) concept has helped reduce diagnostic ambiguity and improved the clinical management of indeterminate thyroid lesions. Nonetheless, the identification of refined diagnostic criteria and additional morpho-molecular markers remains essential for improving accuracy and clinical outcomes.

The predominance of PTC and the presence of FVPTC in exposed cohorts are consistent with observations after other nuclear accidents, such as Chernobyl and Fukushima, as well as previous studies from Semipalatinsk [13].

Overall, the study of thyroid nodular lesions in radiation-exposed populations continues to be a priority for thyroid pathology research. The current findings offer valuable insights into radiation-induced thyroid abnormalities and contribute to the development of early diagnostic and preventive strategies for populations residing in former nuclear testing zones.

FNAB remains the most effective screening tool for evaluating thyroid nodules, particularly in extreme and maximum radiation risk populations. Its ability to accurately distinguish malignant from benign nodules reduces the need for unnecessary surgical interventions and improves patient outcomes. Based on the cytological findings and existing diagnostic criteria, we synthesized practical diagnostic algorithms for differentiating benign and malignant thyroid nodules. These are presented in Figures 2–4 and are discussed in the context of previously published classifications and our clinical observations.

Morphological characteristics play an important role in the differential diagnosis of nodular thyroid diseases, especially in populations exposed to radiation. Taken together, the algorithms for diagnosing malignant and benign tumors illustrate the comprehensive importance of morphological assessment in thyroid pathology. Their implementation in clinical practice not only increases the accuracy of cytological examination by fine-needle aspiration biopsy, but also optimizes patient treatment outcomes by providing a balanced approach between surgical intervention and conservative therapy.

The algorithm for malignant thyroid lesions emphasizes the cytological features that define each nosological unit, clearly describing the diagnostic criteria, which helps to make the correct diagnosis, ensuring timely and correct treatment decisions for high-risk patients.

Equally important is a systematic approach to benign thyroid nodules, where morphological assessment prevents unnecessary surgical interventions. Diagnostic criteria allow benign, inflammatory and autoimmune diseases to be distinguished from malignant ones. The link between these cytological patterns and conservative treatment strategies highlights the practical value of morphological diagnosis in reducing the frequency of overtreatment and determining appropriate treatment tactics for patients.

Table 1. *Distribution of thyroid diagnoses by generation.*

Generation	Suspicious neoplasms	Follicular adenoma	Papillary thyroid carcinoma	Follicular variant of PTC	Medullary carcinoma	Total number	χ^2, p
First generation	23	21	22	2	1	69	
Second generation	15	24	20	2	0	61	24.88
Third generation	2	0	0	2	0	4	0.0016

