RESEARCH ARTICLE

Editorial Process: Submission:11/01/2024 Acceptance:02/09/2025

Epidemiology of Thyroid Cancer in Kazakhstan and in Areas Adjacent to the Former Semipalatinsk Nuclear Test Site in 2013-2023

Maira Zh. Espenbetova[1], Aida M. Bidakhmetova[1]*, Ainur S. Krykpayeva[2], Bayan A. Yespenbetova[3], Dina M. Toleutayeva[4], Askar S. Serikbayev[5], Assel R. Tukinova[4], Laura B. Uasheva[6]

Abstract

Objective: This study aimed to investigate the incidence and mortality of thyroid cancer (TC) in the Republic of Kazakhstan and East Kazakhstan Region, which includes the areas adjacent to the former Semipalatinsk nuclear test site over the past ten years, from 2013 to 2023. **Methods:** The study included information from Form No. 7 Annual "Report on Patients with Malignant Neoplasms" and "Indicators of the Oncological Service of the Republic of Kazakhstan" for the period 2013-2023. Incidence and mortality rates were calculated per 100,000 population, and data were distributed by gender, age groups, clinical stages. The study included an analysis of trends in annual epidemiological indicators, which allows us to observe fluctuations in Incidence and mortality over time. **Results:** Overall, Republic of Kazakstan experienced a gradual increase in incidence, beginning at 2.9 per 100,000 population in 2013, peaking at 7.2 in 2019, and ending at 5.5 in 2023. East Kazakhstan, however, showed greater fluctuation, with rates ranging from 3.2 to 4.3 per 100,000, with a notable increase in 2023 to 4.7 per 100,000 population, the highest value observed in the study period. In East Kazakhstan, mortality remained steady at 0.4 per 100,000 from 2013 to 2016, briefly increasing to 0.9 in 2018, before stabilizing at 0.4 from 2020 to 2023. Nationwide, TC mortality varied between 0.3 and 0.5 per 100,000, with a gradual decline to 0.3 per 100,000 in 2021 and 2023. **Conclusion:** In the areas adjacent to the former Semipalatinsk nuclear test site, significant fluctuations and peaks in morbidity are observed, which differ from the general republican indicators.

Keywords: Thyroid cancer- nuclear test- epidemiology.

Asian Pac J Cancer Prev, **26 (2)**, 691-699

Introduction

Thyroid carcinoma (TC) is the most prevalent malignancy of the endocrine system, with a steadily increasing incidence globally. According to the Global Cancer Observatory's 2020 data, TC accounted for approximately 586,000 cancer cases worldwide [1]. TC encompasses several histological types, including papillary, follicular, medullary, and anaplastic carcinoma, as well as thyroid lymphoma. Clinically, TC manifests with symptoms such as dysphagia, throat pain, hoarseness, cough, weight loss, and sweating. Diagnostic approaches involve ultrasound, MRI, and scintigraphy, with fine-needle biopsy serving as the primary method for cellular confirmation [2].

While TC represents only 2% of all cancers globally, in 2016 alone, 238,000 new cases were reported, with 43,000 deaths [3]. The age-standardized incidence rates stood at 2.2 per 100,000 in men and 4.4 per 100,000 in women. Over the past three decades, TC incidence has risen significantly, particularly in countries like Lithuania, Italy, Austria, Croatia, and Luxembourg. Although mortality rates remain comparatively low, the rising incidence of TC can largely be attributed to advancements in diagnostic technologies, especially for differentiated thyroid cancers such as papillary carcinoma. By contrast, the incidence of other forms, including follicular, anaplastic, and medullary thyroid cancers, has remained constant [4]. In the United States, TC incidence has surged over the past 40 years, partly due to overdiagnosis; however, an increase in more

*[1]Department of Therapy, NJSC "Medical University of Semey", Semey, Kazhakhstan. [2]Department of Nursing, NJSC "Medical University of Semey", Semey, Kazhakhstan. [3]Department "Finance" NJSC "L.N. Gumilyov Eurasian National University", Semey, Kazhakhstan. [4]Department of Epidemiology and Biostatistics, NJSC "Medical University of Semey", Semey, Kazhakhstan. [5]Department of Emergency Medicine, NJSC "Medical University of Semey", Semey, Kazhakhstan. [6]Endocrinologist of "Center for Nuclear Medicine and Oncology", Semey, Kazakhstan. *For Correspondence: aiidavip656@gmail.com*

