Original Article

Evaluation the serum levels of T3, T4, TSH, Thyroglobulin and Galactin-3 in patients with benign and malignant thyroid tumors

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Abstract

Background: Currently, cytological examination of fine needle biopsies is the method used for preoperative differential diagnosis of thyroid nodules, however, the results may be inaccurate in about 20% of cases. Aim: The study aimed to detect a biomarker in the serum to detect and distinguish between benign and malignant thyroid gland tumors. Methods: Seventy-two patients were divided into malignant thyroid tumor (n = 45) and benign thyroid tumor (n = 27), the median age of patients was 45 years. The blood samples were collected from Middle Euphrates Cancer Center /Al- Najaf Al-Ashraf Governorate in Iraq from September 2019 until March 2020. Every patient's study group was divided into subgroups according to age, gender and body mass index (BMI). A physician diagnosed the patients based on history, clinical presentation and fine needle aspirate. Each patient group was distributed into two groups: before and after thyroidectomy. The control group was made out of sixteen healthy male and females the median of age was 47 years. Results: A significant rise (p□0.05) in serum T4 in patients with benign thyroid tumors matched with healthy and malignant thyroid tumor groups could be seen. A significant rise (p□0.05) of T3 and T4 concentration in patients with benign thyroid tumor in male groups compared with female groups was observed. A significant increase (p□0.05) of T4 concentration in patients with malignant thyroid tumor in BMI group (18-24.9) Kg/m2 compared with other BMI groups was observed. A significant increase (p□0.05) of T3 and T4 concentration in patients with benign thyroid tumor in BMI group (18-24.9) Kg/m2 compared with other BMI groups was also observed. Also, serum TSH exhibited a significant increase (p□0.05) in patients with malignant thyroid tumors compared with healthy group and benign thyroid tumor group. On other hand the results demonstrated that that there was a significant increase (p□0.05) in serum Tg and Galactin-3 of patients with malignant thyroid tumors and benign thyroid tumor group compared with healthy group. Regarding the thyroidectomy, there was a significant increase of TSH (p□0.05) in patients with malignant thyroid tumor earlier thyroidectomy matched with that later thyroidectomy. Tg concentration exposed a significant decrease (p□0.05) after thyroidectomy compared with groups before thyroidectomy in benign and malignant thyroid tumor. Conclusions: Depending on the findings of the study, we can conclude that the early detection of abnormal biochemical parameters includes TSH, thyroglobulin, and Galactin-3 can limit complication and it can also help to monitor the progression of the disease in patients with thyroid cancers. But, the findings did not demonstrate that these biomarkers could be used to discriminate between malignant and benign thyroid tumor.

Keywords: Galactin-3, malignant thyroid tumor, benign thyroid tumor, thyroglobulin, TSH.

Introduction

Thyroid cancer (TC) has a greater frequency than other common endocrine malignancies and it creates 3–4% of recently di¬agnosed cancers every year.

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The frequency of TC has also improved markedly over the past 2 decades [1]. Papillary thyroid cancer (PTC) is the most common type of thyroid cancer diagnosed, and it accounts for up to 90% of all TC cases [2]. Physical examinations have had limited efficiency in the differ¬entiation of benign thyroid nodules from malignant thyroid nodules unless there is an marked outcome. Fine-needle as¬piration biopsy (FNAB) of the thyroid is usually well-thought-out an effective screening test [3]. However, this is an inva¬sive practice and can have severe problems. Moreover, one of the main restriction of this method is a great happening of non-diagnostic results and about 10–20% non-diag¬nostic rates [4]. So, there is an increasing essential to identify novel and clinically appropriate biological markers to differentiate ma¬lignant thyroid nodules from benign lesions [5].

The initial use of biological markers was to identify and treat thyroid cancer. The idea of thyroid biomarkers changed as our knowledge of the molecular etiology of thyroid cancer increased. Biomarkers, also known as molecular markers, biological markers, or tumor markers, are now helpful for predicting the success of surgical removal, radioiodine ablation, and chemotherapy as well as for early detection of thyroid cancer and recurring and persistent disease [6].

A member of the galectin family with a preference for β-galactosidis galectin-3 [7]. Through its impact on the cell cycle, it has been postulated to affect cell adhesion and proliferation [8]. Galectin-3 may operate as an adhesion molecule in tumor progression and relax the connection between tumor cells to enhance cancer cell spread because of its physiological roles [9]. According to certain research, galectin-3 is much more abundant in cancer tissues and is linked to cancer metastasis [7].

The identification of serological biomarkers capable to distinguish between malignant and benign nodules would allow to develop a non-invasive assay for the detection of thyroid cancer and evade problems linked with the sampling of biopsies. Therefore the aims of the current study was: Estimate the level of the T3, T4, TSH, thyroglobulin and Galectin-3 in thyroid tumor patients and compare their levels with the healthy control group in addition to examine the possibility of using it as a biomarker for differentiating malignant from benign thyroid neoplasm. In addition to compare the levels of the study parameters in patient with and without thyroidectomy and to assess the effect of some risk factor including age, gender and body mass index on the study parameters in thyroid tumor patients.