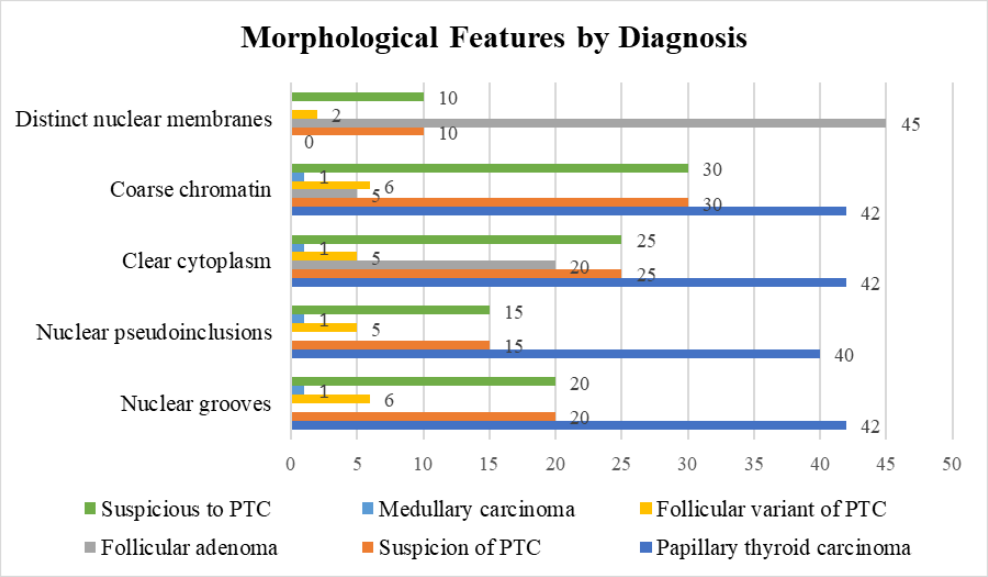

Figure 3. *Distribution of cytomorphological features by thyroid diagnosis.*

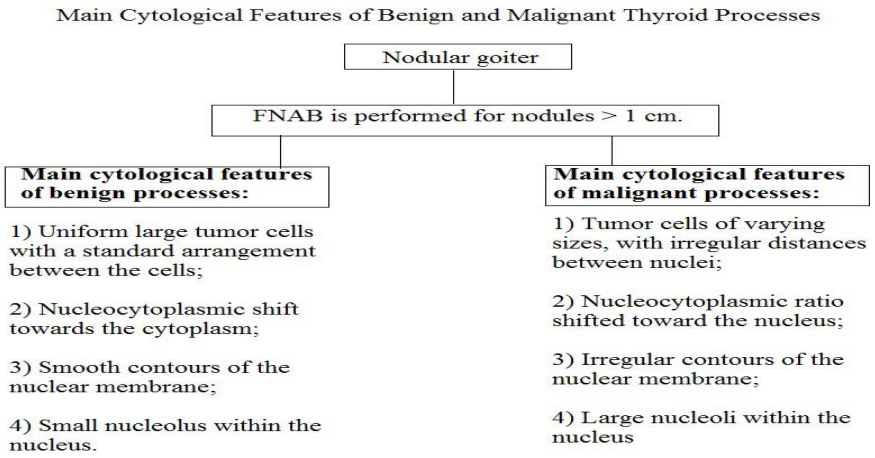

Figure 4. *Main cytological features of benign and malignant thyroid diseases.*

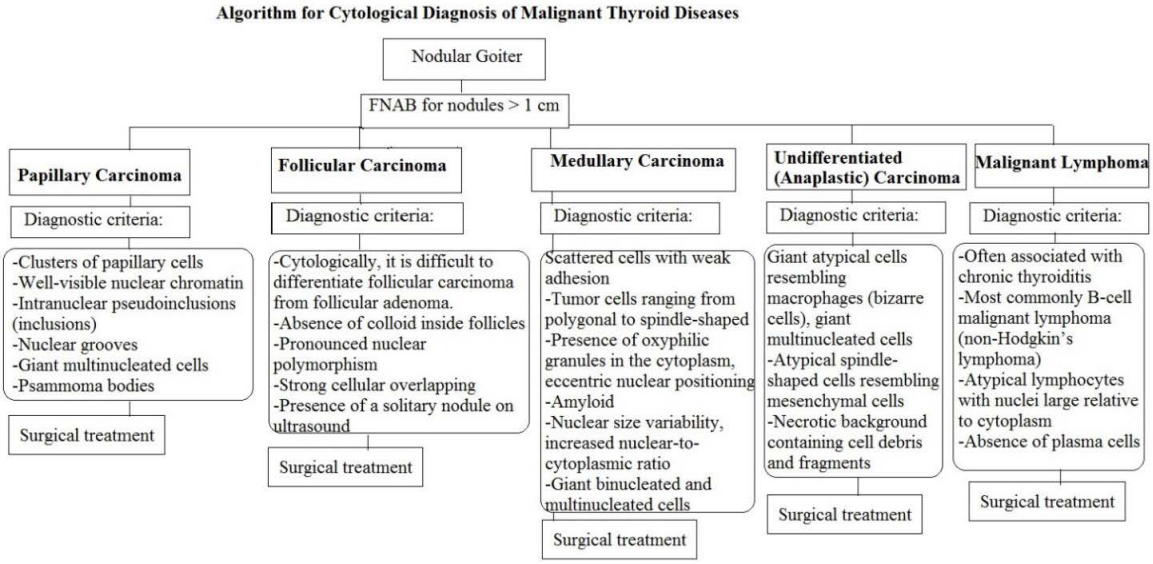

Figure 5. *Algorithm for cytological diagnosis of malignant thyroid diseases.*

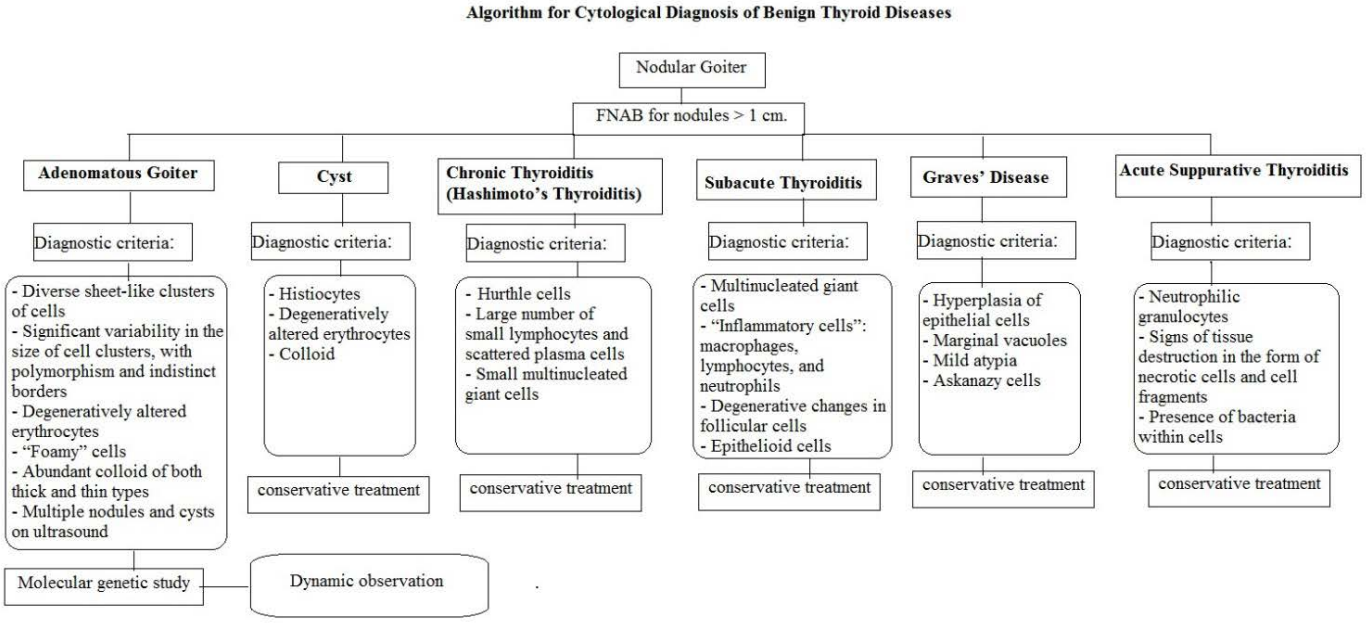

Figure 6. *Algorithm for cytological diagnosis of benign thyroid diseases.*

Advantages.

The study addresses the long-term effects of radiation exposure from the Semipalatinsk Nuclear Test Site (SNTS) on thyroid pathology, which represents a significant public health issue with both scientific and clinical implications. A comparative evaluation of cytological features across three generations of residents provides novel insights into dose-dependent patterns of thyroid pathology associated with different periods of radiation exposure. The integration of clinical, ultrasound, and cytological data strengthens the robustness of the results and ensures a multidimensional assessment of thyroid nodular disease.

Disadvantages.

The predominance of female and Kazakh participants may limit the generalizability of the findings to more diverse populations. Individual radiation doses were not directly quantified and were estimated based on birth period and place of residence, in accordance with the official classification of the studied territories as extreme and maximum radiation risk zones under the Law of the Republic of Kazakhstan. All patients were indigenous and permanent residents of these territories, which minimizes the risk of exposure misclassification. Selection bias may also be present, as the study included only individuals who attended medical facilities and underwent FNAB, however, it should be noted that annual medical check-ups for patients with thyroid nodules are routinely conducted in these regions, which provides broader coverage of the affected population.

Conclusion.

The Semipalatinsk Nuclear Test Site has had a significant impact on the prevalence of thyroid cancer among residents of surrounding territories, especially within the first and second generations. The effects of radiation are reflected in distinctive cytological features, particularly in cases of papillary thyroid carcinoma and its follicular variant. Modern screening techniques enable the detection of these tumors at early stages, which is essential for the prevention and management of radiation-induced malignancies.

