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Risk factors of the thyroid cancer

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Abstract

Introduction and purpose: These days, thyroid cancer (TC) is the most common endocrine cancer. According to „Cancer in Poland in 2022” thyroid cancer affected 47800 women in 2022. A better understanding of the illness will help develop more potent treatment and prevention strategies. The goal of our work is to classify and describe risk factors [RF] for TC.

Review Methods: A systematic search of the “PubMed” database was conducted, focusing on studies published within the last 10 years. The search strategy used relevant key words related to TC and RF. Studies were included if they provided information on RF associated with TC in the adult population. The articles that are most relevant to the topic have been selected.

State of knowledge: It is known that TC has several RF. According to recent research, female sex, radiation, low physical activity, obesity, metabolic syndromes and lifestyle choices are the

most significant RF. Other elements that raise the chance of TC include, for example family history of thyroid cancer, iodine deficiency, inadequate sleep, hormonal and genetic factors, eating meals high in sugar. Adequate physical activity, getting enough good sleep, eating dairy products, oranges and persimmons and a healthy lifestyle are associated with a lower risk of thyroid cancer; nevertheless, smoking and drinking alcohol, also reduces the disease's likelihood.

Summary: Many medical, genetic, and environmental factors are believed to be linked to a higher risk of TC. Research into RF for the disease could be useful in the development of prevention facilitating the application of suitable screening programs, diagnostic and treatment techniques. Further study is required to fully understand the etiopathology of TC, identify all RF, and verify whether they can be used for the procedure of treatment, as they are not well enough recognized.

Key words: thyroid cancer; risk factors

1. Introduction

Thyroid cancer (TC) is a major problem affecting many people in the population, especially women. The National Cancer Registry's "Cancer in Poland in 2022" report that 4107 women were diagnosed with thyroid cancer in 2022. TC accounted for 4.5% of cancer cases in 2022 in women. [1] Thyroid cancer ranked ninth among all cancers in terms of incidence in 2020, with 586 000 new cases worldwide, according to GLOBOCAN estimations.[2] TC is the most common endocrine cancer. In many nations, the incidence of thyroid cancer has significantly grown during the last few decades. [3]

The follicular (FTC) and papillary TC (PTC) types are the two most popular forms. Three to five percent of thyroid tumors are medullary thyroid malignancies (MTC), which are caused by C cells that secrete calcitonin. Although rare, anaplastic thyroid carcinoma (ATC) is extremely aggressive. [4] The most prevalent histological form of differentiated TC is papillary thyroid cancer (PTC). This cancer is characterized by slow growth and a benign clinical course. It spreads mainly through lymphatic vessels, metastasizing to nearby lymph nodes and occasionally to the lungs.

There are several risk factors in TC, such as: female sex, low physical activity, radiation, obesity, high BMI, metabolic syndrome, family history of thyroid cancer, air pollution, genetic factors, eating meals high in sugar, occupational exposure to biocides, stress, using fertility

drugs. [1-39] Because it is a multifactorial disease, a comprehensive understanding of all risk factors is necessary for better prevention, early detection, and treatment results.

Objective: The purpose of our research is to examine the PubMed publications that are currently available regarding thyroid cancer risk factors in order to have a better understanding of the disease's etiology.

2. State of knowledge:

Thyroid cancer risk factors are currently being studied and are not entirely understood. Early disease diagnosis and therapy seem to depend on identifying the right risk factors. Although there is a lot of research, not everything has yet been fully discovered and explained. Both positive and negative factors have been described in many articles.

2.1 Sex and age

The Polish National Cancer Registry claims that women are much more likely to get the disease than men. The number of new cases in 2022 was 905 in men and 4107 in women.[1] This shows how significant this problem is in the female gender. This association has also been found in studies conducted by other scientists worldwide. Myung et al. in their research show that females (OR, 2.08; 95% CI, 1.26 to 3.45) had a higher chance of developing thyroid cancer.[5] Based to the GLOBOCAN 2022 of the International Agency of Research on Cancer in the world was 614729 new cases among women and 206485 among males. The results show that TC is 3-4 times more common in women than in men. According to Maleki's et al.[6] study's findings, women are 8.9 times more likely than males to develop thyroid cancer.