Materials and methods

A- Patients

A total of 88 patients were selected for this study. They were separated in two groups, patients and control groups. From the patients group, 72 patients were distributed into two study groups: 45 patients with malignant thyroid tumor and 27 patients benign thyroid tumor. For both groups, the average of age was 45 years old. The samples were collected from Middle Euphrates cancer center from September 2019 to March 2020. According to the age, gender and body mass index (BMI), all patients were than distributed into subgroups. The patients were identified by physician constructed on history, clinical performance and fine needle aspirate. Moreover, every patient group was distributed into two collections: pre and post thyroidectomy.

B- Control

A total of 16 healthy men and women with average of age of 47 years old were selected. In each of the control subject, a filled history was documented. The control subjects should have no history of thyroid disease, heart disease or diabetes mellitus.

Study Design

Every group of the study was distributed into subgroups according to gender, age and BMI.

A- Patients group with malignant thyroid tumor were divided into:

1. Three subgroups according to age: 13 in the age group (25-39 years), 17 in the age group (40-49 years) and 15 in the age group (50 years).

2. Two subgroups groups according to gender: 35 in the female group and 10 in the male group.

3. Three subgroups groups according to BMI: 10 in the BMI groups (18.5-24.9 kg/m2), 18 in the BMI groups (25-29.9 kg/m2) and 17 in the BMI groups (30- 39.9 kg/m2).

B- Patients group with benign thyroid tumor were divided into:

1. Three subgroups according to age: 10 in the age group (25-39 years), 12 in the age group (40-49 years) and 5 in the age group (50 years).

2. Two subgroups according to gender: 18 in the female group and 9 in the male group.

3. Three subgroups according to BMI: 8 in the BMI group (18.5-24.9 kg/m2), 11 in the BMI group (25-29.9 kg/m2) and 8 in the BMI group (30- 39.9 kg/m2).

Methods:

1. Collection of blood sample

A total of 5 mL of intravenous blood was attained by antecubital venipuncture utilizing needle. The blood was let to coagulate in gel tube at room temperature. The serum is aspirated after centrifugation at 3000rpm for 10 min, divided into aliquots in epindroff tubes and stored at -20 °C until the measurement of the study parameters.

2. Physiological Tests

Body mass index quantities

The measure including the weight (to the nearest kilogram) and height (to the nearest centimeter). At that time,

the body mass index (BMI) was deliberated affording to the resulting equation:

BMI= Weight (kg)/Height(m2)

BMI was classified as follows:

*Normal at a BMI if 18.5- 24.9 kg/m2.

*Grade I obesity (over weight) if a BMI was25- 29.9 kg/m2.

*Grade II obesity (obese) if a BMI was30- 39.9 kg/m2.

*Grade III obesity (morbid obesity) if a BMI was >40 kg/m2.

3. Biochemical and Hormonal tests

T3,T4 and TSH

The concentration of these three hormones identified via (MINI VIDAS) was a compact automated immunoassay system created on the Enzyme Linked Fluorescent Assay (ELFA) principles.

Thyroglobulin

The concentration of Tg well-known via (cobas e 411 analyzer) that was a fully automated analyzer that procedures a patented ElectroChemiLuminescence (ECL) technology for immunoassay analysis.

Galectin-3

Galectin-3 concentration in the serum was identified via enzyme- linked immunosorbent assay (ELISA) affording to procedure arranged by the from Elabscience, China, Catalog No: E-EL-H1470 96T.

4. Statistical Analysis

The data were analyzed using SPSS Statistics version 25 software. P-value □0.05 was considered significant. Kolmogorov Smirnov test was used to analyze whether the data were normally distributed. ANOVA test or Kruskal-Wallis test and Student t- test or Mann-Whitney U-test was useful to compare continuous variables. The results were conveyed as (mean±standard error).

Results

1. Comparison of (T3), (T4), (TSH), thyroglobulin and Galactin-3 between patients with thyroid tumor and control groups

The results of table (1) revealed an insignificant decrease (p□0.05) in serum T3 of patients with malignant thyroid tumors (1.966□0.148 nmol/I) compared with control group (2.212□0.171 nmol/I) and benign thyroid tumor group (2.257□0.200 nmol/I). Also, there was a significant increase (p□0.05) in serum T4 of patients with benign thyroid tumors (165.631□12.993 nmol/I) compared with control group (145.300□11.864 nmol/I) and malignant thyroid tumor group (121.56□8.40531 nmol/I).

The results in the same table indicate that there was a significant increase (p□0.05) in serum TSH of patients with malignant thyroid tumors (12.325□3.379 mlU/I) compared with control group (0.767□0.097 mlU/I) and benign thyroid tumor group (1.571□0.336 mlU/I). While the results indicated that there was a significant increase (p□0.05) in serum Tg of patients with malignant thyroid tumors (48.512□7.527 ng/ml) and benign thyroid tumor group (44.790□6.630 ng/ml) compared with control group (7.400□0.965 ng/ml).

