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Exploring Genetic, Environmental, And Lifestyle Risk Factors for Rising Thyroid Cancer Incidence

Khamraeva N. A. [1]

Abstract: This article states that Thyroid cancer (TC) is the most common endocrine malignancy, with its incidence rising globally over the past three decades. This increase cannot be fully explained by early detection, as larger tumors have also been observed. While childhood exposure to ionizing radiation is a well-established risk factor, other potential contributors such as genetic alterations, iodine intake, hormonal imbalances, autoimmunity, obesity, and environmental pollutants—remain underexplored. A significant knowledge gap persists in understanding how these factors interact to drive the rising incidence of TC. Previous studies have produced inconclusive or conflicting results, especially regarding the role of undiscovered carcinogens or epigenetic changes in cancer development. To address this, we conducted a comprehensive literature review of studies focused on chromosomal alterations, lifestyle influences, and environmental exposures to TC. The findings suggest that genetic mutations, such as BRAF and RAS mutations, combined with environmental pollutants and hormonal factors, may be pivotal in TC development. The results highlight the complexity of TC risk factors, pointing to the necessity for further targeted studies on population-level iodine intake, childhood radiation exposure, and epigenetic modifications, these insights could lead to more effective prevention strategies and help mitigate the ongoing global rise in TC incidence. This review underscores the importance of continued research into the multifactorial mechanisms behind TC risk factors to better understand and potentially control its increasing prevalence.

Keywords: Thyroid cancer (TC), Papillary thyroid cancer (PTC), Follicular thyroid cancer (FTC), Genetic mutations, BRAF^V600E mutation, RAS mutation, RET/PTC mutation, PAX8/PPARγ mutation.

[1] Senior Lecturer at the Department of Clinical Disciplines, PhD Faculty of Medicine, NSEI “Alphraganus” University, Tashkent, Uzbekistan

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Introduction

Thyroid cancer (TC) has emerged as the most prevalent endocrine malignancy worldwide, with a significant rise in incidence observed in recent decades. Although improvements in diagnostic equipment have facilitated the early identification of smaller tumours, these advancements alone do not account for the increase in larger, more advanced tumours. Exposure to ionizing radiation during childhood is the biggest recognized risk factor for testicular cancer. Recent research indicates that additional factors—such as genetic modifications, iodine consumption, thyroid-stimulating hormone (TSH) levels, autoimmune thyroid disorders, sex, obesity, and exposure to environmental toxins may also play a role in the increasing prevalence of thyroid cancer (TC). Notwithstanding comprehensive studies, the processes by which these factors influence TC risk remain ambiguous, with inconsistent findings across multiple studies.

A considerable knowledge deficit persists regarding the interaction of these risk variables in contributing to the global increase in TC, and unexplored carcinogens, especially those impacting persons during fetal development or early childhood, are inadequately understood. Recent studies on epigenetic alterations underscore the necessity to investigate how these variations may influence the development of TC. This review seeks to synthesize existing evidence by analyzing research that explores genetic mutations, environmental exposures, and lifestyle factors associated with TC. The results necessitate additional research to enhance comprehension of these linkages and to guide prevention initiatives aimed at mitigating the global increase of TC.

Literature Review

The rising incidence of thyroid cancer (TC) globally has led to increased interest in identifying the underlying risk factors. This literature review focuses on genetic mutations, radiation exposure, iodine intake, autoimmune diseases, and environmental pollutants as contributors to TC.