Thyroid cancer incidence cases among females and males in 2019 were highest in the 55–59 age group (10 257, 95% UI: 9027 to 11 475), and the 50–54 age group (17 547, 95% UI: 15 534 to 19 685), respectively. [2] et al. in their study have noted that TC was diagnosed at a median age of 49 years for women and 54 years for men in the United States, which is younger than the median age for the majority of other major cancer types. [3]

2.2 Physical activity and lifestyle

Physical exercise and lifestyle choices can also influence how the disease develops. A very important factor that increases the risk of TC is low physical activity. Maleki et al. underlined that reduced physical activity has been demonstrated to raise the risk of thyroid cancer by 1,12 times. [6] Another study found an association between daily walking time vs. risk reduction of TC. The risk of TC was decreased by walking for at least 60 minutes per day (OR: 0.357; 95% CI: 0.157–0.673). Spend at least one hour practicing an activity also has a protective effect. [7] Bui et al. also emphasized in their study the protective effect of physical activity against the

development of TC. The risk of TC was lower for those with the highest degree of physical activity ([HR] = 0.65 [confidence interval, CI = 0.44-0.94], p-trend = 0.028) than for those with the lowest level.[8] As the above studies show, increased physical activity can have a protective effect on disease, while decreased or no physical activity increases the risk of disease.

Feng et al. examined the effects of pattern, body mass index, waist circumference, blood pressure, heart rate, lifestyle, diet, exercise, smoking, alcohol consumption and genetic risk on the risk of thyroid cancer. The group with incident TC had a higher percentage of adverse weighted lifestyle (39.95% vs. 33.59%; $P < .001$) than the group without TC. Participants with TC had a greater negative lifestyle component than those without TC, such as smoking (10.87% vs 7.83%), weight (63.36% vs 55.27%), and moderate to intense physical activity (55.56% vs 46.17%). Moderate-to-intense physical activity was less beneficial for women (47.68% vs. 44.57%). The risk of total cancer was correlated with both lifestyle and genetic variables. According to the study's findings, leading a better lifestyle may help reduce the negative impact of hereditary factors on TC risk, particularly in those with a high genetic risk. [9] A case-control study conducted by Myung et al. examined the relationship between the risk of TC and income, family history of thyroid cancer, smoking, alcohol consumption and body mass index. Results of this study suggest people who are female, have a higher body mass index (BMI), have a family history of TC, are not smokers or drinkers, and have a lower monthly household income are more likely to acquire TC. [5] The relationship between particulate air pollution and cancer risk has been studied by researchers Karzaj et al. They show that after two or three years of exposure, there is a substantial correlation between the incidence of papillary thyroid cancer and the concentration of fine (diameter $\leq 2.5 \mu\text{m}$) particulate matter in air pollution. A $5 \mu\text{g}/\text{m}^3$ increase in fine ($\leq 2.5 \mu\text{m}$) particulate matter concentrations over 2 years (adjusted odds ratio = 1.18, 95% CI: 1.00-1.40) and 3 years (adjusted odds ratio = 1.23, 95% CI: 1.05-1.44) of exposure was linked to an increased risk of developing papillary thyroid carcinoma. Depending on smoking status, this risk varied. The risk of having PTC was highest among current smokers ($n = 623$; adjusted odds ratio = 1.35, 95% CI: 1.12-1.63).[10] Occupational exposure to biocides also has an impact on disease development. Such a relationship has been shown by Zeng et al. Thyroid cancer risk was higher in those who had ever been exposed to biocides at work (OR=1.65, 95% CI 1.16 to 2.35), and the highest risk (OR=2.18, 95% CI 1.28 to 3.73). was shown in those with a high cumulative probability of exposure. Wood preservation, cosmetics, paints, disinfectants, hospitals, and medicinal applications are just a few of the many applications for biocides. [11] The following article aims to describe the correlation between lifestyle, living environment and increased incidence of TC. Smoking, drinking alcohol, getting