The results of the serum galactin-3 concentration in study groups are presented in table (1). The results showed a significant (P□0.05) increase of serum galactin-3 in patients with malignant thyroid tumors (4.64□.31916 ng/ml) and benign thyroid tumor group (4.80□.37553 ng/ml) compared with healthy group (3.14□.46278 ng/ml).

Table (1): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in thyroid tumor patients and control group

Parameters / Groups	Mean ±SE				
	T_3 (nmol/I)	**T_4 (nmol/I)**	**TSH (mlU/I)**	**Tg (ng/ml)**	**Galactin-3 (**ng/ml
Control group n=16	2.212 ± 0.171	145.300 ± 11.864	0.767 ± 0.097	7.400 ± 0.965	3.14 ± 0.462
Malignant tumors n=45	1.966 ± 0.148	121.56 ± 8.40531	12.325 ± 3.379*	48.512 ± 7.527*	4.64 ± 0.319*
Benign tumors n=27	2.257 ± 0.200	165.631 ± 12.993*	1.571 ± 0.336	44.790 ± 6.630*	4.80 ± 0.375*
Sig.	0.098	0.020	0.000	0.032	.0240

*Statically significant difference (p<0.05)

2. Comparison of study parameter levels between patients with and without thyroidectomy

Results in the table (2) revealed a significant increase (p□0.05) in patients with malignant thyroid tumor before thyroidectomy (26.358□7.850 mlU/I) compared with that after thyroidectomy (3.805□0.787 mlU/I). Tg concentration revealed a significant decrease (p□0.05) after thyroidectomy (40.9182□9.853 ng/ml) compared with groups before thyroidectomy (61.02□11.264 ng/ml). The same table revealed a significant decrease (p□0.05) of Galactin-3 in patients with malignant thyroid tumor after

thyroidectomy (4.04□.35221 ng/ml) compared with that before thyroidectomy (5.63□.54658 ng/ml).

Table (2): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in malignant thyroid tumor patients before and after thyroidectomy

Parameters / Groups	Malignant tumor group before thyroidectomy n=17	Malignant tumor group after thyroidectomy n=28	Sig.
	Mean ±SE	Mean ±SE	
T_3 (nmol/I)	1.795±0.2191	2.069±0.198	.4820
T_4 (nmol/I)	127.60±10.95	117.892±11.855	.3990
TSH (mlU/I)	26.358±7.850	3.805±0.787*	.0060
Tg (ng/ml)	61.02±11.264	40.9182±9.853*	0.019
Galactin-3 (ng/ml)	5.63±.54658	4.04±.35221*	.0140

*Statically significant difference (p<0.05)

The results in table (3) showed that Tg concentration was significantly decrease (p□0.05) in patients with benign thyroid tumor after thyroidectomy (31.042□.10.055ng/ml) compared with groups before thyroidectomy (57.5564□7.541ng/ml).

Table (3): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in benign thyroid tumor patients before and after thyroidectomy

Parameters / Groups	Benign tumor group without thyroidectomy n=17	Benign tumor group with thyroidectomy n=28	Sig.
	Mean ±SE	Mean ±SE	
T_3 (nmol/I)	2.595±.3210	1.892±0.197	0.133
T_4 (nmol/I)	178.850±18.99	151.396±17.494	0.308
TSH (mlU/I)	1.8214±.5229	1.302±0.423	0.331
Tg (ng/ml)	57.5564±7.541	31.042±.10.055*	0.052
Galactin-3 (ng/ml)	4.581±0.5976	5.033±0.457	.4170

*Statically significant difference (p<0.05)

3. The effects of age on levels of study parameter in patients with thyroid tumor

The results in the table (4) indicated that there was a significant increases (P□0.05) of TSH in patients with malignant thyroid tumor (16.128□6.961 mlU/I) in age group (40-49) years compared with age group (20-39) years in which TSH concentrations were estimated as (9.340□4.326 mlU/I), and age group (50□) years in which TSH concentrations were estimated as (10.602□5.391 mlU/I).

Additionally, there was significant increases (P□0.05) of Tg in patients with malignant thyroid tumor (41.279□10.463ng/ml) in age group (40-49) years and (83.202□14.455ng/ml) in age group (50□) years compared with age group (20-39) years in which Tg concentrations were estimated as (17.943□6.909 ng/ml).