aggressive forms and a higher mortality rate have been noted, potentially linked to risk factors like childhood exposure to ionizing radiation and obesity. Incidence rates are region-dependent, with women nearly three times more likely to be affected than men. Risk peaks around ages 55 for women and 65 for men, with lifetime diagnosis risks estimated at 1 in 55 for women and 1 in 149 for men [5]. The rising incidence of TC has been particularly evident in Asian countries, such as South Korea, where cases surged from 4.3 to 5.3 per 100,000 for females from 2008 to 2012, with similar trends among men. Trends in more rare forms, including follicular and medullary cancers, have remained stable, while anaplastic TC has shown a slight decline in prevalence [6]. Recent data from the Russian Federation indicate a 49.03% increase in TC incidence from 2008 to 2018, especially among individuals over 55 years. This increase is likely due to an aging population, enhanced diagnostic techniques, and extended medical follow-up periods, with early-stage TC (stages I and II) representing 77.7% of diagnosed cases [7].

In Kazakhstan, the mean age of TC diagnosis is 51.8 years for women and 53.2 years for men. The incidence rate in women is notably higher, with a peak in the 60–69 age group at 4.21 per 10,000 in men and 15.37 per 10,000 in women, demonstrating upward trends in both sexes (7.8% in women, 5.0% in men) [8]. Given Kazakhstan's historical proximity to the Semipalatinsk nuclear test site, regions like East Kazakhstan experience high levels of background radiation, which has likely contributed to an increased cancer burden, including TC [9]. The East Kazakhstan region, particularly its districts that fall within the radiation exposure zone of the Semipalatinsk test site, represents an area with high risks of radioactive contamination. These districts, according to classification, may fall into various categories of radiation risk levels, depending on the magnitude of the effective equivalent dose of radiation to the population exceeding 0.1 rem over the entire period of testing. Specifically, the territories of East Kazakhstan are divided into zones of extreme, maximum, elevated, and minimal radiation risk, which poses a long-term threat to the health of the population [10] (Figure 1).

As the prevalence and impacts of TC rise, understanding regional disparities and their implications on public health has become imperative. Enhanced data on TC incidence and mortality across Kazakhstan is essential to strengthen early diagnosis, preventive strategies, and effective treatment to improve patient outcomes and mitigate the growing burden on public health.

Materials and Methods

This study aimed to evaluate the incidence and mortality rates of thyroid cancer (TC) in Kazakhstan, with a specific focus on East Kazakhstan Region, over a ten-year period from 2013 to 2023. The comparison of thyroid cancer incidence and mortality rates with the general indicators of the country is due to the historical impact of the Semipalatinsk nuclear test site, which was located in the territory of East Kazakhstan. Population data were sourced from the official website of the Bureau of National Statistics of Kazakhstan, and epidemiological data were obtained from official national reports, specifically the Annual "Report on Patients with Malignant Neoplasms" (Form No. 7) and "Indicators of the Oncological Service of the Republic of Kazakhstan" for the years 2013–2023.

The analysis encompassed all recorded cases of TC incidence and mortality within the study period. Incidence and mortality rates were calculated per 100,000 population, and data were stratified by gender, age groups, clinical stages. The study included a trend analysis of annual epidemiological indicators, allowing for the observation of fluctuations in incidence and mortality over time.

Epidemiological indicators, including annual trends, were calculated to determine changes in incidence and mortality over the specified period. The significance of observed trends was evaluated, with particular attention to changes in clinical stage distribution.

Figure 1. Location of the Former Semipalatinsk Nuclear Test Site on the Map of Kazakhstan

Results

The incidence of thyroid cancer (TC) in the Republic of Kazakhstan and East Kazakhstan Region displayed distinct trends over the study period from 2013 to 2023 (Figure 2). Overall, Kazakhstan experienced a gradual increase in incidence, beginning at 2.9 per 100,000 population in 2013, peaking at 7.2 in 2019, and ending at 5.5 in 2023. East Kazakhstan, however, showed greater fluctuation, with rates ranging from 3.2 to 4.3 per 100,000, with a notable increase in 2023 to 4.7 per 100,000 population, the highest value observed in the study period.