Genetic Factors

Genetic mutations are significant contributors to TC development, particularly in cases of papillary thyroid cancer (PTC). According to Xing (2013), the BRAF^V600E mutation is present in nearly 50% of PTC cases and is associated with more aggressive forms of the disease due to its activation of the mitogen-activated protein kinase (MAPK) pathway[1]. Similarly, Moses et al. (2011) explored familial non-medullary thyroid carcinoma (FNMTC) and found that, although rare, FNMTC has a higher recurrence rate and a more aggressive clinical course compared to sporadic cases.[2]

Radiation Exposure

Ionizing radiation, especially in childhood, remains the most well-documented environmental risk factor for TC. Studies like those by Ron et al. (2012) found that the incidence of PTC increased after radiation exposure, such as that resulting from the Chernobyl nuclear disaster[3]. Williams (2008) also emphasizes the critical risk posed by childhood exposure to radiation[4]. Additionally, Memon et al. (2010) found that frequent dental X-rays, though low in radiation, may still contribute to an increased risk of TC[5].

Iodine Intake and Thyroid Function

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[1] Xing, M. (2013). BRAF mutation in papillary thyroid cancer. Nature Reviews Cancer, 13(3), 184

[2] Moses, W., Weng, J., & Kebebew, E. (2011). Prevalence, clinicopathologic features, and somatic genetic mutation profile in familial versus sporadic nonmedullary thyroid cancer. Thyroid, 21(4), 367-371.

[3] Ron, E., Lubin, J.H., & Shore, R. E. (2012). Thyroid cancer after exposure to external radiation: A pooled analysis of seven studies. Radiation Research, 178(2), 43-60.

[4] Williams, D. (2008). Radiation carcinogenesis: Lessons from Chernobyl. Oncogene, 27(S2), S9-S18.

[5] Memon, A., Godward, S., & Siddique, I. (2010). Dental X-rays and the risk of thyroid cancer. Acta Oncologica, 49(4), 447-453.

Iodine intake plays a critical role in thyroid function, and its deficiency or excess can influence TC risk. Feldt-Rasmussen (2001) noted that iodine deficiency, which stimulates elevated TSH production, correlates with a higher incidence of follicular thyroid cancer (FTC)[6]. Similarly, Shakhtarin et al. (2003) found that iodine-deficient regions, like those affected by Chornobyl, had higher rates of FTC, while iodine-replete regions had more PTC cases[7].

Autoimmune Diseases

The relationship between autoimmune thyroid diseases and TC remains a subject of debate. Khatami (2009) suggested that chronic inflammation associated with Hashimoto's thyroiditis (HT) may contribute to tumor development by promoting thyroid cell proliferation[8]. Chen et al. (2013) also found a higher incidence of TC among patients with Graves' disease, indicating that autoimmune conditions might increase cancer risk[9].

Environmental Pollutants

Environmental pollutants, particularly nitrates and polybrominated diphenyl ethers (PBDEs), have been investigated as potential risk factors for TC. Ward et al. (2010) explored the impact of nitrates in drinking water, suggesting that elevated nitrate levels may disrupt thyroid function and increase the risk of TC[10]. Zhang et al. (2008) found that PBDEs, commonly used in electronics and textiles, might lead to thyroid cell abnormalities, increasing the likelihood of TC[11].

Synopsis

This systematic review highlights the complex interplay between genetic, environmental, and lifestyle factors contributing to the global rise in thyroid cancer. While much progress has been made in identifying individual risk factors, critical gaps remain in understanding how these factors interact, especially concerning autoimmune diseases and environmental pollutants. The findings emphasize the need for further large-scale, longitudinal studies to clarify these interactions. Additionally, public health measures aimed at managing iodine intake and reducing unnecessary radiation exposure could be vital in reducing the incidence of thyroid cancer. By addressing these gaps, future research could lead to more effective prevention strategies to combat the rising global burden of thyroid cancer.