Table (4): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in malignant thyroid tumor patients according to age groups

Parameters / Groups	Mean ±SE				
	T_3 (nmol/I)	**T_4 (nmol/I)**	**TSH (mlU/I)**	**Tg (ng/ml)**	**Galactin-3 (ng/ml)**
(20-39) years n=13	2.176 ± 0.352	138.406 ± 18.829	9.340 ± 4.326	17.943 ± 6.909	4.04 ± 0.592
(40-49) years n=17	1.645 ± 0.150	107.086 ± 10.096	16.128 ± 6.961*	41.279 ±10.463*	4.93 ±0.489

(50≤) years n=15	2.146 ± 0.270	123.365 ± 15.360	10.602 ± 5.391	83.202 ± 14.455*	4.83 ± 0.597
Sig.	0.523	0.417	0.037	0.005	.4900

*Statically significant difference (p<0.05)

The results in the table (5) showed that there was insignificant differences (p>0.05) in all study parameters according age groups in patients with benign thyroid tumor.

Table (5): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in benign thyroid tumor patients according to age groups

Parameters / Groups	**Mean ±SE**				
	T_3 (nmol/I)	**T_4 (nmol/I)**	**TSH (mlU/I)**	**Tg (ng/ml)**	**Galactin-3 (ng/ml)**
(20-39) years n=10	1.962 ± 0.270	155.567 ± 17.664	1.103 ± 0.330	31.875 ± 10.487	4.22 ± 0.549
(40-49) years n=12	2.540 ± 0.341	167.382 ± 23.763	1.872 ± 0.630	53.754 ± 9.256	5.36 ± 0.596
(50≤) years n=5	2.166 ± 0.466	181.560 ± 26.049	1.787 ± 0.831	49.108 ± 18.614	4.62 ± 0.93
Sig.	.3400	.7150	.8440	.2000	.3990

4. The effects of gender on levels of study parameter in patients with thyroid tumor

The results of the T3, T4, TSH, Tg and Galactin-3 in male and female malignant thyroid tumor patients are presented in table (6). The results indicated that there was insignificant differences (p>0.05) in all study parameters according gender.

Table (6): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in malignant thyroid tumor patients according to gender

Parameters / Groups	**Females groups of the malignant thyroid tumor patients n=35**	**Males groups of the malignant thyroid tumor patients n=10**	**Sig.**
	Mean ±SE	Mean ±SE	
T_3 (nmol/I)	1.807±0.118	2.521±0.506	0.566
T_4 (nmol/I)	112.771±8.259	152.323±22.740	0.091
TSH (mlU/I)	13.728±4.143	7.413±4.560	0.240
Tg (ng/ml)	50.662±8.6404	40.988±15.855	0.428
Galactin-3 (ng/ml)	4.81±0.34115	4.0417±0.80684	0.199

The results of the effects of gender on study parameter are shown in table (7), which indicate that: a significant increase (p□0.05) of T3 and T4 concentration in patients with benign thyroid tumor (3.005□0.384nmol/I), (235.830□17.09nmol/I) respectively in male group compared with female group in which T3 and T4 concentrations were estimated as (1.882□0.180nmol/I), (130.532□10.05nmol/I).

Also, there was a significant increase (P□0.05) of TSH in patients with benign thyroid tumor (2.156□0.441mlU/I) in female group compared with male group in which TSH concentrations were estimated as (0.402□0.147mlU/I).

Table (7): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in benign thyroid tumor patients according to gender

Parameters / Groups	Females groups of the benign thyroid tumor patients n=18	Males groups of the benign thyroid tumor patients n=9	Sig.
	Mean ±SE	Mean ±SE	
T_3 (nmol/I)	1.882±0.180	3.005±0.384*	0.021
T_4 (nmol/I)	130.532±10.05	235.830±17.09*	0.000
TSH (mlU/I)	2.156±0.441	0.402±0.147*	0.022
Tg (ng/ml)	46.688±7.574	40.995±13.495	0.487
Galactin-3 (ng/ml)	4.708±0.520	4.980±0.465	0.324

*Statically significant difference (p<0.05)

5. The effects of body mass index (BMI) on levels of study parameter in patients with thyroid tumor

The results in the table (8) indicated that there was a significant increase (p□0.05) of T4 concentration in patients with malignant thyroid tumor (162.919□20.879nmol/I) in BMI group (18-24.9) Kg/m2 compared with BMI group (25-29.9) Kg/m2 and (30-39.9) Kg/m2 in which T4 concentrations were estimated as (105.518□12.067nmol/I) (114.2182□11.087 nmol/I) respectively.

Additionally, there was a significant increases (P□0.05) of TSH in patients with malignant thyroid tumor (23.3235□7.920 mlU/I) in BMI group (30-39.9) Kg/m2 compared with BMI group (18-24.9) Kg/m2 and (25-29.9) Kg/m2 in which TSH concentrations were estimated as (3.131□1.311nmol/I) and (7.046□2.550nmol/I) respectively.

Results in the table (8) indicated, there was an insignificant differences (P□0.05) of T3, Tg and Galactin-3 concentration in patients with malignant thyroid tumor according to BMI.

