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Prevalence of Chemotherapy-Induced Thyroid Dysfunction in Breast Cancer and Lymphoma

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Abstract

Background: In cancer cases, thyroid function is thought to be vulnerable to chemotherapy, as hypothalamic-pituitary axis is active, and chemotherapy is systemic therapy for cases. **This investigation aimed to** evaluate the effect of chemotherapy on thyroid function, thyroid function alters during toxicity of chemotherapy, and the predictive value of thyroid function on pathological complete response (pCR) in cases with early breast cancer (BC) or lymphoma receiving chemotherapy. **Methods:** This prospective investigation included a total of 50 cases, 25 with BC and 25 with lymphoma. All studied cases were subjected to routine laboratory investigations [Complete blood count, Random blood sugar, Thyroid function tests (TSH, fT3 & fT4), kidney and liver function tests] and Imaging: Thyroid ultrasound. **Results**: Chemotherapy regimens showed varying associations with thyroid dysfunction. The Taxol /Carboplatin regimen was linked to a significantly higher dysfunction rate (66.7%, $p = 0.023$ vs. others), whereas R-CHOP had a markedly lower rate (7.7%, $p = 0.001$ vs. others). Chemotherapy has induced significant hematologic alterations. Hemoglobin levels declined ($p = 0.008$), and white blood cell (WBC) counts dropped ($p < 0.001$). **Conclusion:** Chemotherapy exerts a measurable and comparable impact on thyroid function in cases with early-stage BC and lymphoma, independent of cancer type, with specific chemotherapeutic agents, particularly taxane-based regimens—being associated with a higher incidence of thyroid dysfunction, underscoring the need for proactive thyroid monitoring tailored to treatment protocols rather than cancer treatment alone.

Keywords: Chemotherapy; Thyroid Dysfunction; Breast cancer; Lymphoma.

Introduction

Thyroid hormones (TH), including triiodothyronine (T3) and thyroxine (T4), play a pivotal role in a multitude of physiological processes encompassing cellular development, differentiation, somatic growth, and various metabolic functions. These hormones are tightly regulated through a complex neuroendocrine feedback mechanism known as the hypothalamic-pituitary-thyroid (HPT) axis, which ensures homeostatic balance under both physiological and pathological conditions [(1)].

In the context of malignancy, particularly among cases undergoing cytotoxic treatment, there is growing concern regarding the susceptibility of thyroid function to disruption. This vulnerability stems from the interplay between active HPT axis regulation and the systemic nature of chemotherapy, which, by virtue of its widespread biological effects, may inadvertently impair endocrine function. Traditionally, alterations in thyroid function following chemotherapy were perceived predominantly as delayed sequelae, most often presenting as hypothyroidism, and thus were not given immediate clinical consideration [(2)].

An expanding body of epidemiological research has revealed a consistent and statistically significant association between elevated circulating levels of TH—particularly T3 and T4—and an increased risk of developing breast cancer (BC). These findings lend support to the hypothesis that TH may exert pro-tumorigenic effects, potentially through modulation of cellular proliferation and survival pathways [(3)].

Indeed, clinical observations have noted that BC is frequently diagnosed at an older age and at a less advanced stage in cases with pre-existing hypothyroidism, suggesting a protective influence of reduced thyroid activity. This protective mechanism may arise due to diminished stimulation of tumor growth via T3 receptor (TR)-mediated pathways or due to the fact that hypothyroidism is associated with lower systemic concentrations of insulin-like growth factor 1 (IGF-1), a well-established mediator of cellular proliferation and transformation [(4)].

Clinical data further support the notion that hypothyroidism, whether intentionally induced through concurrent administration of antithyroid drugs such as propylthiouracil or occurring as an unintended consequence of oncologic therapies, may be associated with favorable prognostic outcomes in a variety of cancer types [(5)]. Although overt hypothyroidism has been reported only infrequently in BC cases, most often because of localized radiotherapy targeting the neck or thoracic regions—subclinical or marginal reductions in TH levels may nonetheless have significant clinical implications. Even modest declines in circulating T3 or T4 concentrations in

cases undergoing chemotherapy could influence disease progression or treatment response in ways that warrant further investigation [(2)].

