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Hashimoto's Thyroiditis Increases Risk for Differentiated Thyroid Carcinoma

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Abstract

Background: Hashimoto's thyroiditis has been found to coexist with differentiated thyroid cancer in surgical specimens, but an association between the two conditions has been discounted by the medical literature. So, we performed this research to determine any potential relationship between Hashimoto's thyroiditis and the risk of developing differentiated thyroid cancer in clinical status. we assessed the related clinical factors linking these conditions, especially serum thyroid-stimulating hormone concentration, family history of thyroid disease, gender& young age group.

Aim of study: to determine that hashimoto's thyroiditis increases risk for differentiated thyroid carcinoma.

Patients and method: This study is a Cross-sectional study carried out in surgical ward of Baghdad teaching hospital, where 82 patients followed up for one year from 1/10/2017 to 1/10/2018. Clinical history and examination with thyroid function tests, ultrasound and FNAC done for them pre operatively, post-operatively all thyroid specimen sent for histopathological study.

Results:

Differentiated thyroid cancer with Hashimoto's thyroiditis patients: (84.6%) had papillary thyroid cancer with Mean age of patients is 37.3±3.3 and Female gender represents 92.3% of differentiated thyroid cancer with Hashimoto's thyroiditis patients. About 53.8%of differentiated thyroid cancer with Hashimoto's thyroiditis patients had high thyroid-stimulating hormone at presentation. About 61.5% of differentiated thyroid cancer with Hashimoto's thyroiditis patients had positive family history of thyroid disease. Most our patients had multinodular goiter 80.5%, only 19.5% had single nodule, in Differentiated thyroid cancer with Hashimoto's thyroiditis patients (papillary thyroid cancer: 81.8% multinodular goiter and18.2% Single nodule, while all Follicular Thyroid Cancer patients had multinodular goiter).Fine needle aspiration biopsy in diagnosis of Hashimoto's thyroiditis pre-operation had Sensitivity 61% & specificity98%.

Conclusion:

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Hashimotos thyroiditis increase risk for DTC.

Female genders, young age group, family history of thyroid disease& TSH level were all considered as a risk factor for DTC in HT patients.

Most DTC with HT patients had PTC.

Most of our patients had MNG.

FNAC was specific but not sensitive in diagnosis of HT cases.

Short period follow up reveal PTC present in earlier stages in patients with HT.

Keywords; Hashimoto's thyroiditis, differentiated thyroid carcinoma.

Introduction

Autoimmune and neoplastic diseases most commonly occur in thyroid gland of these Hashimoto's thyroiditis (HT) and the differentiated thyroid cancer (DTC) take priority (1), when HT come together with differentiated thyroid carcinoma the disease represent in less aggressive and better prognosis way(2). The incidence of both diseases increasing in non-explaining way (3).

Hashimoto thyroiditis:

Is an autoimmune disease of thyroid specifically, destroy thyroid cell by antibodies, first described by Japanese pathologist Hakaru Hashimoto in 1912(4, 5, 6). .

In developed countries and iodine sufficient areas HT is the leading cause of hypothyroidism (3, 4, 9). Hashimoto thyroiditis, present itself in adolescents and young adults, cause either hypothyroidism or hyperthyroidism; these patients usually have a strong family's thyroid disease history (7, 8).

Diagnosed by antibodies against thyroid antigen. antithyroid peroxidase and antithyroglobulin antibodies titers found in 90% of cases. (4, 6).

Diagnosis of differentiated thyroid cancer:

In 5% of the thyroid nodules thyroid malignancy discovered. US features associated with malignancy are hypoechoegenic, micro-calcifications, no peripheral halo, borders irregularity, solid, hyper vascular and taller than width.

The fine-needle cytology of the aspiration is significant to diagnose the nodules of the thyroid. The FNAC must be carried out in any of the thyroid nodules that are bigger than 1cm and in the ones that are less than 1cm with a neck and head radiation history or a history of the thyroid cancer in the family (10).

Differentiated thyroid cancer and Hashimotos thyroiditis:

more than a century a relationship between cancer and inflammation has been found, at 1863, R.

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Virchow recognized leukocytes in the neoplastic tissues and assumed that this is the cancer origin at the chronic inflammation sites, based on the epidemiological and clinical findings (3).

A link between the DTC and Hashimoto's thyroiditis depend on either surgical or clinical source of report, this explain by either the thyroid gland completely destroyed by autoimmune process which is clinically evident but no more tissue to have carcinoma, or partially destructive have no clinical(hypothyroidism) but pathological evidence of carcinoma(3).

The patients that have less destructive (i.e. non-clinically evident) Hashimoto's thyroiditis could be at higher risks to develop the DTC compared to the unaffected patients, or the patients who are affected by the destructive (i.e. the clinically evident) Hashimoto's thyroiditis (3).