Table (8): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in malignant thyroid tumor patients according to BMI

Parameters / Groups	Mean ±SE				
	T_3 (nmol/I)	**T_4 (nmol/I)**	**TSH (mlU/I)**	**Tg (ng/ml)**	**Galactin-3 (ng/ml)**
(18-24.9) Kg/m^2 Normal n=10	2.281±0.435	162.919±20.879*	3.131±1.311	37.221±13.298	4.20±0.660
(25-29.9) Kg/m^2 Over w. n=18	1.932±0.190	105.518±12.067	7.046±2.550	54.394±13.513	4.80±0.536
(30-39.9) Kg/m^2 Obese n=17	1.8165±.22801	114.2182±11.087	23.3235±7.920*	48.926±11.897	4.73±0.513
Sig.	0.623	0.051	0.054	0.633	.7680

*Statically significant difference (p<0.05)

The results in the table (9) showed that there was a significant increase (p□0.05) of T3 and T4 concentration in patients with benign thyroid tumor (3.063□0.434 nmol/I), (212.765□23.344nmol/I) respectively in BMI group (18-24.9) Kg/m2 compared with BMI groups (25-29.9) Kg/m2 and (30-39.9) Kg/m2 in which T3 and T4 concentrations were estimated as (1.972□0.217ng/ml, 1.841□0.296 ng/ml) and (137.558□18.662ng/ml, 157.100□20.115 ng/ml) respectively. The results indicated in the same table that there was insignificant differences (P□0.05) of TSH, Tg and Galactin-3 in patients with benign thyroid tumor according to BMI.

Table (9): Comparison of serum level of T3, T4, TSH, Tg and Galactin-3 in benign thyroid tumor patients according to BMI

Parameters / Groups	Mean ±SE				
	T_3 (nmol/I)	**T_4 (nmol/I)**	**TSH (mlU/I)**	**Tg (ng/ml)**	**Galactin-3 (ng/ml)**
(18-24.9) Kg/m^2 Normal n=8	3.063±0.434*	212.765±23.344*	0.976±0.343	32.544±12.664	3.92± 0.660
(25-29.9) Kg/m^2 Over w. n=11	1.972±0.217	137.558±18.662	1.723±0.508	48.594±9.796	5.01±0.561
(30-39.9) Kg/m^2 Obese n=8	1.841±0.296	157.100±20.115	1.958±0.848	51.806±13.074	5.38 ±0.738
Sig.	0.048	0.047	0.741	0.223	.3040

*Statically significant difference (p<0.05)

Discussion

1. Hormonal parameter in patients with thyroid tumor

The results in table (1) exposed an insignificant decline (p□0.05) in serum T3 of patients with malignant thyroid tumors compared with control and benign thyroid tumor group. Also, in the patients with benign thyroid tumors there was a significant rise (p□0.05) in serum T4 compared with control and malignant thyroid tumor groups.

The main reason for these outcomes was explicated by the researchers who found that the patient with a cancerous thyroid nodule will have an fT4 value which seems normal [10], and the levels of thyroid hormones were normal in most of the study participants. However, moderately higher FT4 levels exposed a positive connotation with thyroid cancer risk [11], Yeh et al., 2013 indicated that it is probable that raised levels of thyroxine (T4) and triiodothyronine (T3) may also be interconnected with malignancy. And that free T4 (fT4) raised in patients with thyroid tumor [12]. Though, the inverse has been revealed to be true for total T3 (TT3) by, to the preeminent of our understanding, there is no evidence-based assumption which elucidates this liaison [13].

The data in the same table specify that there was a significant rise (p□0.05) in serum TSH of patients with malignant thyroid tumors compared with control group and benign thyroid tumor group.

Franco et al. (2011), demonstrated that TSH acting a key role in induced PTC beginning [14]. Another research recounted that upper TSH levels are not only linked with dominance of DTC but moreover with the aggressive characteristics of DTC [15]. Shi et al in 2012 described that TSH level might be linked to progressive stage, that is, progression of thyroid cancer, but not with the development of thyroid cancer; increase TSH level was also accompanied with lymph node metastasis and advanced disease (stages III and IV) [16]. Further studies proposed the association between tumor mass and TSH levels is evaluated with correlation test and exposed a very tough positive linear correlation concerning them [17], TSH level that is in the upper range of normal or even more than the normal range is hypothetical to increase the probability that a thyroid nodule is malignant [18].

Concerning TSH, the results in table (2) showed a significant rise (p□0.05) in patients with malignant thyroid tumor earlier thyroidectomy matched with that later thyroidectomy. In table (3) TSH results showed an insignificant deference (p□0.05) between two groups in patients with benign thyroid tumor.

The reason for this increase in TSH in patients with malignant thyroid tumor before thyroidectomy compared with that after thyroidectomy was a penchant toward a lower TSH in the groups which had go through thyroidectomy [19] (Kostev et al., 2018).