Figure 2 presents a comparative analysis of thyroid cancer (TC) incidence in the East Kazakhstan Region and the Republic of Kazakhstan (2013 to 2023) per 100,000 population. Thyroid cancer mortality in East Kazakhstan Region and Kazakhstan revealed stable trends, with notable regional differences (Figure 3). In East Kazakhstan, mortality remained steady at 0.4 per 100,000 from 2013 to 2016, briefly increasing to 0.9 in 2018, before stabilizing at 0.4 from 2020 to 2023. Nationwide, TC mortality varied between 0.3 and 0.5 per 100,000, with a gradual decline to 0.3 per 100,000 in 2021 and 2023.

Figure 3 shows the dynamics of thyroid cancer mortality in East Kazakhstan Region and the Republic of Kazakhstan (2013 to 2023) per 100,000 population.

Gender disparities in TC incidence were pronounced (Figure 4). Female incidence rates showed an upward trend, from 2.9 per 100,000 in 2013 to 4.2 in 2023, with peaks in 2016 (3.6) and 2019 (3.7) and a notable dip to 2.8 in 2020. Male incidence rates, however, remained consistently low, fluctuating between 0.4 and 0.6 per

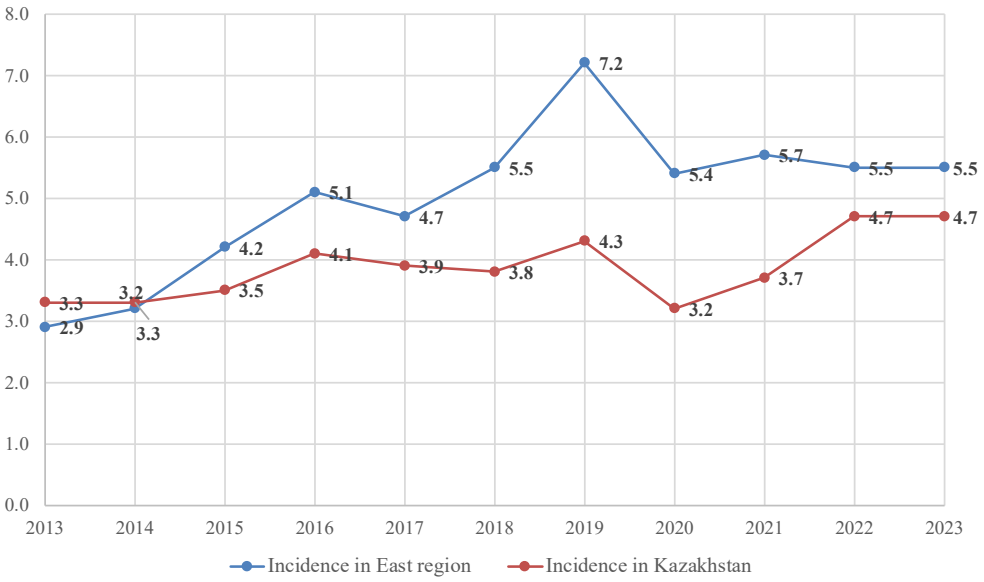

Figure 2. Trend Dynamics of Thyroid Cancer in Kazakhstan and East Kazakhstan Region (2013-2023) per 100,000 Population

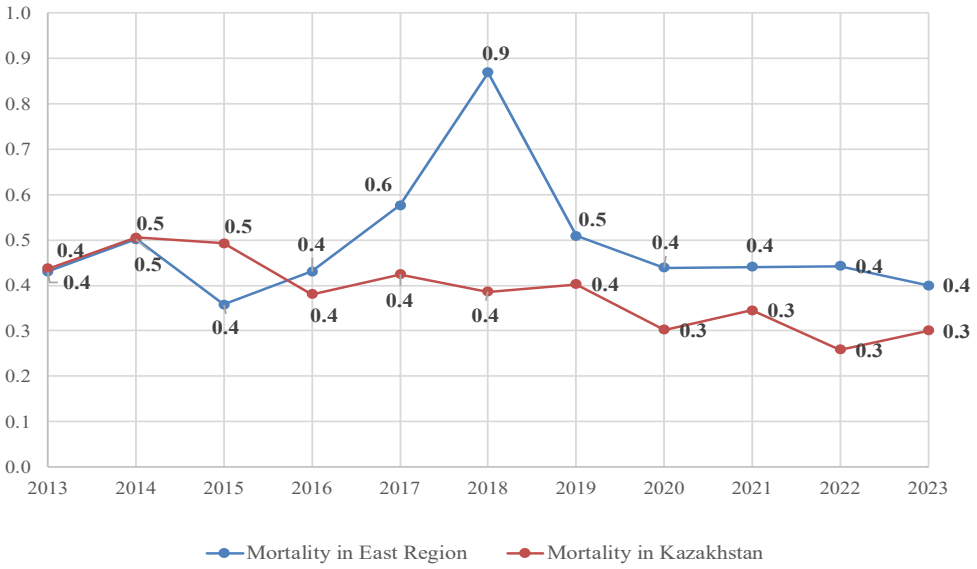

Figure 3. Dynamics of Thyroid Cancer Mortality in East Kazakhstan Region and the Republic of Kazakhstan (2013 to 2023) per 100,000 Population

