Journal of Techniques, ISSN: 2708-8383, Vol. 4, No. Special Issue, November 2022, Pages 170-174

JOURNAL OF TECHNIQUES

Journal homepage: http://journal.mtu.edu.iq

RESEARCH ARTICLE - MEDICAL TECHNIQUES

Neutrophil to Lymphocyte Ratio as a Predictive Factor in Iraqi Patients with Thyroid Cancer

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Article Info.

Article history:

Received
28 July 2022

Accepted
28 August 2022

Publishing
15 November 2022

Abstract

Thyroid cancer is one of the fastest growing malignancies in recent years, with an increase of 14.51% per year. It has been shown that there is an association between some biomarkers and the progression of thyroid cancer. In this study, we aim to assess the Neutrophil to Lymphocyte Ratio (NLR) levels and Thyroid function test (TSH, T3, T4) in patients with thyroid cancer. In the current study, (145) participants were divided into 3 groups: G1: (60 malignant thyroid gland patients, G2: (35 benign thyroid gland patients), and G3: (50 healthy control individuals as a control group). The patients attended to AL-Amal oncology Hospital in Baghdad and Imam Sadiq Hospital in Babylon province, Iraq during the period from November 2021 to February 2022. Depending on hematology analyzer the level of NLR and by Mini Vida's the TSH, T3, T4 were estimated in the studied groups. The results showed that the highest number and percentage of malignant thyroid tumors 21 (35%) was among the age group (50-≥ 60) years, while the lowest number and percentage of malignant tumors 10 (16.7%) was among the age groups (20-29) and (30-39) years. The results also demonstrated that the number and percentage of female patients with malignant thyroid tumors was 43 (71.7%) and males 17 (28.3%). A highly significant increase ($P<0.01$) in the levels of both NLR and TSH was observed in patients with malignant thyroid cancer when compared with their levels in the control group and benign tumor groups. The current study revealed that the age group (50-≥ 60) years and female patients were most affected by thyroid cancer and both NLR and TSH levels were highly increased in thyroid cancer patients. when compared with healthy group.

Publisher : Middle Technical University

Keywords: Malignant & benign; Thyroid gland; T3; T4; TSH; Neutrophil–lymphocyte ratio.

1. Introduction

Thyroid cancer is the most prevalent malignant tumor of the endocrine system and the head and neck, and its frequency is increasing year after year, causing global worry [1]. Thyroid cancer is the most frequent endocrine cancer, accounting for approximately 96% of all endocrine malignancies and 3% of all cancers [2]. Radiation exposure, a family history of thyroid cancer, lymphocytic thyroiditis, low iodine intake, and female gender are all established risk factors for thyroid cancer [3, 4]. Thyroid cancer is principally classified histologically into three types: papillary thyroid carcinoma (PTC), anaplastic thyroid carcinoma (ATC), and follicular thyroid carcinoma (FTC) [5]. Papillary thyroid carcinoma (PTC) is the predominant histological type of thyroid malignancy, accounting for 80%–85% of cases [6, 7], which is identified as the least aggressive form of thyroid tumor [8]. Biomarkers of cancer can be genetic materials, proteins, chemical modifications, and characteristics that can be measured in the field of thyroid cancer [9]. The neutrophil-to-lymphocyte ratio (NLR) is commonly accepted as a biomarker of systemic inflammation [10]. As a result, it serves as a predictor of metastasis and poor prognosis in a variety of malignancies, including breast, colon, head, neck, and thyroid cancers [11-13]. Furthermore, neutrophils indicate the presence of inflammation, whereas lymphocytes demonstrate the function of the immune system. As a result, it may serve as a possible predictor of metastasis and poor prognosis in thyroid cancer patients, as it does in other malignancies [14]. Increased neutrophil-to-lymphocyte ratio (NLR), which measures the ratio of peripheral circulating neutrophil and lymphocyte counts, has been found to be an indicator of a bad prognosis in several malignancies, including those of the breast, colon, and head and neck [15].