The results in the table (4) indicated a significant rise (P□0.05) of TSH in patients with malignant thyroid tumor in age group (40-49) years compared with age group (20-39) years and age group (50□) years. Also, the results in the table (5) exhibited an insignificant deference (p>0.05) of T3, T4 and TSH concentration in patients with benign thyroid tumor in age group (40-49) years and age group (50□) years compared with age group (20-39) years.

A study suggesting that TSH levels was identified to progressively rise with age, a change that extends into later age [20]. Another study was shown that the elevated TSH levels observed at old age might partly outcome from selective survival of subjects with constitutionally low down thyroid occupation [21]. However, additional studies was indicated that TSH with the lowest value found in the age group of 40±49 years and greater values noted in age groups of 10±19 [22].

The results of the hormonal parameter in man and woman patients are offered in table (6). The outcomes showed an insignificant increase (p>0.05) of T3, T4 and TSH concentration in patients with malignant thyroid tumor in male group compared with female group. In table (7), results

indicate that there was a significant rise (p□0.05) of T3 and T4 concentration in patients with benign thyroid in male group compared with female group. Also, there was a significant decline (P□0.05) of TSH in patients with benign thyroid tumor in male group matched with female group.

The main reason for these outcomes was explained by the researchers who establish that the TSH was significantly elevated in females than Males [22], and TSH level based on BMI groups were significantly upper in women than those in men in all age groups (P < 0.05), and the median FT3 level was lesser in female subjects; but, there was no significant variation between male and female subjects in medium FT4 level. [23]. Also, TSH was lower in males than in females, while FT3 and FT4 were higher in males than in females [24].

The data in the table (8) recognized a significant rise (p□0.05) of TSH in patients with malignant thyroid tumor in BMI group (30-39.9) Kg/m2 matched with BMI group (18-24.9) Kg/m2 and (25-29.9) Kg/m2. The results in the table (9) exhibited a significant rises (p□0.05) of T3 and T4 concentration in patients with benign thyroid tumor, in BMI group (18-24.9) Kg/m2 matched with BMI groups (25-29.9) Kg/m2 and BMI groups (30-39.9) Kg/m2.

Numerous studies have pronounced the association between BMI and levels of thyroid hormones, and the consequences were diverse, one study exhibited that BMI was positively correlated to serum TSH and negatively to serum free T4 (FT4) and had no correlation to serum free T3(FT3) [25] lesser FT4 concentration were accompanied by elevated BMI values, but no association between BMI and FT3 was establish [26]. Serum FT4 (not TSH) was establish to have a negative correlation with BMI. It was too negatively associated with total cholesterol and triglycerides and positively associated with HDL. But, the serum TSH serum concentration were positively interrelated to triglycerides only [27]. There has been established positive correlation between serum leptin and TSH which likewise means positive correlation between BMI and TSH. Instead, FT4 was declined with cumulative BMI [28]. TSH serum levels exhibited a significantly rising tendency with rising BMI. Contrariwise, a negative tendency was observed concerning participants' mean serum levels of fT4 with their BMI, there were great fT4 levels among participants with normal BMI and low among obese patient , on the other hand no significant differences were detected in serum fT3 levels agreeing to BMI [29] (Al-Musa, 2017).

These outcomes are in agreement with those of Solanki et al 2013 who explained a significant positive relationship between patients' BMI and their TSH serum concentrations and they found that BMI was adversely interconnected with serum fT4 but had no connotation with serum fT3 [30]. In contrast, Figueroa et al. (2008) establish no correlation between serum concentration of the thyroid hormones and BMI [31]. But, another studies establish that thyroid activity and obesity may affect each other, such that adipose tissue secretes leptin, which have a role to the changes in the excretion of thyrotropin-releasing hormone (TRH) and affects the secretion of TSH [32].

2. Thyroglobulin in patients with thyroid tumor

The data in table (1) indicated that there was a significant rise (p□0.05) on the Tg in patients with malignant thyroid tumors and benign thyroid tumor group matched with control group.

Giovanella et al. in 2014 indicated that the Tg molecule may become unregulated in thyroid tumor cells resulting in differences in the structure of the circulating Tg protein [33]. In addition, patients with differentiated thyroid cancer (DTC) and makes whole thyroidectomy, the serum thyroglobulin (Tg) level is an vital marker in the follow-up of them, and it assists as an gauge for cancer recurrence [34]. Serum Tg is a very specific tumor marker for patients with DTC and shows high specificity for detecting DTC reappearance [35]. Lee et al. (2012) indicated that sequential measurements of serum Tg levels significantly greater level in PTC patients (Lee et al., 2012) [36].

Numerous benign tumors can consequence in amplified production of thyroid hormone (toxic nodules or Grave's disease) or improved release of thyroid hormone (thyroiditis) and can be the etiology for greater serum TG levels , Hence, an raised serum TG in an individual with a thyroid nodule does not always specify thyroid cancer [37]. In healthy persons, minor quantity of Tg is released physiologically into the circulation but in DTC it is aggressively released into circulation [38].