enough good sleep, eating dairy products, and engaging in regular, long-term exercise are all factors that help avoid TC. On the other hand, extended and regular usage of mobile phones increases the risk of thyroid cancer in people with certain genetic abnormalities. Additionally, people who live close to volcanoes or in areas where pesticides are present, work night shifts, or have high-pressure occupations are more likely to acquire thyroid cancer. [12] Sleep features and their impact on TC rated Zong et al. In the Finnish population, a 7.307-fold increased risk of TC was linked to a 1.30-hour reduction in sleep duration (OR = 7.307, 95% CI: 1.642–32.519). In the Finnish population, sleep disturbances raised the risk of TC (OR = 2.298, 95% CI: 1.194–4.422). According to the findings, there was a lower incidence of TC in the Italian population for those who woke up early (OR = 0.055, 95%CI: 0.004–0.741) and napped during the day (OR = 0.031, 95%CI: 0.002–0.462). In conclusion, Reduced sleep duration was linked to a higher risk of thyroid cancer, highlighting the significance of getting enough sleep in order to prevent TC. [13] Another study, on the other hand, did not confirm a significant negative effect of cell phone use on the occurrence of thyroid cancer, so this topic still needs further research. There was no significant correlation between cell phone use and an increased risk of TC (OR: 1.05, 95% CI: 0.74–1.48). There was no discernible correlation between the number of daily calls and any statistical significance. But longer duration of use and higher daily hours of use were associated with a considerable increase in TC risk compared to non-users (>15 years: OR: 1.29, 95% CI: 0.83–2.00; 1–2 hours per day: OR: 1.51, 95% CI: 0.90–2.53; >2 hours per day: OR: 1.40, 95% CI: 0.83–2.35). [14]

As studies show, there are many modifiable risk factors that affect the occurrence of thyroid cancer. Some studies have a different view of selected factors, so it is very important to intensify efforts to discover and classify factors that affect positively and negatively. Physical activity deserves special attention. Its absence significantly increases the risk of the disease.

2.3 Smoking

Cigarette smoking as a risk factor for thyroid cancer is classified differently in various studies on the subject. Both as a protective factor and as a factor that increases the risk of the disease. Cigarette smoking and second-hand smoke (SHS) were categorized as RF for thyroid cancer in the study. However, many other studies indicate otherwise. [6] More research on this topic is therefore needed. Cho et al. stated that TC in men is inversely correlated with pack-years, current smoking and dosage dependence. Adjusted hazard ratios (95% CIs) for TC comparing present and former smokers to never smokers were 0.58 (0.45–0.75) and 0.93 (0.73–1.18), as well, after controlling for covariates. Following additional correction for TSH and BMI as putative mediators, this link was marginally diminished but still significant. Although

this link did not achieve statistical significance, current smokers tended to have a decreased risk of TC for women. [15] In a meta-analysis Lee et al. proves that the link between cigarette smoking and thyroid cancer is negative (OR, 0.798; 95% CI, 0.681 to 0.935). Both men (OR, 0.734; 95% CI, 0.553 to 0.974) and women (OR, 0.792; 95% CI, 0.700 to 0.897) had a lower risk of TC. However the relationship did not achieve statistical significance, current smokers seemed to have a decreased risk of thyroid cancer for women. [16] As the examples above indicate, further research is needed on this topic, as it is an important modifiable factor.

2.4 Body Mass Index, Obesity and Metabolic Syndrome

High BMI, metabolic syndrome and obesity are affecting an increasing number of people around the world. These factors are responsible for the increased incidence of many diseases of civilization. The following research shows their relationship to the occurrence of thyroid cancer. Obesity is the accumulation of excess body fat and is intimately linked to the start of a number of disorders. BMI and waist circumference are examples of indicators of obesity. A person's BMI is determined by their weight and height. The BMI, which is expressed in kilograms per square meter, is calculated by dividing the body mass by the square of the body height.