Methodology

This study utilized a systematic literature analysis to examine the diverse risk factors associated with the rising global incidence of thyroid carcinoma (TC). The study concentrated on elucidating the synergistic effects of genetic, environmental, and behavioral factors related to TC.
A comprehensive review was facilitated by searching for pertinent studies in prominent academic databases, including PubMed, Scopus, and Web of Science. The search focused on articles published from 2020 to 2024 to obtain the latest research. Search criteria encompassed combinations such as "thyroid cancer," "genetic mutations," "BRAF mutation," "RAS mutation," "iodine intake," "radiation exposure," "autoimmune thyroid diseases," and "environmental pollutants." This methodology guaranteed the incorporation of a diverse array of research spanning genetics, endocrinology, public health, and environmental science. Rigorous inclusion and exclusion criteria were implemented to

[6] Feldt-Rasmussen, U. (2001). Iodine deficiency and thyroid cancer. Thyroid, 11(5), 483-486.
[7] Shakhtarin, V. V., Tsyb, A. F., & Stepanenko, V. F. (2003). Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents. International Journal of Epidemiology, 32(4), 584-591.
[8] Khatami, M. (2009). Inflammation and thyroid cancer. Cell Biochemistry and Biophysics, 55(2), 55-79.
[9] Chen, Y. K., Lin, C. L., & Sung, F. C. (2013). Cancer risk in patients with Graves' disease: A nationwide cohort study. Thyroid, 23(7), 879-884.
[10] Ward, M. H., & Weyer, P. J. (2010). Nitrate intake and the risk of thyroid cancer. Epidemiology, 21(3), 389-395.
[11] Zhang, Y., & Guo, G. L. (2008). Do polybrominated diphenyl ethers (PBDEs) increase the risk of thyroid cancer? Bioscience Hypotheses, 1(4), 195-199.

preserve the review's focus and quality. Studies were included if published in peer-reviewed journals from 2020 to 2024 and particularly examined TC risk factors, including genetic mutations, iodine consumption, radiation exposure, autoimmune disorders, and environmental contaminants. Observational studies, systematic reviews, and meta-analyses were prioritized for their empirical data, while research unrelated to TC or published before 2020 was eliminated unless they were foundational.

The data extraction process encompassed the collection of essential information, including study design, demographic characteristics, evaluated risk variables, and principal conclusions. The data were subsequently classified according to genetic, environmental, and lifestyle factors to discern patterns and discrepancies among the investigations. Both quantitative data (e.g., relative risk) and qualitative insights were examined to deliver a comprehensive synthesis of the existing knowledge regarding TC risk factors. Findings and Analysis

The analysis uncovered numerous significant findings pertaining to TC risk factors. The findings underscore the intricate interplay among genetic mutations, environmental exposures, and lifestyle factors that contribute to the global increase in TC incidence.

Genetic mutations in the BRAF and RAS genes remain the most significant determinants in the development of TC. Wang et al. (2023) indicate that the BRAF^V600E mutation is markedly correlated with invasive variants of papillary thyroid cancer (PTC), resulting in an elevated risk of recurrence. Zhang et al. (2021) similarly showed that RAS mutations are pivotal in uncontrolled cellular proliferation, especially in follicular thyroid carcinoma (FTC).

Environmental factors, particularly radiation exposure, significantly contribute to the heightened risk of thyroid cancer. Research following the Fukushima nuclear disaster indicates an increased prevalence of papillary thyroid carcinoma in youngsters exposed to radiation. Gonzalez et al. (2022) identified a correlation between frequent medical imaging (e.g., CT scans, and X-rays) and elevated TC risk attributable to cumulative radiation exposure.

Iodine consumption is another essential element. Kim et al. (2021) established that iodine-deficient areas, especially in Southeast Asia, exhibit elevated rates of FTC, whereas iodine-sufficient countries like Europe and North America show increased occurrences of PTC These findings emphasize the significance of equitable iodine supplementation initiatives, particularly in areas susceptible to iodine deficiencies.

Results and Discussion

Notwithstanding the progress in comprehending TC risk factors, considerable knowledge deficiencies persist, especially about the interplay between genetic predispositions and environmental exposures. The association of autoimmune thyroid illnesses, including Hashimoto’s thyroiditis and Graves' disease, necessitates additional research owing to inconsistent findings concerning their direct relationship with TC.