In the tables (2) and (3) concentration of Tg exposed a significant decline (p□0.05) later thyroidectomy matched with groups earlier thyroidectomy in patients with malignant and benign thyroid cancer. These results representative a probable role of this biomarker in the progress of malignant and benign thyroid tumor in addition to the likelihood of using as a tool for monitoring patients with malignant and benign thyroid tumor because thyroglobulin assay performed subsequently surgery but beforehand radioiodine treatment has been demonstrated to be beneficial in predicting the presence / absence of distant metastasis. Serum TG concentration is practiced as a tumor marker as well as in the continuation care of well-differentiated thyroid cancer DTC , because serum TG concentrations are predictable to be low following complete thyroidectomy [39]. The TG levels was well-known to reduction to fewer than 5-10 ng/mL 25 days afterward thyroidectomy [40], the majority patients do have a level slighter than 2 ng/ml within the first year next complete thyroidectomy. Subsequent RAI ablation, Tg levels are lesser than 0.15 or 0.27 ng/ml [41]. Nascimento and his colleagues exposed that Tg level was reduced in the 76 patients at a mean time of nine months later surgical treatment [42].

The outcomes in the table (4) refers to that there was significant rises (P□0.05) of Tg in patients with malignant thyroid tumor in age group (40-49) years and age group (50□)

years matched with age group (20-39) years. One study indicated that established correlated reference values for age that rise Tg level exceeding the 40 years old [43], in addition to in patients underneath the age of 20 and beyond 60 years [44].

The results in table (6) and (7) specified that there was an insignificant deference (P□0.05) of Tg in patients with malignant and benign thyroid tumor in woman group matched with man group. The scientists assessment differed on the interpretation of this finding, one study definite that there were no significant variations in Tg according to sex [43]. Another study indicated that Tg had highest frequency in women [45] (Alagić-S. et al., 2012). Additional study specified that there were no noteworthy Tg changes between sexes [46]. By using a logistic studies, Kim et al , showed that Serum Tg not associated with age at diagnosis, sex (male or female) and tumor size [18].

Results in the table (8) and (9) indicated that there was an insignificant decrease (P□0.05) of Tg concentration in patients with malignant and benign thyroid tumor in BMI group (18-24.9) Kg/m2 linked with other BMI groups. Kim et al showed that the higher BMI groups have a tendency to be older (P=0.011) and have elevated TG (P=0.006) [47], while Van Do et al showed that Tg levels, however, are not affected by age, sex, or body weight [48]

3. Galectin-3

The results of the serum galectin-3 concentration in study groups are presented in table (1). The results presented a significant (P□0.05) rise of serum galectin-3 in patients with malignant thyroid tumors and benign thyroid tumor group matched with control group.

Išić et al. in (2010) compared preoperative levels of Galectin-3 in serum of patients with thyroid tumors with tissue expressions. Extreme serum Galectin-3 concentration was found in thyroid carcinomas but as well in adenomas. No significant association was establish between serum and tissue Galectin-3 concentration. Accordingly, Galectin-3 was appraised as being respectable tissue marker; however, serum concentration of these markers was not a reliable indicator for the diagnosis of thyroid malignant and follow out of thyroid cancers [49]. In 2013, Xue et al., have identify Galectin-3 concentration in serum and surgical sections of a group having 159 patients with thyroid malignant and 16 patients without thyroid malignant. They establish noticeably elevated concentration in patients with malignant. They indicated that Galectin-3 measurements in serum and surgical specimens would product in greater investigative degrees in thyroid cancers [50]. Makki et al., 2013 have showing noticeably elevated serum Gal-3 levels in patients with thyroid papillary malignancy matched with that in the normal group [51].

Additional researchers have investigated the immunoexpression of CK19, Galectin-3, RET oncoprotein and HBME-1 in thyroid FNAB specimens and confirmed that Galectin-3 was the mainly sensitive and specific marker in distinctiving benign thyroid nodules from the malignant ones [52]. However, further studies found Galectin-3 was to be a highly sensitive marker in the diagnosis of PTC, but was found to be expressed in only a minor amount of cases including further kinds of thyroid lesions [7].

Song et al. establish that Galectin-3 positive rate in nodular goiter (52.58%), follicular adenoma (48.15%) and in papillary thyroid carcinoma (97.17%) [53] (Song et al., 2011). Arcolia et al found indicator existence for Galectin 1 and Galectin 3 was ever-present, in cooperation in tumor cell (cytoplasmic and nuclear staining) and the stromal accompanying to malignant tumor and adenomas, and it is found that cytoplasmic immunostaining exposed that the intensity expression of the four markers (gal 1, gal 3, CK19 and HBME 1) was significantly greater in cancer cells of papillary thyroid carcinoma matched to epithelial cells [54]. Another study showed that Galectin-3 was highly expressed in papillary tumor tissues compared to its adjacent noncancerous thyroid tissues [55]. Furthermore, additional study indicated in 50 malignant cases galectin-3 have revealed positivity in 48 cases (96%) and in the 70 nonmalignant cases, galectin-3 was positive in 45 cases (64.28%) [56]. Also, Pennelli et al. supposed the great mass of benign lesions with positivity of Gal-3 were secreted by adenomas and thyroiditis, may be because Gal-3 is expressed in the cytoplasm of Follicular cells and blocks the apoptotic passageway [57].