2. Materials and Methods

2.1. Samples

Venous blood samples were withdrawn from the patients along with the diagnosis period before any surgical operation. And collected into two tubes; The first gel tube was used for routine thyroid function tests including TSH, total thyroxine (T4), and total triiodothyronine (T3), which were analyzed using Mini Vida's; Biomerieux Diagnostics, enzyme-linked fluorescent immunoassay (ELFA).

Nomenclature			
CBC	Complete blood count	NLR	Neutrophil-lymphocyte ratio
PTC	Papillary thyroid carcinoma	TSH	Thyroid stimulating hormone
T3	Triiodothyronine	FTC	Follicular thyroid cancer
T4	Thyroxine	ATC	Anaplastic thyroid cancer
ELFA	Enzyme linked fluorescent immunoassay		

The second EDTA tube was used for CBC to detect the neutrophil to lymphocyte ratio by using a hematology analyzer, NLR calculated by dividing the neutrophil number by lymphocyte number, from peripheral blood sample.

2.2. Statistical analysis

Data were revised, coded, and analyzed using the "Statistical Package of Social Science(SPSS) version 26.0.

3. Results and Discussions

3.1 Distribution of studied groups according to age

In this case-control study, the serum levels of NLR and thyroid function test were studied in the patients with malignant and benign thyroid tumors and compared with the healthy control group. Table 1 showed that the highest number and percentage of malignant thyroid tumors 21 (35%) were among the age group (50-≥ 60) years, while the lowest number and percentage of malignant tumors 10 (16.7%) was among the age groups (20-29) and (30-39) years. The highest number and percentage of benign thyroid tumors 11 (31.4%) was among the age group (50-≥ 60) years, while the lowest number and percentage of benign tumors 4 (11.4%) was among the age groups (20-29) years, while the highest number and percentage of healthy controls 16 (32%) was among the age group (20-29) years, and the lowest number and percentage of controls 8 (16%) was among the age groups (40-49) years.

Table 1 Distribution of studied groups according to age

Age			groups		
	Age Groups		Benign	Malignant	Healthy
	(20-29)	No.	4 / 11.4%	10 / 16.7 %	16 /32.0 %
	(30-39)	No.	10 / 28.6%	10 / 16.7 %	14 / 28.0 %
	(40-49)	No.	10 / 28.6 %	19 / 31.7 %	8 / 16.0 %
	(50--≥60)	No.	11 /31.4%	21 /35.0 %	12 / 24.0 %
	Total	No.	35 / 100.0 %	60 / 100.0 %	50 / 100.0 %
			X^2=10.919	P=.091 (NS)	

3.2. Distribution of studied groups according to gender

The distribution of the studied groups according to gender demonstrated that the number and percentage of female patients with malignant thyroid tumors were 43 (71.7%) and males were 17 (28.3%), while the number and percentage of female patients with benign tumors were 27 (77.1%) and males were 8 (22.9%), whereas the number and percentage of female controls was 31 (62%) and males were 19 (38. %) as shown in Table 2.

Table 2 Distribution of studied groups according to gender

	Gender Groups		Benign	Malignant	Healthy
Gender	Female	No.	27 /77.1 %	43 / 71.7 %	31 / 62.0 %
	Male	No.	8 / 22.9 %	17 / 28.3 %	19 / 38.0 %
	Total	No.	35 / 100.0 %	60 / 100.0 %	50 / 100.0 %
			X^2=2.429	P=.297 (NS)	

3.3. Comparison of the studied groups according to NLR

Results in Table 3 revealed that the (Mean±SD) of NLR % among healthy controls was (2.242±0.709), and among patients with benign thyroid tumor was (2.767±2.101), while among patients with malignant thyroid cancer was (5.241±2.010) with a non-significant difference between the benign and control groups (P>0.05), while there was a highly significant difference between the healthy controls and malignant tumor patients (P<0.01), and also a highly significant difference between the benign tumor group and malignant group (P<0.01).

