

Hypothyroidism Increases the Risk of Malignancy in Thyroid Nodules

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Objective

To assess the correlation between malignancy in thyroid nodules with thyroid autoantibodies or serum thyroid stimulating hormone (TSH) levels as diagnosed by ultrasound-guided thyroid fine needle aspiration biopsy (USGFNAB).

Introduction

- Thyroid nodule incidence varies depending on the method used for diagnosis; 4–7% by palpation¹ and 17–67% by high-resolution ultrasound^{1,2}
- Thyroid malignancy is much less common and accounts for 1% of all new malignant disease (0.5% of cancers in men and 1.5% in women)²
- Rate of malignancy among thyroid nodules is relatively low (5%)¹
- Amongst the thyroid malignancies, papillary thyroid carcinoma is the most common (accounting for around 70-85% of thyroid cancers)^{3,4}
- Hashimoto Thyroiditis (HT) is the most common autoimmune thyroid disease, with an incidence of 30–150 per 100,000 individuals worldwide with a predominance in females (5–20:1)⁴
- Relationship between HT, TSH levels, and thyroid cancer has not yet been fully explored and remains controversial

Materials and Methods

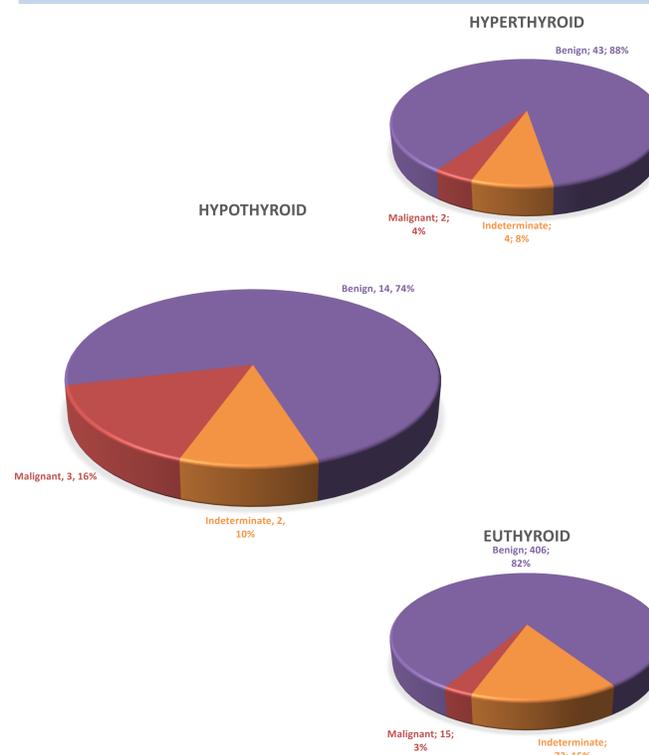
- Cytology results were retrospectively analyzed in patients who underwent USGFNA biopsy in our outpatient clinic between 2016 and 2019.
- Between two and six passes were made for each nodule. USGFNA was performed with 23 or 25 gauge needle attached to a 10 cc syringe.
- Each nodule was considered as its own case for data presentation and statistical analysis
- Cytology results were categorized as malignant, benign, and indeterminate
- Patients were categorized as euthyroid, hyperthyroid, and hypothyroid based on TSH results

Results

- 695 nodules were biopsied but 133 unsatisfactory results were eliminated
- 290 nodules (52%) were from the right, 244 (43%) from the left, and 28 (5%) were isthmus
- Amongst Euthyroid nodules, 3% were malignant, 82% were benign, and 15% were indeterminate
- Amongst hyperthyroid nodules, 4% were malignant, 88% were benign, and 8% were indeterminate
- Amongst hypothyroid nodules, 16% were malignant, 74% were benign, and 10% were indeterminate
- Hypothyroid nodules more likely to be malignant (df=4, p=.035)
- Amongst biopsies without Hashimoto (n=216), 4% were malignant, 83% were benign, and 13% were indeterminate
- Amongst biopsies with Hashimoto present (n=60), 2% were malignant, 80% were benign, and 18% were indeterminate
- No statistical significance between HT and risk of malignancy (df=2, p=.399)

Thyroid Status and Outcomes					
Thyroid_Status		Outcome			Total
		Malignant % (n)	Benign % (n)	Indeterminate % (n)	
Thyroid_Status	Euthyroid	3 (15 _a)	82 (406 _a)	15 (73 _a)	494
	Hyperthyroid	4 (2 _a)	88 (43 _a)	8 (4 _a)	49
	Hypothyroid	16 (3 _a)	74 (14 _a)	10 (2 _{a,b})	19
Total		4 (20)	82 (463)	14 (79)	562

Different subscript letters horizontally denotes a subset of Outcome categories whose column proportions differ significantly from each other at the .05 level.
Thyroid status at the time of biopsy showed a significant correlation to benign and indeterminate results, but there was a lack of correlation to malignant results due to the small collected sample size. It was noticed that there was a significant correlation of the hypothyroid status having a less likely outcome of being benign. Chi Square test, df = 4 p=0.035



Hashimoto's Thyroiditis Outcomes					
Hashimoto's Thyroiditis		Outcome			Total
		Malignant % (n)	Benign % (n)	Indeterminate % (n)	
Hashimoto's Thyroiditis	Hashimoto (-)	4 (8 _a)	83 (181 _a)	13 (27 _a)	216
	Hashimoto (+)	2 (1 _a)	80 (48 _a)	18 (11 _a)	60
Total		3 (9)	83 (229)	14 (38)	276

Each subscript letter denotes a subset of Outcome categories whose column proportions do not differ significantly from each other at the .05 level.
Chi Square test, df = 2 p=0.399

Discussion

- Study was conducted to analyze the relationship of TSH levels and thyroid antibodies with the occurrence of differentiated thyroid cancer
- Increased levels of TSH has the potential to stimulate tumor growth, leading to thyroid cancer, as it physiologically simulates normal follicular cells^{1,4,5}
- One study demonstrated a significant relationship between increased TSH levels and risk of thyroid malignancy² while another did not show this association as a significant predictor of suspicious cytology⁶
- Our data demonstrated higher TSH levels had a higher risk of malignancy when compared with normal or decreased TSH levels
- Associations between HT and thyroid malignancy were first suggested in 1955 and later confirmed in 1995^{5,7}
- Surgical studies reported a higher incidence of malignancy among patients with HT than cytological studies suggesting a selection bias⁴
- Several studies found a significant association between Hashimoto's thyroiditis and thyroid cancer,^{1,3,5,7,8}
- Our study did not show a statistically significant correlation between HT and thyroid cancer

Limitations

- This was a single-center retrospective analysis with a small sample size of 562 nodules.
- 70 patients who were actively being treated for hypothyroidism were also included in the analysis and were classified according to their most recent TSH levels
- Many patients who would have been classified as hypothyroid were classified as euthyroid based on their TSH status
- Ongoing treatment with Levothyroxine would reduce TSH level, therefore, in theory would also decrease the risk of thyroid cancer

Conclusion

- Nodules from the hypothyroid category had more malignant and less benign cytology results compared to nodules from the euthyroid or hyperthyroid category
- TSH has the ability to stimulate normal thyroid follicular cells as well as malignant thyroid cells
- Elevated TSH level but not the presence of elevated thyroid antibodies should be considered as a risk factor for thyroid cancer

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