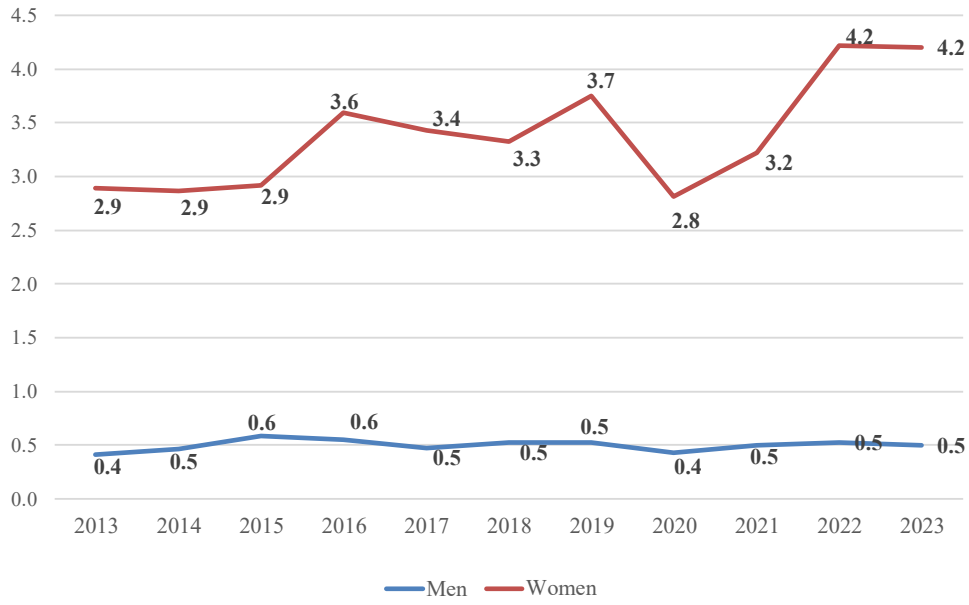

Figure 4. Thyroid Cancer Incidence among Male and Female Populations in the Republic of Kazakhstan (2013-2023) per 100,000 Population

100,000 without significant changes over the period.

Figure 4 illustrates the dynamics of thyroid cancer incidence among men and women in the Republic of Kazakhstan (2013-2023) per 100,000 population. Age group analysis indicated that TC incidence was highest among individuals aged 50-69 and 30-49 years (Figure 5). The 50-69 age group showed the highest incidence, reaching 2.0 per 100,000 in both 2019 and 2023. The 30-49 age group increased steadily from 1.0 in 2013 to 1.9 in 2023. In contrast, incidence in individuals under 29 and over 70 years remained low, with minor increases observed only in the 70+ age group, from 0.3 to 0.5 per 100,000 by 2023.

Figure 5 presents the age group of thyroid cancer incidence in the Republic of Kazakhstan (2013-2023) per 100,000 population. Improvements in early detection rates of TC at stages I-II were observed in East Kazakhstan and across Kazakhstan (Figure 6). In East Kazakhstan, the proportion of cases diagnosed at stages I-II rose from 67.5% in 2013 to 86.7% in 2023. Similarly, the national rate of early-stage detection increased from 79.5% in 2013 to 91.1% in 2023, reflecting advancements in diagnostic imaging and early detection efforts.