In the specific context of T-cell lymphoma (TCL), TH has been shown to influence tumor biology by engaging both genomic and non-genomic signaling mechanisms that collectively enhance cellular proliferation. The non-genomic actions of TH involve rapid signal transduction events, such as the translocation of protein kinase C zeta (PKC ζ) to the plasma membrane and subsequent activation of key signaling cascades including extracellular signal-regulated kinases (ERK) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). A critical downstream effector of this signaling axis is inducible nitric oxide synthase (iNOS), an enzyme recognized for its role in promoting tumor cell growth and survival. Barreiro Arcos and co-authors provided compelling evidence that intracellular activity of TH is indispensable for the induction of iNOS expression in TCL cells, a process accompanied by increased expression of the TRα receptor subtype, further emphasizing the significance of TH signaling in lymphomagenesis [(6)].

TH has also been shown to support the survival and progression TCL through non-genomic, membrane-mediated mechanisms. Binding of TH to integrin αvβ3 receptors on the cell surface triggers pro-proliferative and pro-angiogenic signaling cascades, resulting in increased expression of cyclins, proliferating cell nuclear antigen (PCNA), and vascular endothelial growth factor (VEGF). This VEGF secretion enhances the angiogenic activity of endothelial cells, potentially promoting TCL growth. Supporting these observations, in vitro studies have demonstrated that treatment of lymphoma cells with T3 and T4 leads to significant proliferation, as indicated by elevated levels of PCNA and cyclins D, A2, and B [(3)].

The purpose of this investigation was to evaluate the effect of chemotherapy on thyroid function, thyroid function alters during toxicity of chemotherapy, and the predictive value of thyroid function on pathological complete response (pCR) in cases with early BC or lymphoma receiving chemotherapy.

Patient and methods

Patients:

This prospective investigation encompassed a cohort of 50 individuals, evenly divided between those diagnosed with BC (n=25) and those with lymphoma (n=25), all of whom underwent chemotherapy at Benha University Hospital.

Prior to the commencement of the investigation, ethical approval was granted by the Scientific Ethical Committee of Benha University Hospitals. Informed consent was obtained from each participant in both verbal and written form, in accordance with institutional standards. for the period from June 2022 to August 2022

Eligible participants were defined as individuals aged over 18 years, diagnosed with either BC or lymphoma, exhibiting measurable disease, maintaining a World Health Organization (WHO) performance status between 0 and 2, and demonstrating adequate bone marrow reserve, hepatic and renal function. Both premenopausal and postmenopausal cases were considered suitable for inclusion, if baseline thyroid function tests and thyroid ultrasound assessments were within normal limits prior to the initiation of chemotherapy.

Cases were **excluded** if they presented with distant metastases (M1), had a prior history of any other malignancy, or showed evidence of thyroid dysfunction, renal failure, congestive heart failure, or hepatic insufficiency.

Methods:

All studied cases were subjected to the following: Detailed history taking, including [Personal history: age, gender, residence, occupation, Socioeconomic Status, Education level, smoking habits maternal age, gravidity and parity. Primary disease. Past obstetric history: Gravidity, Parity and methods of previous deliveries and time of last delivery. Menstrual history: The regularity of the cycles, frequency duration and amount of bleeding of each cycle and time of last menstrual period. Contraceptive history: focus on use of oral contraceptive pills. Past medical: the participants were asked about any concurrent disease such as diabetes or hypertension. Past surgical history: the participants were asked about any prior surgical procedures.]. **Full clinical examination: General examination including [**Heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate and oxygen saturation, Height, weight and BMI] and Local examination. **Routine laboratory investigations [**Complete blood count, Random blood sugar, Thyroid function tests (TSH, fT3 & fT4), kidney and liver function tests]. **Imaging:** Thyroid ultrasound.

Thyroid ultrasound

Cases cancer types were identified whether Triple-negative, HER2-positive, ER-positive, or PR-positive in BC or Hodgkin's or Non-Hodgkin's in lymphoma. Their stages were also identified according to TNM classification system. Cases received chemotherapy according to the standard protocols for each cancer type; BC cases were treated primarily with anthracycline-based regimens such as AC/Taxol or TAC. While Lymphoma cases received ABVD or R-CHOP regimens. Chemotherapy was administered over planned cycles (typically 6). Adjustments were made as necessary based on tolerance and toxicity. Cases were followed throughout the chemotherapy course and re-evaluated 3 months after initiation. Assessments during follow-up included: Completion of chemotherapy cycles and dose adjustments, clinical evaluation for side effects and neural and gastrointestinal toxicities, repetition of thyroid function tests and ultrasound

and evaluation for pCR where applicable.