In the destructive (clinically evident) type have high titer thyroid peroxide antibodies (TPOAb) (3). Others said Antithyroglobulin antibody (TgAb), not thyroid peroxidase antibody (TPOAb), was the risk factor for Thyroid carcinoma (4), other responsible for the potential impact of other factors, which include the thyroid-stimulating hormone (TSH) levels as one of the DTC risk factors (5). Others have discovered increased TSH levels, stimulating the follicular epithelial proliferation, leading to the differentiated thyroid gland carcinoma (11).

Finally, the patients who have prolonged exposures to the inflammations (i.e. prolonged disease) can be at higher cancer risks compared to the patients that had a recent beginning of Hashimoto's thyroiditis. (3)

Here the correlation of hashimoto’s thyroiditis and DTC have been researched, considering the clinical autoimmune disease state as has been expressed by existence of the residual function of the thyroid. (i.e. either had normal or high TSH level), and the effect of other variable(age, gender, family history of thyroid disease).

Patients and methods

Patients

In our study 82 patients have been followed up for 1 year between 1/10/2017 and 1/10/2018.

Study design & settings:

This is a Cross-sectional research that has been conducted in surgical ward of the Baghdad teaching hospital in the medical city, in Baghdad, Iraq. In the period between 1/10/2017 and 1/10/2018 studied the relationship between HT and DTC.

The HT subjects were subdivided into either euthyroid (normal TSH level) or hypothyroid (high TSH level) based on their preoperative thyroid function test & either with PTC or with FTC based on FNAC &histopathological results.

Inclusion Criteria:

Adults (age>20 years).

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Patients that have FNAC results which has been positive for the malignancy, highly suspicious for the follicular neoplasm or the PTC, or the undetermined significance follicular cells.

Patient with 2 non-diagnostic or benign FNAC with 2 or more US characteristics which are suggestive of the thyroid cancer (such as micro calcifications, irregular margins, and hypo echoic pattern) or increase in the size.

Exclusion Criteria:

Patients diagnosed as Undifferentiated Thyroid CA.

Toxic goiters.

Failures of following up the patients.

Recurrent carcinomas of thyroid.

Statistical analysis:

The data were analyzed using SPSS 24 Program. . In all of the statistical analyses, the significance level (p value), has been set to ≤ 0.05 and result which are presented as graphs, tables, or both. The statistical analyses of this study have been carried out by the community of the medical experts.

RESULTS

The present study involved 82 patients had DTC: 69 patients had DTC without HT {(81.2%) 56patients of them had PTC, and (18.8%) 13 patients of them had FTC} and 13 patients had DTC with HT {(84.6%)11 patients of them had PTC and (15.4%) 2 patients of them had FTC } as shown in table 1. We found most DTC with HT patients had PTC.

Table 1: pts. Distribution according to type of DTC to either with or without HT.

	Without Hashimotos	%	With Hashimotos	%
Papillary thyroid ca	56	81,2%	11	84,6%
Follicular thyroid ca	13	18,8%	2	15,4%
Total	69	100%	13	100%

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Mean age of DTC without HT patients were 34.5±9.9 years, 31.8%of them were in age group (20-30), 42% were in age group (31-40), 11.6% were in age group (between 41 and 50), and 14.5% were in age group (between 51 and 60). While mean age of DTC with HT patients were 37.3±3.3years, 15.3%of them were in age group (between 20 and 30), 61.5% were in age group (between 31 and 40), 7.60% were in age group (between 41 and 50), and 15.3% were in age group (between 51 and 60) .as shown in table 2 .

Table 2: age groups distribution of pts.to either DTC With HT or DTC without HT

Age group	Pts. with DTC without Hashimotos	%	Pts. with DTC with Hashimotos	%
20-30	22	31.8%	2	15.3%
31-40	29	42%	8	61.5%
41-50	8	11.6%	1	7.6%
51-60	10	14.5%	2	15.3%
Total	69	100%	13	100%
Mean	34.5		37.3	
Standard deviation	9.9		3.3	

P value 0.08(insignificant)

Table 3: Gender distribution according to either DTC with HT or DTC without HT

	Female	%	male	%
DTC with HT	12	18	1	6.6
DTC without HT	55	82	14	93.4
Total	67	100	15	100
%from total DTC pts.(82)	81.7%		18.3%	

P value (0.9) insignificant

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Table4: distribution of DTC with HT & DTC without HT according to TSH level.

	DTC with HT	%	DTC without HT	%	
high TSH	7	53.8%	29	42%	
Normal TSH	6	46.2%	40	58%	
Total	13	100%	69	100%	

Table 5: family history of thyroid disease in pts. With & without HT

	DTC with Hashimotos	%	DTC without Hashimotos	%	P value 0.04(significant)
Positive Fam. Hx of thyroid dis.	8	61.5%	23	33.3%	
Negative Fam. Hx of thyroid dis.	5	38.5%	46	66.6%	
Total	13		69		

P value 0.04(significant)

Discussion:

Both thyroid autoimmunity and TC have been increasing, several studies discovered the likelihood of an association between those two conditions with contradictory results. Several have discovered that the Hashimoto's thyroiditis linked with the TC while others didn’t.