Hoang et al. have demonstrated the relationship between genetic variants, BMI and thyroid cancer risk. In the subclasses of overweight (23-24.9 kg/m²; adjusted OR, 1.50; 95% CI, 1.12 to 2.00) and obese (≥ 25 kg/m²) (adjusted OR, 1.62; 95% CI, 1.23 to 2.14), Body Mass Index was linked to an elevated risk of TC. The FTO genetic variations rs8047395 and rs8044769 were positively correlated with a higher risk of TC. Furthermore, in the codominant (rs17817288), dominant (rs12149832, rs9937053, rs1861867 and rs7195539), and recessive (rs17817288 and rs8044769) models, the combination of BMI subclasses and FTO gene variations was strongly linked to this disease risk. [17] Jinyoung et al. try to determine the relationship between metabolic syndrome and thyroid cancer risk. With the exception of impaired fasting glucose criterion, every component of metabolic syndrome exhibited a marked rise in hazard ratio in relation to the number of diagnoses. According to the Korean definition, metabolic syndrome was identified when three or more of the five criteria listed below were satisfied: Serum triglycerides > 150 mg/dL, HDL-C < 40 mg/dL in men or < 50 mg/dL in women, blood pressure $\geq 130/85$ mmHg or current use of anti-hypertensive medications, fasting blood glucose ≥ 100 mg/dL or up-to-date use of oral hypoglycemic agents or insulin for diabetes, and waist circumference > 90 cm for men or > 80 cm for women. The survey included people aged 20-39 years old. [18] As we can see, this problem can even effects very young people. Kwon et al. conducted a nationwide cohort study evaluating the association of thyroid cancer

with BMI, waist circumference (WC) and weight change. Following multivariate analysis, participants with higher BMI and bigger WC had a significantly higher incidence of TC ($P < 0.001$ and $P < 0.001$, as well.). The incidence of the disease grew drastically in lean people who developed obesity (hazard ratio [HR] 1.15 [1.11-1.19]), especially in women (HR 1.17 [1.13–1.22], $P < 0.001$). Thyroid cancer incidence was considerably lower in obese people who lost weight (HR 0.89 [0.86-0.93]). As the study shows increased TC risk was linked to weight growth in lean people, while lower risk was linked to weight loss in obese patients. [19] Another study found an association between PTC, BMI, urinary iodine concentration (UIC) and thyrotropin hormone levels (TSH). TSH levels (3.38 vs. 1.59, $p < 0.05$) and BMI (23.71 vs. 22.66, $p < 0.05$) were greater in PTC patients. PTC was independently predicted by UIC (OR=1.005, $p < 0.05$). Both UIC ($r=0.737$, $p < 0.05$) and BMI ($r=0.593$, $p < 0.05$) showed favorable correlations with TSH levels. [20] TC risk was linked to low HDL-C levels, and this association was more pronounced in those with metabolic disorders as Kim et al. stated. When diabetic patients had low HDL-C levels in four consecutive tests, the HR for the incidence of TC was 1.714 (95% CI, 1.529 to 1.921), while it was for patients with hyperlipidemia. Patients with central obesity (P for interaction = 0.062), high blood pressure (P for interaction = 0.057), impaired fasting glucose (P for interaction = 0.051), and hyperlipidemia (P for interaction = 0.126) were more affected by low HDL-C levels. Low HDL-C levels that are frequently assessed may be a risk factor for TC. [21] Yin et al. underlined that patients with insulin resistance (RR = 1.59, 95% CI = 1.12-2.27, $P = 0.01$), dysglycemia (RR = 1.40, 95% CI = 1.15-1.70, $P < 0.001$), high body mass index (RR = 1.35, 95% CI = 1.23-1.48, $P < 0.001$), and hypertension (RR = 1.34, 95% CI = 1.22-1.47, $p < 0.001$) are at a higher risk of TC. [22] These findings could aid in the identification of those at high risk for thyroid cancer and the adoption of healthy lifestyle choices. Interestingly, there are also studies addressing the topic of growth in correlation with thyroid cancer. The male groups with heights of 165-168 cm and ≥ 169 cm had HRs of 3.92 (95% CI; 1.33-11.55, $P = 0.013$) and 4.24 (95% CI; 1.32-13.61, $P = 0.015$), respectively, in comparison to the male group with height ≤ 160 cm. The HR per 5-cm increase in height was 1.12 (95% CI 1.06-1.18, $P < 0.001$). Using data from a huge population-based cohort in Japan, we found that men's height considerably enhanced their risk of developing TC. [23] Kitahara et al. underlined that HR (CIs) for height (per 5 cm) = 1.07 [1.04-1.10], BMI (per 5 kg/m²) = 1.06 [1.02-1.10], waist circumference (per 5 cm) = 1.03 [1.01-1.05], young-adult BMI (per 5 kg/m²) = 1.13 [1.02-1.25] and adulthood BMI gain (per 5 kg/m²) = 1.07 [1.00-1.15] were all positively correlated with the incidence of TC. A statistically significant 23% higher risk [CI 6–42%] was linked to an adult BMI gain of 5.0–9.9 kg/m² as opposed to a BMI growth of 0–4.9 kg/m². [24]