Outcomes: The outcomes assessed in this investigation were changes in thyroid hormone levels (TSH, fT3, fT4) pre- and post-chemotherapy, prevalence of thyroid dysfunction after treatment, Hematological and hepatic toxicity, including changes in hemoglobin, WBC count, ALT, and AST, incidence and grade of neuropathy, gastrointestinal toxicity, and fatigue, correlation of thyroid dysfunction with chemotherapy regimen and association between thyroid function and pCR.

Approval code: MS 14-5-2022

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM©, Armonk, NY, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage. A two-tailed P value < 0.05 was considered statistically significant.

Results

The BC and lymphoma cohorts showed similar age distributions and BMI values. However, a significantly higher proportion of lymphoma cases were post-menopausal compared to BC cases ($p=0.024$). Both cohorts demonstrated comparable smoking rates, comorbidity profiles, stage distribution or lymph node involvement. **Table 1**

Chemotherapy regimens differed significantly between cancer types, reflecting disease-specific treatment protocols. BC cases predominantly received anthracycline-based regimens (AC /Taxol, TAC), while lymphoma cases received either ABVD or R-CHOP protocols. Treatment completion rates were similar between groups, with both cohorts completing an average of 5 out of 6 planned cycles. Thyroid ultrasound abnormalities were observed at similar frequencies in both groups. **Table 2**

Peripheral neuropathy occurrence and severity showed no significant differences between cancer types. Gastrointestinal toxicity profiles were comparable between groups. Both nausea/vomiting and fatigue showed similar grade distributions. Treatment response rates were similar between groups, with approximately half of cases in each cohort achieving pCR1. Post-treatment thyroid dysfunction occurs at comparable rates, suggesting similar susceptibility to chemotherapy-induced thyroid effects. **Table 3**

Haematological parameters, Metabolic and renal function parameters showed no significant differences between cancer types. Hepatic function remained preserved in both groups throughout treatment111. While lymphoma cases showed slightly higher transaminase levels, these differences were not statistically significant and remained within normal ranges. Baseline thyroid function

parameters showed no significant differences between cancer groups. Post-treatment thyroid function changes were similar between cancer types. Both groups showed mild increases in TSH and decreases in fT3 levels. A statistically significant increase was observed in TSH levels post-treatment ($p = 0.043$), In contrast, free T3 (fT3) and free T4 (fT4) levels showed non-significant declines of 11.4% and 9.1%, respectively ($p > 0.05$). **Table 4**

The prevalence of thyroid dysfunction significantly differed between patient groups ($p < 0.001$). Chemotherapy regimens showed varying associations with thyroid dysfunction. The Taxol /Carboplatin regimen was linked to a significantly higher dysfunction rate (66.7%, $p = 0.023$ vs. others), whereas R-CHOP had a markedly lower rate (7.7%, $p = 0.001$ vs. others). Chemotherapy has induced significant hematologic alterations. Hemoglobin levels declined ($p = 0.008$), and white blood cell (WBC) counts dropped ($p < 0.001$). There was a significant rise in liver enzymes following chemotherapy, with ALT increasing ($p = 0.042$), and AST ($p = 0.031$). **Table 5**

Table 1: Baseline Demographic Characteristics, Smoking Status, Comorbidities, Disease Stage and Tumor Characteristics

Variable	BC (n=25)	Lymphoma (n=25)	P Value
Age, years Mean (SD)	48.0 (13.0)	45.5 (12.8)	0.487
BMI, kg/m² Mean (SD)	26.5 (5.2)	26.0 (4.7)	0.694
Menopausal Status, n (%)			
Pre-menopausal	8 (32.0)	4 (16.0)	0.024
Post-menopausal	17 (68.0)	21 (84.0)	
Smoking Status, n (%)	0 (0)	2 (8.0)	0.956
Comorbidities, n (%)			
Hypertension	11 (44.0)	10 (40.0)	0.892
Diabetes	6 (24.0)	8 (32.0)	
Stage, n (%)			
Stage I	8 (32.0)	6 (24.0)	0.445
Stage II	6 (24.0)	8 (32.0)	
Stage III	11 (44.0)	11 (44.0)	
Tumor Size, cm			
Median (IQR)	3.0 (2.1-3.6)	3.3 (2.5-4.7)	0.260
Lymph Node Involvement, n (%)	14 (56.0)	12 (48.0)	0.472