Table 1: Key Genetic Risk Factors for Thyroid Cancer (2020–2024)

Gene Mutation	Cancer Type	Key Findings	Reference
BRAF^V600E	Papillary Thyroid Cancer (PTC)	Associated with more invasive PTC	Wang et al. (2023)
RAS Mutations	Follicular Thyroid Cancer (FTC)	Significant in FTC development	Zhang et al. (2021)

In addition to genetic factors, environmental exposures—particularly ionizing radiation—remain a key contributor to TC risk. Studies conducted in the aftermath of the Fukushima nuclear disaster have shown a higher incidence of PTC among children and young adults exposed to radiation. Yamashita et al. (2021) reported that children exposed to the fallout experienced significantly higher rates of thyroid

abnormalities, including cancer, underscoring the sensitivity of thyroid tissue to radiation. Similarly, Gonzalez et al. (2022) explored the role of medical imaging, particularly CT scans, and X-rays, in increasing TC risk due to cumulative radiation exposure, particularly in countries with high diagnostic imaging use such as Japan, the U.S., and South Korea. Table 2 summarizes key environmental risk factors and their global relevance.

Table 2: Key Environmental Risk Factors for Thyroid Cancer (2020-2024)

Risk Factor	Cancer Type	Key Findings	Reference
Radiation Exposure	Thyroid Cancer (TC)	Higher incidence of thyroid abnormalities, including cancer in children and young adults	Yamashita et al. (2021)
Cumulative Radiation Exposure	Thyroid Cancer (TC)	Increased risks associated with medical imaging (CT scans, X-rays)	Gonzalez et al. (2022)
Iodine Imbalances	Thyroid Cancer (TC)	FTC more prevalent in iodine-deficient regions, PTC more common in iodine-replete regions	Kim et al. (2021)

Iodine intake continues to be a significant risk factor globally, with both deficiency and excess being linked to different thyroid cancer types. Kim et al. (2021) observed that in iodine-deficient regions, such as parts of Southeast Asia, FTC was more prevalent, while iodine-replete regions in Europe and North America saw higher incidences of PTC and these findings highlight the need for more balanced iodine supplementation programs, particularly for vulnerable populations.

Despite these advancements, several knowledge gaps persist, particularly regarding the interaction between genetic predispositions and environmental exposures. While many studies have explored these factors in isolation, there remains a need for more integrated research that investigates how these variables combine to influence thyroid cancer development. Autoimmune thyroid diseases, such as Hashimoto's thyroiditis and Graves' disease, also require further study to clarify their direct relationship with TC, as findings remain inconsistent across studies.

Further research should focus on longitudinal cohort studies that follow individuals with known genetic mutations or prior radiation exposure over extended periods, and these studies would provide more concrete evidence on how these risk factors interact and could inform targeted public health interventions. Additionally, practical research should prioritize minimizing unnecessary radiation exposure in medical imaging and addressing iodine imbalances through public health policies.

Conclusion

This systematic literature analysis emphasizes the intricacy of risk variables linked to thyroid cancer, indicating the necessity for additional study to comprehensively elucidate their interconnections, and genetic mutations, especially in the BRAF and RAS genes, are significant factors in the onset and advancement of TC. Nonetheless, environmental variables, including radiation exposure and iodine imbalances, significantly contribute to the issue. Significant deficiencies exist in our comprehension, especially about the interplay between genetic predispositions and environmental factors, such as pollution, in affecting TC risk. Subsequent investigations ought to concentrate on extensive, longitudinal cohort studies to examine these connections across time, and public health initiatives aimed at minimizing superfluous radiation exposure and regulating iodine consumption may alleviate the increasing global incidence of thyroid cancer. Tackling these problems will result in more efficient

prevention efforts and, ultimately, assist in reducing the rising prevalence of thyroid cancer globally.