Table 3 Comparison of the studied groups according to NLR

NLR	Compared with Healthy				Compared Benign with Malignant	
	Group	Mean± Std.	t-test	p-value	t-test	p-value
			Healthy	2.242±0.709		
		Benign	2.767±2.101	1.642	.104(p>0.05 NS)	
	Malignant	5.241±2.010	10.037	0.000(p<0.01 HS)	5.690	0.000(p<0.01 HS)

3.4. Comparison of the studied groups according to T3

Result in Table 4 revealed that the (Mean±SD) of T3 (miu\ml) among healthy controls was (2.286±0.588), and among patients with benign thyroid tumor was (1.300±0.727), while among patients with malignant thyroid cancer was (1.433±1.311) with a high significant difference between the benign and control groups (P<0.05), while there was a highly significant difference between the healthy controls and malignant tumor patients (P<0.01) , and also a non-significant difference between the benign tumor group and malignant group (p>0.05).

Table 4 Comparison of the studied groups according to T3

T3	Compared with Healthy				Compared Benign with Malignant	
	Group	Mean± Std.	t-test	p-value	t-test	p-value
			Healthy	2.286±0.588		
		Benign	1.300±0.727	6.897	0.000(p<0.01 HS)	
	Malignant	1.433±1.311	4.255	0.000(p<0.01 HS)	0.553	0.553(p>0.05 NS)

3.5. Comparison of the studied groups according to T4

Result in Table 5 revealed that the (Mean±SD) of T4 (miu\ml) among healthy controls was (8.556±2.604), and among patients with benign thyroid tumor was (11.035±8.556), while among patients with malignant thyroid cancer was (8.705±4.337) with a non-significant difference between the benign and control groups (P>0.05), and non- significant difference between the healthy controls and malignant tumor patients (P>0.05) , and also non- significant difference between the benign tumor group and malignant group(p>0.05).

Table 5 Comparison of the studied groups according to T4

T4	Compared with Healthy				Compared Benign with Malignant	
	Group	Mean± Std.	t-test	p-value	t-test	p-value
			Healthy	8.556±2.604		
		Benign	11.035±8.556	1.930	.060(p>0.05 NS)	
	Malignant	8.705±4.337	0.213	.832(p>0.05 NS)	1.761	.081(p>0.05 NS)

3.6. Comparison of the studied groups according to TSH

Result in Table 6 revealed that the (Mean±SD) of TSH (miu\ml) among healthy controls was (2.632±4.893), and among patients with benign thyroid tumor was (1.607±2.612), while among patients with malignant thyroid cancer was (25.454±33.960) with a non-significant difference between the benign and control groups (P>0.05), while there was a highly significant difference between the healthy controls and malignant tumor patients (P<0.01) , and also a highly significant difference between the benign tumor group and malignant group (p<0.01).

Table 6 Comparison of the studied groups according to TSH

TSH	Compared with Healthy				Compared Benign with Malignant	
	Group	Mean± Std.	t-test	p-value	t-test	p-value
			Healthy	2.632±4.893		
		Benign	1.607±2.612	1.131	.261(p>0.05 NS)	
	Malignant	25.454±33.960	4.708	0.000(p<0.01 HS)	4.138	0.000(p<0.01 HS)