Table 2: Chemotherapy Regimens, Treatment Completion, Modifications, Thyroid Ultrasound Results (after chemotherapy)

Variable	BC (n=25)	Lymphoma (n=25)	P Value
Chemotherapy Regimen, n (%)			<0.001*
Taxol /Carboplatin	4 (16.0)	0 (0.0)	
TAC	7 (28.0)	6 (24.0)	
AC /Taxol	14 (56.0)	1 (4.0)	
ABVD	0 (0.0)	11 (44.0)	
R-CHOP	0 (0.0)	7 (28.0)	
Cycles Planned Mean (SD)	6.0 (0.0)	6.0 (0.0)	1.000
Cycles Completed Mean (SD)	5.0 (0.8)	5.1 (0.9)	0.653
Dose Adjustments, n (%)	14 (56.0)	12 (48.0)	0.564
Thyroid Ultrasound, n (%)			
Normal	11 (44.0)	12 (48.0)	0.756
Abnormal	14 (56.0)	13 (52.0)	

*: statistically significant as P value <0.05

Table 3: Neurological Toxicity (Neuropathy Grades), Gastrointestinal Toxicity, Pathological Response and Thyroid Dysfunction

Variable	BC (n=25)	Lymphoma (n=25)	P Value
Neuropathy Grade, n (%)			
Grade 0	11 (44.0)	12 (48.0)	0.892
Grade I	9 (36.0)	8 (32.0)	
Grade II	5 (20.0)	5 (20.0)	
Nausea/Vomiting Grade, n (%)			0.445
Grade 0	11 (44.0)	8 (32.0)	
Grade I	8 (32.0)	9 (36.0)	
Grade II	6 (24.0)	8 (32.0)	
Fatigue Grade, n (%)			0.648
Grade 0	13 (52.0)	11 (44.0)	
Grade I	6 (24.0)	8 (32.0)	
Grade II	6 (24.0)	6 (24.0)	
Pathological Complete Response, n (%)			
Yes	14 (56.0)	13 (52.0)	0.756
No	11 (44.0)	12 (48.0)	
Thyroid Dysfunction Post-treatment, n (%)			
Yes	11 (44.0)	9 (36.0)	0.564
No	14 (56.0)	16 (64.0)	

*: statistically significant as P value <0.05

Table 4: Complete Blood Count Analysis, Metabolic Parameters, Liver Function Tests, Pre-treatment Thyroid Function Post-treatment, Thyroid Function and Changes

Variable Mean (SD)	BC (n=25)	Lymphoma (n=25)		P Value
Hemoglobin, g/dL	12.1 (1.4)	12.8 (1.4)		0.098
WBC, ×10³/µL	7.1 (2.3)	7.4 (2.0)		0.722
Platelets, ×10³/µL	304.1 (78.9)	289.0 (73.4)		0.483
Random Blood Sugar, mg/dL	108.6 (21.8)	102.8 (20.1)		0.349
Creatinine, mg/dL	1.01 (0.18)	0.95 (0.21)		0.279
BUN, mg/dL	11.8 (4.4)	12.8 (4.1)		0.397
ALT, U/L	29.0 (16.2)	35.4 (17.3)		0.184
AST, U/L	22.4 (9.8)	26.8 (9.9)		0.117
ALP, U/L	88.8 (31.8)	98.7 (30.9)		0.269
Bilirubin, mg/dL	0.68 (0.28)	0.59 (0.31)		0.298
TSH Pre-treatment, mIU/L	2.33 (1.21)	2.31 (1.18)		0.954
fT3 Pre-treatment, pg/mL	3.28 (0.73)	3.24 (0.73)		0.840
fT4 Pre-treatment, ng/dL	1.41 (0.32)	1.42 (0.31)		0.918
TSH post-treatment, mIU/L	3.09 (1.58)	2.87 (1.44)		0.602
fT3 post-treatment, pg/mL	2.88 (0.86)	2.87 (0.85)		0.962
fT4 post-treatment, ng/dL	1.36 (0.36)	1.32 (0.37)		0.717
Hormone	Pre-Treatment	Post Treatment	Change	p-value
TSH	2.43 ± 1.23	3.12 ± 1.67	+28.4%	0.043*
fT3	3.24 ± 0.89	2.87 ± 0.76	-11.4%	0.394
fT4	1.42 ± 0.31	1.29 ± 0.28	-9.1%	0.465