High BMI, metabolic syndrome, obesity, tall height and increased waist circumference are all associated with an elevated risk of thyroid cancer. Obesity is a major problem affecting populations worldwide and is a significant public health issue. Obesity increases the risk of many diseases, including TC. It is therefore an important problem that needs to be countered and public awareness of the issue raised.

2.5 Diet

Thyroid hormone secretion is influenced by diet, which makes it a critical factor contributing to the likelihood of developing in TC. According to research, eating meals high in sugar, such as starchy foods, processed meats, refined grains, fatty foods high in nitrates and confections, may increase the risk of TC, especially in women. High iodine consumption protects against TC, especially follicular TC, in areas with severe iodine deficiency. Consuming cruciferous vegetables, beans, milk and dairy products is associated with a lower risk. Increased fruit intake, particularly of oranges and persimmons, is also linked to this risk reduction. [12] While chronically excessive iodine intake may raise the risk of PTC and more aggressive histology tumor characteristics, like lymph node metastases, iodine shortage is linked to an increased risk of FTC. Reduced T3 and T4 production and the ensuing hypersecretion of thyroid stimulating hormone might result from an iodine shortage. This encourages the development of cancer by causing thyroid follicular cells to enlarge and proliferate. [25] According to research by Stojšavljević A. et al., blood samples from patients with Thyroid Cancer had an average Zn concentration of 1613 ng/g, which was significantly lower ($p < 0.05$) than those from the control group (5147 ng/g). This finding may be significant from a clinical perspective for diagnostic and trace purposes. Examining more research, comparable findings provide credence to the idea that low zinc levels are linked to TC. [26] The differentiated TC risk was positively correlated with a diet high in sweetened drinks (HR_{Q4vs.Q1} = 1.26; 95% CI:0.99-1.61; P-trend = 0.07) as Zamora-Ros et al. stated. In particular, the consumption of sweetened beverages was positively correlated with papillary TC risk (HR_{100mL/d} = 1.07; 95% CI:1.01-1.13) and differentiated TC risk (HR_{100mL/d} = 1.05; 95% CI:1.00-1.11). [27] Cao et al. underlined that a high intake of saltwater fish (at least three times per week or twelve times per month) may reduce the incidence of TC (OR 0.72; 95% CI 0.55, 0.95; $P = .02$). High seafood consumption (≥ 3 times per week or ≥ 12 times per month) may also reduce the incidence of Thyroid Cancer (OR 0.70; 95% CI 0.52, 0.96; $P = .03$). The analysis shows that higher iodine intake (≥ 300 $\mu\text{g/d}$), high intake of marine fish and shellfish were protective factors for this disease. [28] As you can see, food choices have a significant impact on health and can both raise the risk of illness and protect against it.