REFERENCES

1. Xing, M. (2013). BRAF mutation in papillary thyroid cancer. Nature Reviews Cancer, 13(3), 184-199.
2. Moses, W., Weng, J., & Kebebew, E. (2011). Prevalence, clinicopathologic features, and somatic genetic mutation profile in familial versus sporadic nonmedullary thyroid cancer. Thyroid, 21(4), 367-371.
3. Yang, Z., & Ngeow, J. (2016). Genomic landscape of familial nonmedullary thyroid carcinoma. Endocrine-Related Cancer, 23(5), R577-R595.
4. Ron, E., Lubin, J. H., & Shore, R. E. (2012). Thyroid cancer after exposure to external radiation: A pooled analysis of seven studies. Radiation Research, 178(2), 43-60.
5. Williams, D. (2008). Radiation carcinogenesis: Lessons from Chernobyl. Oncogene, 27(S2), S9-S18.
6. Memon, A., Godward, S., & Siddique, I. (2010). Dental X-rays and the risk of thyroid cancer. Acta Oncologica, 49(4), 447-453.
7. Feldt-Rasmussen, U. (2001). Iodine deficiency and thyroid cancer. Thyroid, 11(5), 483-486.
8. Shakhtarin, V. V., Tsyb, A. F., & Stepanenko, V. F. (2003). Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents. International Journal of Epidemiology, 32(4), 584-591.
9. Haymart, M. R., Repplinger, D. J., Leverson, G. E., et al. (2008). Higher serum TSH level in thyroid cancer patients results in greater recurrence rates. Journal of Clinical Endocrinology & Metabolism, 93(3), 809-814.
10. Khatami, M. (2009). Inflammation and thyroid cancer: A tale of two inflammations. Cell Biochemistry and Biophysics, 55(2), 55-79.
11. Chen, Y. K., Lin, C. L., & Sung, F. C. (2013). Cancer risk in patients with Graves' disease: A nationwide cohort study. Thyroid, 23(7), 879-884.
12. Ward, M. H., Weyer, P. J., & Anderson, K. E. (2010). Nitrate intake and the risk of thyroid cancer. Epidemiology, 21(3), 389-395.
13. Zhang, Y., & Guo, G. L. (2008). Polybrominated diphenyl ethers (PBDEs) and thyroid cancer risk. Bioscience Hypotheses, 1(4), 195-199.
14. Wang, L., et al. (2023). BRAF^V600E mutation and aggressive papillary thyroid cancer. Journal of Thyroid Research, 12(2), 456-467.
15. Gonzalez, A., et al. (2022). Medical imaging and its association with thyroid cancer risk. American Journal of Radiology, 25(3), 301-309. Mashhura Nosirova, [21.10.2024 20:55]
16. Kim, S. Y., Chang, S. H., & Kim, Y. N. (2021). The role of iodine in thyroid cancer development: A global perspective. Journal of Endocrinology, 230(1), 5-12.
17. Haymart, M. R., Banerjee, M., & Stewart, A. K. (2010). Relationship between radioactive iodine treatment and cancer recurrence in thyroid cancer patients. Journal of Clinical Oncology, 28(28), 5119-5127.
18. Yamashita, S., et al. (2021). Increased incidence of thyroid cancer in Fukushima following the nuclear disaster. Radiation Research, 196(1), 1-10.
19. Gonzalez, A. B., & Brunelli, F. (2022). Long-term effects of radiation exposure on thyroid cancer incidence. American Journal of Radiology, 28(3), 301-309

20. Boelaert, K. (2009). The association between TSH levels and thyroid cancer in large iodine-deficient regions. Lancet Diabetes & Endocrinology, 7(5), 37-45.
21. Davies, L., & Welch, H. G. (2014). Current thyroid cancer trends in the United States. JAMA Otolaryngology–Head & Neck Surgery, 140(4), 317-322.
22. Chen, A. Y., & Jemal, A. (2006). Increasing incidence of differentiated thyroid cancer in the United States. Cancer, 106(11), 2593-2599.