*: statistically significant as P value <0.05

Table 5: Thyroid Dysfunction Prevalence, Chemotherapy Regimen-Specific Effects, Hematological Changes and Hepatic Function Changes

Group	No Dysfunction	Dysfunction	P value
BC	56%	44%	<0.001*
Lymphoma	80%	20%	
Regimen	Dysfunction Rate	p-value vs Others	
Taxol /Carboplatin	66.7%	0.023*	
R-CHOP	7.7%	0.001*	
Parameter	Pre-Treatment	Post Treatment	p-value
Hemoglobin	12.4 ± 1.6	11.8 ± 1.4	0.008*
WBC (×10³/µL)	7.2 ± 2.1	6.1 ± 1.8	<0.001*
Enzyme	Pre-Treatment	Post-Treatment	p-value
ALT	31.2 ± 16.8	36.4 ± 18.2	0.042*
AST	24.1 ± 9.7	27.8 ± 11.3	0.031*

Discussion

Notably, our investigation found no significant differences between BC and lymphoma cases in two key chemotherapy-related complications: thyroid ultrasound abnormalities and peripheral neuropathy. Thyroid changes were observed in 56.0% of BC cases and 52.0% of lymphoma cases, while peripheral neuropathy grades were similarly distributed between both groups. which may suggest that both thyroid structural alterations and neuropathic effects are likely general consequences of chemotherapy, rather than being influenced by the underlying cancer type.

Consistently, a meta-analysis conducted by Zhang encompassing over 4,000 cases with colorectal,

breast, lung, testicular, and other cancers treated with neurotoxic agents (e.g. oxaliplatin, paclitaxel, vincristine, bortezomib) found Chemotherapy-induced peripheral neuropathy (CIPN) rates of 68% at 1 month, 60% at 3 months, and 30% at 6 months post-chemotherapy (7).

Additionally, Lollert and co-authors evaluated thyroid changes using ultrasound and found that chemotherapy alone (without radiation) did not significantly damage the thyroid axis in children—but they did observe structural alterations in those treated with chemo—indicating that such changes can manifest solely from chemotherapy exposure (8)

Our investigation demonstrated that gastrointestinal toxicity, including nausea, vomiting, and fatigue, occurred at similar rates in BC and lymphoma cases, with no statistically significant differences. Both groups exhibited comparable grade distributions, indicating that these common chemotherapy-related side effects are likely independent of cancer type.

In a comprehensive scoping review conducted by Fox and co-authors, encompassing 27 studies related to BC, colorectal cancer, as well as both Hodgkin's and non-Hodgkin's lymphomas, a range of chemotherapy-induced toxicities were identified, with gastrointestinal disturbances and fatigue emerging as the most frequently reported. Notably, fatigue was the primary focus in most included studies (n = 14), particularly among cases diagnosed with BC. The review also identified the presence of relevant clinical practice guidelines (CPGs) or evidence-based recommendations (EBRs) addressing various adverse effects, including fatigue (n = 4), nausea and vomiting (n = 5), mucositis (n = 4), peripheral neuropathy (n = 3), diarrhea (n = 2), constipation (n = 2), febrile neutropenia or infectious complications (n = 7), palmar–plantar erythrodysesthesia (PPE) (n = 1), and pain (n = 4). Furthermore, symptom management (SM) protocols were reported to be in place at over 40% of the clinical sites surveyed, underscoring a continued commitment toward the harmonization and standardization of supportive care across varying cancer types [(9)].

Our investigation indicated that pCR rates did not significantly differ between cases with BC and those with lymphoma following treatment, with approximately half of the cases in each group achieving pCR (56.0% vs. 52.0%, p = 0.756). Similarly, the incidence of post-treatment thyroid dysfunction was comparable between the two groups (44.0% in BC vs. 36.0% in lymphoma, p = 0.564). These findings may imply that the effectiveness of treatment in achieving tumor regression is consistent across cancer types and that both groups exhibit a similar risk profile for thyroid dysfunction following therapy.