Figure 6 illustrates detection rate of thyroid cancer at stages I-II, III-IV in East Kazakhstan Region and Kazakhstan (2013 and 2023). The proportion of TC cases

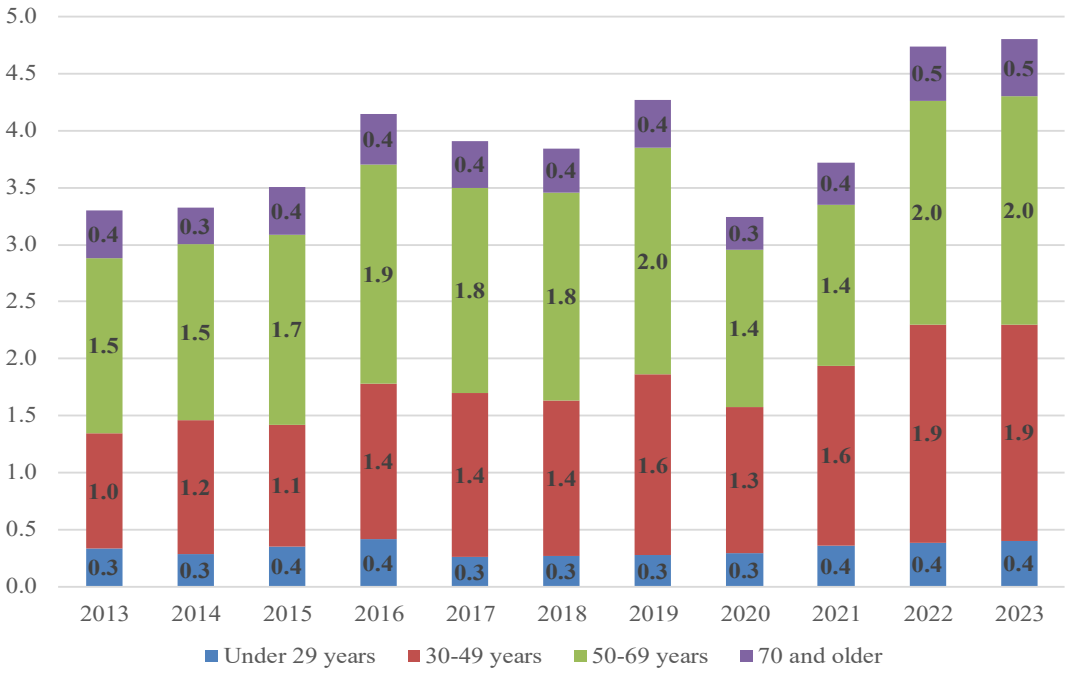

Figure 5. Age Group of Thyroid Cancer Incidence in the Republic of Kazakhstan (2013-2023) per 100,000 Population

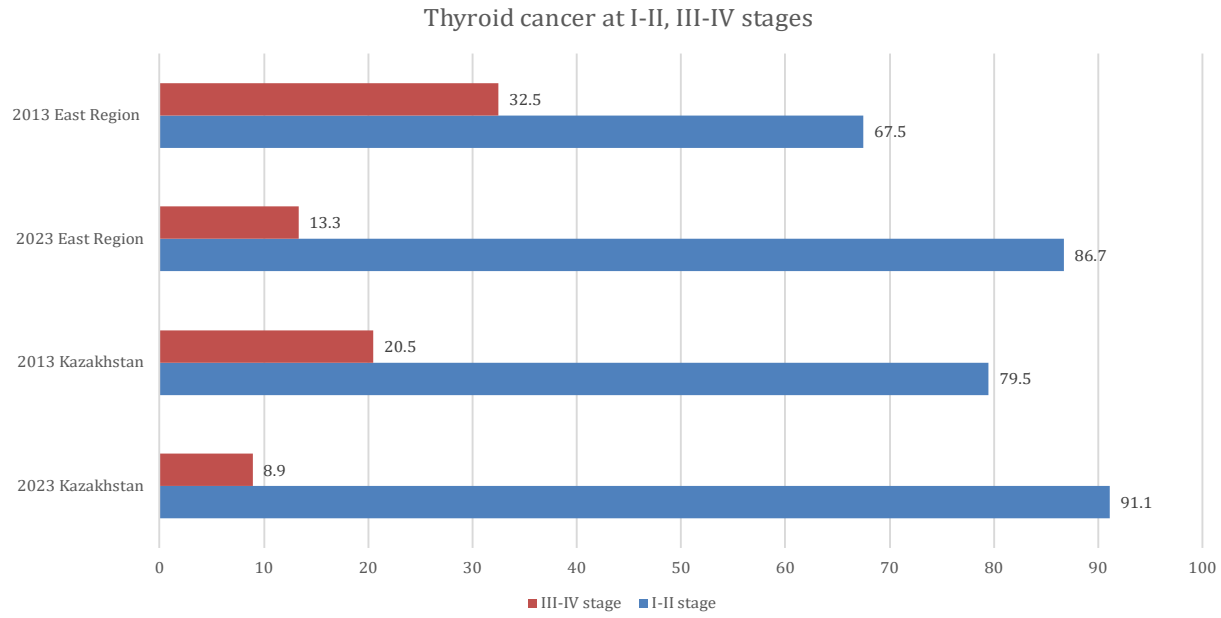

Figure 6. Dynamics of Thyroid Cancer Detection at Stages I-II, III-IV in East Kazakhstan Region and Kazakhstan (2013 and 2023)