2.6 Radiation

Radiation is one of the main risk factors for thyroid cancer. According to the results of the current study, a history of head and neck radiation increases the risk of thyroid cancer by more than six times. The aftermath of the Chernobyl disaster demonstrated that PTC is commonly developed in people, especially youngsters, who are exposed to radiation in the head and neck area. Also, ionizing radiation, particularly to the cervix and thyroid gland, especially through X-rays, is a documented RF. Multiple dental x-rays are also responsible for increased exposure to the disease. A history of head and neck radiography was identified as a risk factor for TC (OR: 6.65; 95%CI: 2.53–17.49). [29] The radiation dose administered to the thyroid gland and the age of exposure are the two primary risk factors for the development of TC. Exposure to a mean dosage greater than 0.05-0.1 Gy (50-100mGy) raises the risk. The risk is lower in adults, diminishes with increasing exposure age, and is greatest in children. It takes at least five to ten years after exposure for thyroid cancer to manifest. The most common type of thyroid cancer identified following radiation exposure is PTC. The Radiation Effects Research Foundation studied the impact of the Hiroshima and Nagasaki bomb detonations. After being exposed to 1Gy at age 10, the estimated elevated relative risk of TC at age 60 was 1.28 (95% CI: 0.59–2.70). For people exposed after the age of 20, the risk was negligible and declined with increasing exposure age. Radiation exposure was responsible for about 36% of TC cases in those exposed before the age of 20. [30] Cottagiri et al. have demonstrated the relationship between living near a nuclear power plant and the risk of thyroid cancer. The risk of TC was 1.09 (95% CI: 0.93-1.29) for those who lived close to NPPs (defined as being within ≤ 25 km) or jurisdictional regions (e.g., community, county) compared to people who lived farther away. Studies that modeled closer residential proximity (≤ 5 km) to NPPs had higher risk estimates than those that modeled farther distances (≤ 25 km and jurisdictional areas). According to the research, the risk of TC is increased by residing close to a nuclear power station. [31]

2.7 Female

There are many risk factors for thyroid cancer that only affect women, and significantly affect the incidence of the disease. A study conducted by Yu et al. examined the effects of using infertility drugs, including clomiphene citrate and gonadotropin, and the incidence of thyroid cancer. The usage of fertility medications was significantly positively correlated with the risk of thyroid cancer in infertile women (relative risk [RR] = 1.35; 95% CI [1.12-1.64; P = 0.002). Furthermore, using clomiphene citrate was linked to a higher incidence of TC in infertile

women than in those who did not use fertility medications (RR = 1.45; 95% CI 1.12-1.88; P = 0.005). [32] Younger age at menarche (<10 vs. 10-11 years; HR, 1.28; 95% CI, 1.00-1.64), a younger age at menopause (<40; HR, 1.31; 95% CI, 1.05-1.62) and older age (≥ 55 ; HR, 1.33; 95% CI, 1.05-1.68), history of menopausal hormone therapy use (HR, 1.16; 95% CI, 1.02-1.33), and prior hysterectomy (HR, 1.25; 95% CI, 1.13-1.39) were all factors linked to a higher risk of differentiated thyroid cancer. [33] Wang et al. underlined that an elevated risk of PTC was linked to late menopausal age (RR = 1.39, 95% CI 1.03-1.89, P = 0.032). [34] The Uterine Fibroids cohort had a greater overall incidence of TC (3.90 vs. 2.36 per 10,000 person-years) than the control cohort as Li-Min et al. stated. As an adjusted hazard ratio of 1.67 (95% CI: 1.22–2.30), patients in the uterine fibroids cohort aged 35–49 years had a considerably greater age-specific risk of thyroid cancer than those in the control cohort. [35] Another study found an association between parity and the risk of TC. Women with one, two, or three children as well as parous women had a noticeably greater risk of TC (HR = 1.45, 95% CI: 1.20, 1.75). Women with 2 children had the most important risk (HR = 1.60, 95% CI: 1.32, 1.93). [36] Breastfeeding, on the other hand, may have a protective effect on the disease. Yi et al. after combining relevant research, they found a substantial negative correlation between the incidence of thyroid cancer and ever nursing (RR = 0.91, 95% CI 0.83-0.99). A one-month increase in breastfeeding duration was associated with a summary RR of 0.983 (95% CI 0.98-0.99) for TC risk. So, a longer period of breastfeeding may further reduce the risk of disease. [37] Such a conclusion is also shown in the study conducted by Wang et al. There was a significant correlation between a longer period of breastfeeding (for 6-12 months against ≤ 6 months, OR: 0.49, 95% CI 0.24-0.98) with a lower incidence of TC. [38]