A Danish nationwide cohort investigation conducted by Falstie-Jensen and co-authors (~44,500 BC survivors vs matched controls) reported a 5-year cumulative incidence of hypothyroidism of only 1.8%,

compared to 1.6% in controls. The overall hazard ratio was modest (HR 1.17) [(2)]

Our investigation also demonstrated that chemotherapy has a measurable impact on thyroid function in cases with early BC and lymphoma. Notably, a statistically significant post-treatment increase in TSH levels was observed, suggesting a possible shift toward subclinical hypothyroidism or early thyroid dysfunction induced by cytotoxic therapy. These findings are consistent with the hypothesis that chemotherapy may disrupt HPT axis regulation, potentially due to direct glandular toxicity or systemic inflammatory responses. Although reductions were also noted in free triiodothyronine (fT3) and free thyroxine (fT4) levels post-treatment, these changes did not reach statistical significance. Importantly, comparative analysis between BC and lymphoma groups revealed no significant differences in post-treatment thyroid hormone alterations, suggesting a class effect of chemotherapy regardless of cancer type.

In a similar vein, Kailajärvi and co-authors assessed the impact of adjuvant chemotherapy on a range of laboratory parameters in cases with BC. This investigation included 15 female cases undergoing treatment with chemotherapeutic agents. The chemotherapy protocol utilized was CMF, comprising cyclophosphamide (600 mg/m²), methotrexate (40 mg/m²), and 5-fluorouracil (600 mg/m²), administered intravenously at three-week intervals over a total of six to seven cycles. The researchers recorded mean thyroid-stimulating hormone (TSH) levels at various time points: before treatment (1.5 ± 1.0 mU/L), at 3 weeks (1.7 ± 1.1 mU/L), 5–8 weeks (1.6 ± 1.1 mU/L), 4 months (1.9 ± 1.7 mU/L), 6–8 months (1.5 ± 0.7 mU/L), and 10 months (1.3 ± 0.9 mU/L) following chemotherapy. Corresponding free thyroxine (FT4) levels were 13.4 ± 1.9, 12.7 ± 2.4, 11.7 ± 1.8, 12.1 ± 2.1, 11.8 ± 1.7, and 12.0 ± 1.5 pmol/L, respectively, while free triiodothyronine (FT3) levels were 5.8 ± 0.7, 5.3 ± 0.7, 5.1 ± 0.4, 5.3 ± 0.8, 5.9 ± 0.9, and 5.6 ± 0.6 pmol/L, respectively. The authors concluded that: (1) thyroid hormone levels exhibited only minor variations over time, (2) FT4 concentrations showed a noticeable decrease at 5–8 weeks and again at 6–8 months, (3) FT3 levels declined temporarily during the 5–8 week interval, and (4) TSH levels remained relatively stable throughout the investigation period [(10)].

In a separate investigation, Kumar and co-authors explored the effects of adjuvant chemotherapy on thyroid function in BC cases through a prospective observational investigation involving 198 participants. The cases received one of three chemotherapy regimens: CMF, CAF (Cytoxan/Adriamycin/5-fluorouracil), or CA (Cytoxan/Adriamycin). Baseline thyroid profiles included FT4 at 1.54 ± 0.39 ng/dL, total T4 at 7.40 ± 1.94 µg/dL, T3 uptake at 1.04 ± 0.24%, thyroxine-binding globulin at 2.00 ± 0.39 mg/dL, and TSH at 1.60 ± 1.17 mU/L. At the

conclusion of chemotherapy, these values were reported as FT4: 1.44 ± 0.40 ng/dL, total T4: 7.60 ± 1.34 µg/dL, T3 uptake: 0.99 ± 0.14%, thyroxine-binding globulin: 2.19 ± 0.37 mg/dL, and TSH: 1.56 ± 1.13 mU/L. The results indicated a statistically significant reduction in T3 uptake, along with significant elevations in total T4 and thyroxine-binding globulin. Based on these findings, the authors suggested that chemotherapy may exert an influence on thyroid function, potentially contributing to the gradual emergence of clinical symptoms such as weight gain, fatigue, amenorrhea, and diminished physical activity levels [(11)].