diagnosed at stages III-IV decreased significantly from 2013 to 2023 in both East Kazakhstan and Kazakhstan as a whole (Figure 6). In East Kazakhstan, cases at stages III-IV fell from 32.5% in 2013 to 13.3% in 2023. Nationwide, late-stage detection dropped from 20.5% in 2013 to 8.9% in 2023, indicating enhanced early diagnosis and potentially improved prognosis for TC patients.

Discussion

As a result of our study, data analysis suggests that the East Kazakhstan Region, where the territory adjacent to the former Semipalatinsk nuclear test site, deviates from the general trendobserved across the Republic of Kazakhstan presenting more substantial fluctuations and peaks in incidence rate. This could indicate regional characteristics that require further investigation. Additionally, there are significant differences in mortality trends between East Kazakhstan Region and the average indicators across Kazakhstan, highlighting essential fluctuations and peaks in areas adjacent to the former Semipalatinsk nuclear test site. During the study period, a noticeable decline in late-stage cancer cases and a rise in early-stage thyroid cancer cases were observed in the East Kazakhstan region and Kazakhstan. The gender aspect is crucial in understanding thyroid cancer incidence, as women face a significantly higher risk. The highest risk of thyroid cancer is observed among middle-aged and elder adults (30-69 years), which requires attention to these age groups in prevention and early diagnosis.

For decades, the incidence rate was higher in women than men, across all global regions, including areas with lower rates of overdiagnosis [11]. Studies show that women seek medical care more than men [12] There are also factors specific to women that make them more susceptible to thyroid cancer, such as recent pregnancy, a history of infertility problems, abnormal menstrual cycles, and a history of breast cancer [13] The results of the study were consistent with our study. In Kazakhstan, females demonstrated a higher incidence rate than males over the past ten years.

The national statistics in the UK in 2015 reported the highest incidence rate of thyroid cancer in the age group of 65–69 years, which is an older age group compared to our study. [14]. Wang et al. [15] reported that a peak incidence in the age group of 50-54 years, and while we also found the highest number of cases in this age group, the peak incidence was observed between the ages of 50-69 years.

Thyroid cancer arises under the influence of various factors, such as ionizing radiation, adenomas, hereditary syndromes, and genetic mutations. The increase in thyroid cancer incidence is associated with anthropogenic factors, environmental pollution, and the use of xenobiotics, especially in urban areas with high levels of urbanization. The incidence of thyroid cancer has been rising due to environmental pollution and iodine deficiency in Kazakhstan [16]. Kazakhstan is an endemic area of thyroid diseases. This leads to an increase in morbidity among the population, especially among women and children, negatively impacting public health. Furthermore, this situation requires active preventive measures, including salt iodization and educational programs on the importance of iodine for health [17]. At the Semipalatinsk Nuclear Test Site (SNTS), 456 nuclear explosions were conducted between 1949 and 1989 with significant radiation exposure resulting from early tests, particularly the 1949, 1951, and 1953 tests [18]. Radiation is an environmental factor that elevates the risk of developing thyroid cancer. Ionizing Radiation exposure of the thyroid at a young age (especially in childhood) is a recognized risk factor for the development of thyroid cancer. Low doses of radiation increase the number of cells with mutations

which, in the long term, contribute to the development of malignant neoplasms. Saenko et al. reported that patients undergoing radiation therapy for the neck and who got radiation exposure due to radiation accidents are susceptible to thyroid cancer [19]. The incidence of thyroid cancer (TC) in Kazakhstan has increased and it is caused by the availability of better, more accessible diagnostic tools as highly sensitive ultrasound imaging. It leads to overdiagnosis and unnecessary treatment of patients without clinical manifestations which negatively impacts health and creates a socio-economic burden. The risks of thyroid cancer are increased in benign thyroid diseases, family history, certain intestinal diseases (e.g., familial adenomatous polyposis), acromegaly, benign breast diseases, radiation and the reproductive history of women. These factors may also contribute to expanding thyroid cancer incidence in the country [20].