4. Discussion

The highest incidence of thyroid cancer in our study appeared in the older adults aged ((50-≥ 60). This result almost agrees with the majority of studies that indicated this finding. Thyroid cancer can strike anyone at any age, while it seldom affects children. Most malignancies are discovered between the third and sixth decade of life. For the papillary form, the median age at diagnosis is between 40 and 50 years old; for the follicular and medullary types, it is 50 years old; and for the poorly differentiated and undifferentiated kinds, it is 60 years old. [16]. One of the most reliable indicators of prognosis in patients with papillary and follicular thyroid cancer is the patient's age upon diagnosis. As people

age, their risk of death and recurrence rises, especially beyond the age of 40 [17].The results of the current study found that women were more likely than males to develop thyroid cancer, and this finding was supported by data from the Chinese Cancer Incidence Study between 2007 and 2009, which showed a considerable rise in the incidence of thyroid cancer, particularly in women. There are three to four times as many ladies who contract this disease as there are males [18]. Alternatively, if males seek medical assistance later in life with a more severe illness or if women do so earlier and are subjected to a more comprehensive screening for illness, a gender-related ascertainment bias may develop. For instance, women more frequently than males use healthcare services and take part in cancer screenings for the skin and colon [19].
Numerous recent investigations have demonstrated that inflammatory stimulation is a significant element in the beginning and progression of thyroid cancer [20]. The neutrophil-to-lymphocyte ratio (NLR) is commonly accepted as a biomarker for systemic inflammatory disease [21]. As a result, it may serve as a possible predictor of metastasis and poor prognosis in thyroid cancer patients, as it does in other malignancies. Several research has confirmed this notion. For example, Xu et al found that NLR was an independent predictor of metastasis (odds ratio = 5.918, 95 percent confidence intervals [CI]: 1.147-30.541; P =.034) in patients with MTC following multivariate logistic regression analysis [22]. However, there were some inconsistencies in the findings: Jiang et al found no significant relationships between the NLR and lymph node metastasis (P =.461) or DFS (P =.124) in MTC patients [23]. Anti-tumor immunity is primarily governed by CD4 and CD8 T lymphocytes, and these immune cells' activities are mediated by a variety of cytokines and chemokines. According to reports, NLR reflects the profile of various cytokines and chemokines [24]. As a result, NLR may be used to predict anti-tumor immunity and prognosis in cancer patients. In a prior study, greater NLR was linked to a higher risk of recurrence and a worse prognosis in PTC [25]. Higher NLR was found to be associated with extra thyroidal invasive, bilateral, multifocal, and lymph node-positive PTC [26]. It has been well documented that there is a relationship between levels of thyroid stimulating hormone (TSH) and thyroid malignancy. A TSH level that is above the normal range or even in the upper range of normal is thought to increase the likelihood that a thyroid nodule is malignant [25]. It stands to reason that if the levels of TSH are elevated in patients with thyroid cancer, it is possible that elevated levels of thyroxine (T4) and triiodothyronine (T3) may also be correlated with malignancy as well. Cho et al. has shown that free T4 (fT4) is elevated in patients with thyroid cancer (odd's ratio (OR) of 1.73) [27]. However, the inverse relationship has been shown to be true for total T3 (TT3) by [28]. By studying serological data taken from patients who have undergone thyroid surgery, we hope to better understand the relationship between the levels of fT4 and fT3 and differentiated thyroid cancer which can be used as a clinical tool to help understand the true nature of indeterminate thyroid nodules [27]. Haymart et al. revealed that there was a correlation between the higher serum content of TSH with the last stage of thyroid carcinoma [29]. The result of the research of (Boelaert, 2009) gave him the impression that TSH content might play its role in the development of thyroid carcinoma [30].

5. Conclusions

Serum neutrophil to lymphocyte ratio levels higher significantly in patient's groups, especially in thyroid cancer when compared with healthy group.

6. Recommendation

Perform same research with a bigger samples size from different areas in Iraq.

Acknowledgement

The authors would like to thank AL-Amal oncology Hospital in Baghdad and Imam Sadiq Hospital in Babylon province.

Ethical approval

The research was conducted in agreement with the Institutional Board Review's ethical approval (IRB) at Middle Technical University's College of Health and Medical Technologies; on the date of 10/11/2021. All subjects gave written informed consent before collecting their blood for this study.

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