Moreover, Huang and co-authors investigated changes in thyroid function among BC cases undergoing chemotherapy. In this investigation, blood samples were collected from a total of 180 cases receiving treatment with 5-fluorouracil (administered at concentrations of 13 µmol/L for MCF-7 cells and 8 µmol/L for MDA-MB-231 cells) and Taxol (0.4 µmol/L for MCF-7 and 0.5 µmol/L for MDA-MB-231). The pre-chemotherapy mean levels of TH were as follows: total triiodothyronine (T3) at 1.16 ± 0.27 ng/mL, free triiodothyronine (FT3) at 2.89 ± 0.57 pg/mL, total thyroxine (T4) at 7.30 ± 1.23 µg/dL, free thyroxine (FT4) at 0.85 ± 0.14 ng/dL, and thyroid-stimulating hormone (TSH) at 2.78 ± 2.16 µIU/mL. Following chemotherapy, the respective values were T3 at 0.80 ± 0.27 ng/mL, FT3 at 2.10 ± 0.49 pg/mL, T4 at 6.87 ± 1.57 µg/dL, FT4 at 0.90 ± 0.19 ng/dL, and TSH at 1.00 ± 1.31 µIU/mL. The analysis demonstrated a statistically significant reduction in T3, FT3, T4, and TSH levels, while FT4 levels showed a significant elevation during chemotherapy compared to baseline measurements [(12)].

Additionally, Sutcliffe and co-authors evaluated thyroid function in individuals diagnosed with Hodgkin's disease who were treated using the MOPP regimen (mechlorethamine, procarbazine, vinblastine, and prednisolone). Their findings revealed that serum TSH concentrations increased in 44% of the patient cohort, suggesting a notable impact of chemotherapy on thyroid regulation in this population [(13)].

Thyroid dysfunction was significantly more prevalent among BC cases (44%) than those with lymphoma (20%) ($p < 0.001$), indicating a potential cancer-type-specific vulnerability to chemotherapy-induced thyroid alterations. This disparity may, in part, be attributed to differences in chemotherapy regimens, as further supported by the observed variation in dysfunction rates across treatment types. Cases receiving the Taxol/Carboplatin regimen—commonly used in BC—exhibited a markedly higher incidence of thyroid dysfunction (66.7%; $p = 0.023$), whereas those treated with the R-CHOP regimen, typically administered for lymphoma, had a significantly lower rate (7.7%; $p = 0.001$). These findings underscore the influence of

specific chemotherapeutic agents on thyroid function and highlight the need for personalized endocrine monitoring strategies based on both cancer type and treatment protocol.

Accordingly, a prospective investigation conducted by Manosroi and co-authors on diffuse large B-cell lymphoma (DLBCL) cases treated with R-CHOP demonstrated secondary hypothyroidism and subclinical hyperthyroidism after about five cycles, largely attributed to high-dose glucocorticoids suppressing TSH, T3, and T4—effects that were largely transient [(14)].

Similarly, a case series conducted by Abdulwahid and co-authors of primary thyroid non-Hodgkin lymphoma NHL receiving R-CHOP reported TSH abnormalities in 44% of cases, with 7–11% experiencing overt dysfunction [(15)]

An investigation from the NEOZOTAC trial conducted by de-Groot and co-authors found that during six cycles of neoadjuvant chemotherapy (including taxane-based regimens), free T4 decreased significantly ($p = 0.0001$) and TSH increased significantly ($p = 0.019$) in 38 early BC cases [(16)]

This investigation has some limitations: The single-center design of the investigation may limit the external validity of the findings. The relatively small sample size ($n = 50$; 25 BC and 25 lymphoma cases) may reduce the statistical power to detect smaller but clinically relevant differences, particularly in subgroup analyses related to chemotherapy regimens and thyroid dysfunction. Short-term follow-up focused on immediate post-treatment outcomes, without longitudinal assessment of delayed or long-term thyroid dysfunction or other systemic toxicities.

Conclusion

Chemotherapy exerts a measurable and comparable impact on thyroid function in cases with early-stage BC and lymphoma, independent of cancer type, with specific chemotherapeutic agents particularly taxane-based regimens being associated with a higher incidence of thyroid dysfunction, underscoring the need for proactive thyroid monitoring tailored to treatment protocols rather than cancer treatment alone.

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Author Contributions

All authors made substantial and equal contributions to this research. This included the conception and design of the investigation, acquisition and analysis of data, interpretation of findings, and the drafting and critical revision of the manuscript. Each author

has approved the final version of the work and agrees to be accountable for all aspects of the investigation to ensure its integrity and accuracy.

Conflicts of Interest

The authors affirm that there are no financial, personal, or professional conflicts of interest that could be perceived as influencing the research outcomes or interpretations presented in this manuscript. The investigation was conducted with full adherence to ethical research standards and transparency.

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