According to the clinical practice guideline of 2023 "Malignant neoplasms of the thyroid gland" by the Ministry of Healthcare of the Republic of Kazakhstan, thyroid cancer symptoms include: growth of a neck mass, rapid tumor growth, hoarseness of the voice and difficulty breathing. A history of thyroid disease, prolonged use of antithyroid medications, exposure to ionizing radiation, prior radiotherapy to the head and neck are significant factors. Physical exam may reveal neck deformity and nodules, laboratory tests as cytological and histological changes, and immunohistochemical examination are crucial. Ultrasonography, CT, and MRI help assess the condition of the thyroid gland and regional lymph nodes. Specialists in field of cardiology, neurology, gastroenterology, and endocrinology are indicated depending on comorbidities and contraindications for patient with thyroid cancer.

Diagnosis, prevention, and treatment of thyroid cancer can be improved through raising awareness, educating healthcare workers and the public about modern diagnostic methods and the importance of early disease detection. Implementation of thyroid cancer screening, iodine intake and access to diagnostic imaging, regional centers should be provided for the population. Additionaly, update clinical practice guidlines based on international guidelines, realization of multidisciplinary teams to treatment, and support science. Setting up of support groups for patients and families will help to manage the psychological aspects of the disease. Finally, systems for monitoring the incidence and mortality of thyroid cancer will allow for the assessment of the effectiveness of implemented programs. These steps should help improve the quality of public health and medical care in Kazakhstan.

In conclusion, the study highlights significant differences in thyroid cancer (TC) incidence between East Kazakhstan and the national trends from 2013 to 2023. While Kazakhstan saw a steady increase in TC cases, East Kazakhstan exhibited more pronounced fluctuations, which may be linked to the long-term effects of radiation from the Semipalatinsk nuclear test site.

Mortality trends remained stable in both East Kazakhstan and the country overall, with some regional variations. Notably, the study showed improvements in early detection, with a marked increase in cases diagnosed at stages III, which likely contributed to a decrease in late-stage diagnoses.

Gender disparities were evident, with women, particularly those aged 30-69, experiencing higher and steadily rising TC incidence rates. These findings underscore the continued impact of historical radiation exposure and the need for targeted health interventions and improved early detection efforts.

Author Contribution Statement

A.B., D.T. – Data collection and preparation, initial processing of the material, and its verification. D.T., A.T., B.E., L.U. – Statistical processing and analysis of the material, drafting of the article (materials and methods, results). A.B., D.T., A.T., A.S. – Drafting of the article (introduction, discussion). M.E., A.S. – 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 express their deep gratitude to the Nuclear Medicine and Oncology Center of the Health Department of the Abai Region for providing the data necessary to conduct this study. We sincerely thank Zeinelova L.T. and Zhumanbaeva Z.M. for their participation in data collection and their contribution to this work.

Funding Statement

This work was supported by the Ministry of Science and Higher Education of the Republic of Kazakhstan, project: IRN AP19860072 "The Role of Molecular Diagnostics in Thyroid Neoplasms," funded by the Ministry of Education and Science of the Republic of Kazakhstan.

Ethical Declaration

This study was conducted with the approval of the Ethics Committee of Semey Medical University, Semey, Kazakhstan (Protocol No. 2, November 7, 2022).

Informed Consent

As patient-identifying information was not accessible to the research team, informed consent was not required. All procedures adhered to relevant ethical guidelines and standards.

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.