With the attempt of uncovering the likelihood of a hidden correlation between the DTC and Hashimoto's thyroiditis in the clinical status, the histologically diagnosed DTC with HT have been divided to the hypothyroid group and euthyroid group according to the TFT and the preoperative clinical status.

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Present study showed that most DTC with HT were PTC (about 84.6%), only 15.4% of DTC with HT were FTC. In study in Denmark, University of Copenhagen by Christina Resende de Paiva et al. an association was found between Hashimoto's thyroiditis and PTC, no correlation has been discovered between HT and FTC (11). in our study we have discovered an association of the HT with the FTC even in less percentage than do PTC with HT. In our study PTC with HT represents 84.6%of total DTC with HT patients& PTC without HT represents 81.2% of total DTC without HT patients, in study in china published in ActaOtorhinolaryngol Ital. by J.Liang et al, More PTC has been found in the patients that had Hashimoto's thyroiditis compared to it in those who did not have it (21.20% versus 18.20%, p = 0.007) (12).

Current study showed that mean age group of DTC with HT 37.3±3.3years and for DTC without HT 34.5±9.9 years, younger than previous Chinese study by J.Liang et al, as they found mean age of PTC with HT patients were 45.04 ± 12.47 years, and also younger than previous Denmark study by Christina Resende de Paiva et al as they found median age amongst the patients that have HT and TC has been 45.9 years whereas it was 47 years amongst the patients that had the TC without the HT (11, 12),while in study in Athens, Greece by C. Avgoustou et al. found Co-existence of the diseases (PTC & HT) has been considerably associated to the younger women(13), same of our study. I.e. DTC tend to present in young age group both with &without HT in our study this may related to that most our patients were PTC which tend to present in younger age group than do FTC.

Our study shows most DTC with HT patients were female 92.3%, while only 7.7% was male. In Chinese research that has been conducted by J.Liang et al. they found in PTC patients with HT: males (20%) and females (80.80%); with M\F ratio 1:4 (12). Also the study in Denmark by Christina Resende de Paiva et al. found most patients were females (82.1%) (11). similar to our study. This means that female gender is a risk factor for DTC in HT patients in our and previous two studies. While in study by Kim KW et al, found that men and the presence of the Hashimoto's thyroiditis (p <.001) increased risks of the PTC.(14).

In our study we found 53.8% DTC with HT patients had high TSH, from them all FTC had high TSH, and 54.6%of PTC with HT patients had normal TSH, in study in Wisconsin madison by RodisPaparodis et al. where he found significant correlation between Hashimoto's thyroiditis and PTC in euthyroid Hashimoto's thyroiditis, while the risk of the thyroid cancer has been lower in the hypothyroid HT populations on the high LT4 replacement dosage (3) which is with us in PTC patients and against us in FTC patients. While, in study in Denmark, University of Copenhagen by Christina Resende de Paiva et al. found elevated TSH levels that stimulates follicular epithelial

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proliferations that lead to differentiated carcinoma of thyroid gland, which is against us in PTC patients and with us in FTC patients. (11). So TSH level which changes according to degree of destruction of thyroid gland by chronic inflammation in HT is the most significant risk factor for developing the DTC in the HT patients.

In our study we found significant association between DTC with HT patients and the presence of thyroid disease in the family history (which is about 61.5%), while only 33.3% of DTC without HT patients had family history of thyroid disease (P = 0.04). In a study that has been published in American thyroid association ATA they found that the overall risks of 1st degree relatives of HT patients, has been 9-fold higher in comparison with general population (15). in study in university of Birmingham, UK reported HT patients had family history, P value 0.001(16). So family history of thyroid disease is a factor of risk to developing the DTC in the patients with HT.

Conclusion

Hashimotos thyroiditis increase risk for DTC.

Female genders, young age group, family history of thyroid disease, normal TSH level were all considered as a factor of risk for DTC in HT patients.

Most DTC with HT patients had PTC.

Most of our patients had MNG.

FNAC was specific but not sensitive in diagnosis of HT cases.

Short period follow up reveal PTC present in earlier stage in patients that have Hashimoto's thyroiditis than the ones who do not have it.

Recommendations

More care in follow up of HT cases especially when nodularity developed.

Risk factor for development of DTC in HT cases; normal or mild high TSH level, female gender, young age group and family history of thyroid disease has to be taken in consideration by surgeon.

Antibodies; Anti-thyroglobulin antibody (Tg-Ab) as well as the thyroid peroxidase antibody (TPO-Ab) need to be added in future research after it availability in governmental laboratories because of its validity in similar research.

Large size multi-centers studies need to be supported.

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