2.8 Genetic factors

Thyroid cancer risk is also influenced by genetic factors. The relationship between the effects of genetic variants on thyroid cancer has been studied by Feng et al. Higher polygenic risk score were linked to TC (hazard ratio, 2.25; 95% CI, 1.91-2.64; P = 8.65×10^{-23}). In comparison to those with the lowest PRS, those with medium PRS had a 1.71-fold risk associated with bigger TC risk (95% CI, 1.28-2.28, P = 2.56×10^{-4}), whereas those with high PRS had a 2.82-fold risk connected with higher TC risk (95% CI, 2.16-3.68; P = 2.34×10^{-14}). [9] In the analysis by Myung et al. when the family history was positive, it increased the risk of the disease (OR, 3,64; 95% CI, 1,87 to 7,09). [5] Precise studies have identified a number of genome variants linked to PTC susceptibility, such as the rs965513 (9q22.33) nucleotide polymorphism near FOXE1. The odds ratios for the A allele of the rs965513 polymorphism were 1.58 (95% CI 1.32-1.90) in all populations, 1.65 (95% CI 1.31-2.07)) in Caucasian

populations, and 1.49 in Asian populations, indicating a strong correlation with the incidence of TC. They found that the homozygous model had the highest odds ratio (OR = 2.80, 95% CI 2.12-3.69) when compared to both the dominant and recessive models. The rs965513 polymorphism is important RF for TC, according to these findings. [39] The risk of thyroid cancer is increased by a number of genetic alterations. Such mutations have been found in more numbers. This demonstrates how genetic alterations are linked to an increased risk of disease. It is very important to continue research on this topic, it may allow, for example, earlier detection of the disease and identification of those at risk.

3. Conclusions

Many factors, both environmental, medical, genetic and lifestyle-related, influence the risk of thyroid cancer. It is feasible to implement suitable diagnostic procedures, preventive measures, screening programs, and more effective therapy by completely comprehending and identifying all of the risk factors associated with TC. As the above examples show, there are many factors contributing to the incidence of this cancer. Many of them have yet to be known, despite a lot of research and tremendous efforts by scientists. The main risk factors for TC are: low physical activity, obesity, high BMI, metabolic syndrome and radiation. Eating meals high in sugar, having a family history of TC, lower monthly household income, air pollution, extended and regular usage of mobile phones, having high pressure occupations, working night shifts, having a history of menopausal hormone therapy use have been proposed as TC risk factors as well. It is also observed that women are more likely to get TC. To completely comprehend the carcinogenesis of TC, more investigation into the risk factors is required. Since maintaining a healthy lifestyle can reduce the risks associated with hereditary and environmental exposure factors for thyroid cancer, the role of knowing modifiable factors is crucial. In one case, regular physical activity can help lower the incidence of thyroid cancer. There are also a number of studied factors that have a protective effect on thyroid cancer incidence, these include regular physical activity, breastfeeding, getting enough good sleep, eating dairy products, saltwater fish and oranges. Surprisingly the protective effect was also shown by drinking alcohol. Smoking still needs more research, although most studies indicate that it has a protective effect. Reduced morbidity and mortality from thyroid cancer would result from the use of early screening diagnosis and appropriate preventative measures. Certainly, the study of thyroid cancer risk factors still needs a lot of research. Knowing them accurately would make it possible to introduce appropriate screening tests, increase public awareness of how they can reduce the risk

of the disease, and increase the speed of detection of the disease in risk groups, which would allow faster and more effective treatment.

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