References

1. Grimm D. Recent Advances in Thyroid Cancer Research. Int J Mol Sci. 2022;23(9):4631. https://doi.org/10.3390/ijms23094631
2. Sharifovna YH. Thyroid cancer diagnostics, classification, staging. Ijtimoiy Fanlarda Innovasiya Onlayn Ilmiy Jurnali. 2021;1(5):63-9.
3. de Morais Fernandes FCG, de Souza DLB, Curado MP, de Souza TA, de Almeida Medeiros A, Barbosa IR. Incidence and mortality from thyroid cancer in Latin America. Trop Med Int Health. 2021;26(7):800-809. https://doi.org/10.1111/tmi.13585
4. Filetti S, Durante C, Hartl D, Leboulleux S, Locati LD, Newbold K, et al. ESMO Guidelines Committee. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30(12):1856-83. https://doi.org/10.1093/annonc/mdz400
5. Kitahara CM, Schneider AB. Epidemiology of Thyroid Cancer. Cancer Epidemiol Biomarkers Prev. 2022;31(7):1284-1297. https://doi.org/10.1158/1055-9965
6. Miranda-Filho A, Lortet-Tieulent J, Bray F, Cao B, Franceschi S, Vaccarella S, et al. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol. 2021;9(4):225-234. https://doi.org/10.1016/S2213-8587(21)00027-9.
7. Shurgaya MA, Pogosyan GE, Puzin SN, Achkasov EE, Memetov SS. Epidemiological aspects of the incidence of thyroid cancer in the Russian Federation. Medical and Social Expert Evaluation and Rehabilitation. 2020;23(2):27-32. https://doi.org/10.17816/MSER34885
8. Yerlankyzy M, Sakhanov SB, Turebayev DK, Kulmirzaeva DM, Urazova SN, Amanshayeva AK, et al. Assessment of thyroid cancer incidence in Kazakhstan. Meditsina. 2020;11-12(221-222):2-7. https://doi.org/10.31082/1728-452X-2020-221-222-11-12-2-7
9. Espenbetova MZ, Krykpayeva AS, Zhumanbaeva ZM, Glushkova NE, Abenova AS, Serikcan AS, Magzumov ZM. Frequency of occurrence of thyroid cancer in the East Kazakhstan region. Sci Health. 2018;5(20):88-95
10. The Law of the Republic of Kazakhstan dated December 18, 1992 N 1787-XII. On social protection of citizens affected by nuclear tests at the Semipalatinsk Nuclear Test site. Available from: https://adilet.zan.kz/rus/docs/Z920003600_
11. Ferlay J, Colombet M, Soerjomataram I, Parkin D, Pineros M, Znaor A, et al. Cancer statistics for the year 2020: An overview. Int J Cancer. 2021;5. https://doi.org/10.1002/ijc.33588
12. Alseddeeqi E, Altinoz A, Oulhaj A, Suliman A, Ahmed LA. Incidence of thyroid cancer in Abu Dhabi, UAE: A registry-based study. J Cancer Res Ther. 2023;19(2):321-326. https://doi.org/10.4103/jcrt.jcrt_999_2
13. Zamora-Ros R, Rinaldi S, Biessy C, Tjønneland A, Halkjaer J, Fournier A, et al. Reproductive and menstrual factors and risk of differentiated thyroid carcinoma: the EPIC study. Int J Cancer. 2015;136(5):1218-27. https://doi.org/10.1002/ijc.29067.
14. Cancer Research UK, Thyroid Cancer Statistics [Internet]. [Last accessed on 2021 May 20]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/thyroid-cancer
15. Wang J, Yu F, Shang Y, Ping Z, Liu L. Thyroid Cancer: Incidence and Mortality Trends in China, 2005-2015. Endocrine. 2020;68(1):163–73. https://doi.org/10.1007/s12020-020-02207-6
16. Kamynina LL. Thyroid health in the realities of big cities. Health of the Megapolis. 2021;2(2):84-95. https://doi.org/10.47619/271-2617.zm.2021.v2i2;84-95
17. Kadyrova KI, Zhatkanbayeva GZh, Imanbayeva ZhA, Utebayeva ZhA, Myrzabayeva NN. Criteria of hormonal contraception in patients with inflammatory diseases and autoimmune tyroiditis. Actual Problems of Theoretical and Clinical Medicine. 2019;(2):27-31
18. Maeda S, Meirmanov S, Adylchanov T, Sandybaev M, Hayashida N, Eguchi S, et al. Accuracy of thyroid cancer diagnosis and surgery in patients with thyroid cancer may be affected by the Semipalatinsk Nuclear Test Site: A collaboration between Nagasaki (Japan) and Semipalatinsk (Kazakhstan) medical centers. Acta Med Nagasaki. 2021;64(3):77-80. https://doi.org/10.11343/amn.64.77
19. Saenko V, Mitsutake N. Radiation-Related Thyroid Cancer. Endocr Rev. 2024;45(1):1–29. https://doi.org/10.1210/endrev/bnad022
20. Igissinov N, Kozhakhmetov S, Zhantubetova M, Igissinova G, Bilyalova Z, Akpolatova G, et al. Thyroid Cancer in Kazakhstan: Component Analysis of Incidence Dynamics. Asian Pac J Cancer Prev. 2019;20(9):2875-80. https://doi.org/10.31557/APJCP.2019.20.9.2875