Galectin-3 was considered as a serum marker; inappropriately a small number of studies on minor series have been reported in this topic and no significant variation among cancers and benign lesion was established. These discoveries are possibly caused by the sub- intra-cellular localization of Gal-3 and the deficiency of its secretary pathway [58]. High degree of thyroid cancers at histology has Galectin-3 over expression in addition to great percentage of thyroid benign nodules has negative Galectin-3 assessment [59].

In thyroid tumors of undefined malignant potential, galectin-3, cytokeratin-19, HBME-1, and CD56 stained negatively in the preponderance of cases (83.9.90.3, 87.1 and 61%, respectively), and no statistically significant alterations were detected when compared with the immune profile of benign thyroid lesions [60]. Galectin-3 is firstly shown to have helpfulness in the differential diagnosis between benign and malignant thyroid lesions. But, certain novel studies proposed that it is not trustworthy [61]. However, that marker had discovered some boundaries because positivity was also conveyed in some benign tumors [62]. Definite study specified that galectin-3 was expressed in a great percentage of multinodular goiters, Hashimoto's thyroiditis and follicular adenomas [63].

Table (2) presented a significant decline (p□0.05) of Galectin-3 in patients with malignant thyroid tumor later thyroidectomy matched with that earlier thyroidectomy.

The results in table (3) exposed an insignificant

deference (p□0.05) of Galectin-3 in patients with benign thyroid tumor earlier thyroidectomy as linked with that later thyroidectomy. We suggest that Galectin-3 is released from cancerous tissue, but when cancer tissue removed so there was no tissue to produce this high amount of Galectin-3.

The results in the table (4) exhibited an insignificant rise (p>0.05) of Galectin-3 in patients with malignant thyroid tumor in age group (40-49) years and age group (50□) years compared with age group (20-39) years. Results in the table (5) exposed that there was insignificant rise (p>0.05) of Galectin-3 in patients with benign thyroid tumor in age group (40-49) years compared with age group (50□) years and age group (20-39) years. This results is explained because the illness age was generally in 40~50 years old [64]. Moreover, galectin-3 is not related with age, sex and body mass index, because it a stable biomarker (Dong et al., 2018). Additional studies verified that galectin-3 expression levels in tumor tissues were not significantly related with age and sex [66] further studies revealed that the levels of circulating galectin-3 have been exposed to correlate positively with age , however additional indicated that Galectin-3 was not correlate to age and sex [67] and Galectin-3 expression was not significantly connected with age but higher in group >45 years old [66]. Additional study displayed that many parameters including age and sex were insignificantly with Galectin-3 [68].

The results in the table (6) and (7) presented an insignificant differences (p>0.05) of Galectin-3 in patients with malignant and benign thyroid tumor in female group compared with male group. In terms of sex, no statistically significant alteration was detected between male and female group, [69]; and Galectin-3 expression was not significantly related with sex but some higher in females [66]. Also, galectin-3 is a steady biomarker and is not linked with age, gender or (BMI) [70]. Additional studies confirmed that galectin-3 expression levels in tumor tissues were not significantly connected with age, sex [66].

The results in the table (8) and (9) presented an insignificant rise (p>0.05) of Galectin-3 in patients with malignant and benign thyroid tumor in BMI groups (25-29.9) Kg/m2 and BMI groups (30-39.9) Kg/m2 compared with BMI group (18-24.9) Kg/m2. Some studies have explained an absence of relationship between Galectin-3 and BMI as indicated that galectin-3 is a constant biomarker and is not linked with age, body mass index or sex [71]. Other studies indicated that overweight individuals display significantly higher Galectin-3 concentration than skinny individuals. Besides, Galecin-3 concentration are positively interconnected to BMI and suggestive for assistant in insulin resistance in male. Gal-3 treatment in vitro causes in hepatocytes, muscle cells, and adipocytes by inhibiting insulin receptor action, leading to decreased downstream signaling to the insulin action cascade. [72].Grupper et al indicated that Gal-3 not significant for age and BMI [73], Gal-3 shown immaterial relation to age and body mass index (Binas et al. 2018). Additional study exposed that the concentration of galectin-3 in circulation relate positively with age and occurrence of obesity [75]. Weigert et al described that circulating galectin-3 levels was upper in 30 overweight subjects, in compare with 23 normal-weight controls. These entire subject exposed galectin-3 levels that connected positively with BMI [76].

Declarations

Study Limitations: This study is limited to the number of patients selected, age, nationality, gender. Other outcomes can be find by using different sample criteria.

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