Cytological features remain a critical tool in the differential diagnosis of thyroid tumors. Among radiation-exposed individuals, PTC and FVPTC are characterized by nuclear grooves and pseudoinclusions, whereas follicular adenomas retain benign nuclear contours and lack pseudoinclusions. Fine-needle aspiration biopsy (FNAB) facilitates accurate tumor characterization and helps prevent unnecessary surgical interventions in benign cases.

Author Contribution Statement.

A.B., A.K. – Data collection and preparation, initial processing of the material, and its verification, A.B., M.E., A.K. - statistical processing and analysis of the material, drafting of the article (materials and methods, results). M.E., A.K. – Drafting of the article (introduction, discussion). M.E., A.Z – Concept, design, and oversight of the study, approval of the final version of the article. All authors have approved the final version of the manuscript.

Acknowledgements.

The authors would like to thank the administration of the Semey Medical University. We thank the study participants for taking time to complete our questionnaire.

Funding Statement.

This work was supported by the Ministry of Science and Higher Education of the Republic of Kazakhstan, project: IRN AP19680072 "The Role of Molecular Diagnostics in Thyroid Neoplasms," funded by the Ministry of Education and Science of the Republic of Kazakhstan.

Ethical Declaration.

This retrospective cross-sectional study was approved by the Ethics Committee of Semey Medical University (Protocol № 2, November 7, 2022).

Informed Consent.

As the study was based solely on anonymized archival data and no patient-identifying information was available to the investigators, the requirement for individual informed consent was formally waived by the Ethics Committee.

Availability of Data.

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest.

The authors declare no conflicts of interest related to this study.

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