

# Assessment of Thyroid Nodules in Children: A Single Center Experience

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## ABSTRACT

Thyroid nodules in children are less common than adults, but with a higher risk of malignancy, metastasis and recurrence. Therefore, detection, follow-up and treatment of thyroid nodules in children is very important. Our study retrospectively analyzed the demographic features, concomitant diseases and ultrasonography (USG) findings of thyroid nodules in children and aimed to obtain information about incidence of malignancy.

We retrospectively analyzed the clinical, laboratory, thyroid USG, Fine needle aspiration biopsy (FNAB) and surgical results of 45 pediatric patients with thyroid nodules.

Forty-five patients were included in the study, female domination was present, and most of the patients were adolescents. Six (13.3%) of the patients had a family history of thyroid cancer, and one had a history of radiation. Thyroid-related disease was present in 53.3% of the patients. Five patients had non-thyroid disease. Thyroid function tests were within normal limits in 33 (73.3%) of the patients. In our patients with pediatric thyroid nodules, FNAB was underwent in 46.6% according to the nodule size, and malignancy was detected in 2.2% of our patient group.

Careful evaluation of thyroid nodules that are rarely seen in adults but higher in malignancy than adults should be evaluated. Diagnostic research for thyroid cancer is mostly done in adult patients, our study contributes to the assessment of risk conditions in thyroid nodules in children.

**Key Words:** Thyroid nodule, thyroid carcinoma, thyroid disease

## Introduction

Thyroid nodules are rarely seen in children. However pediatric thyroid nodules have a higher malignancy rate, metastasis and recurrence risk as compared to the thyroid nodules in adults (1). This condition requires evaluating the children and adolescents with thyroid nodules in detail. Thyroid nodules are separate lesions than thyroid tissue. Palpable and incidental thyroid nodules carry the same risk for thyroid cancer. The studies investigating the prediction methods for thyroid cancer were mostly conducted with adults (2,3). On the other hand, the studies in pediatric population are relatively insufficient. In the present study, we retrospectively analyzed the clinical features, laboratory data and thyroid ultrasonography (USG) findings, and also the results of fine needle aspiration biopsy (FNAB) and surgical outcomes in children under 18 years of age and aimed to detect the incidence of thyroid cancer.

## Material and Methods

A total of 45 patients below 18 years of age who were admitted to Pediatric Endocrinology Outpatient Clinic between October 2018 and January 2020 were analyzed retrospectively. Age, gender, body mass index (BMI), presence of clinical symptoms, thyroid staging on physical examination (according to goiter staging of World Health Organization), family history of thyroid cancer, history of radiation exposure, thyroid function tests (TFT) including free T4 and thyroid stimulating hormone (TSH) at the time of diagnosis were evaluated. Free T4 (fT4), TSH, serum anti-thyroglobulin (Tg) antibodies and anti-thyroid peroxidase (TPO) antibodies were measured with chemi-luminescence immune analysis method by using Abbott Ci 16200 system. Ultrasonography results with regard to thyroid size and nodule characteristics, presence of thyroid disorder or non-thyroid disorders, pathology results of the patients who underwent FNAB (indications: nodule size > 10 mm, solid nodule, microcalcification, history of

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radiotherapy) and who underwent thyroid surgery were evaluated retrospectively. Approval for this study was obtained from the Local Ethical Committee (Approval number:2020/03-07).

#### Statistical Analysis

Descriptive statistics for continuous variables are expressed as mean, standard deviation, minimum and maximum values, while for categorical variables, they are expressed as numbers and percentages. SPSS statistical software was used for calculations.

## Results

A total of 45 patients were included in the study. Mean age of the patients was 12.8 years, and 38 (84.4%) were girls and 7 (15.6%) were boys. Clinical symptoms at the time of first admission included swelling in the neck in 18 patients (40%) (difficulty to swallow in 2 of these patients) and remaining 27 (60%) were asymptomatic. Thyroid was non-palpable in 28 patients (62.2%), stage 1 palpable in 2 (4.4%) and stage 2 and stage 3 palpable in 15 (33.3%). There was the family history of thyroid cancer in 6 patients (13.3%). History of radiation was detected in one patient who was receiving radio-therapy for non-Hodgkin's lymphoma (NHL). Twenty four (53.3%) patients had thyroid disorders [congenital hypothyroidism (CH) in 12, Hashimoto's thyroiditis (HT) in 7, Graves disease (GD) in 1, multi-nodular goiter (MNG) in 2, subclinical hypothyroidism in 1 and Pendred syndrome in 1 patient] and there was no thyroid disorders in 19 patients (42.2%). When non-thyroid disorders were analyzed, hearing loss was detected in 1 patient with Pendred syndrome, NHL was detected in 1 patient, ectopic kidney in 1 patient, type 1 diabetes mellitus (DM) in 1 patient (the same patient had also HT) and xeroderma pigmentosum in 1 patient (Table 1).

Ultrasonography findings included hypoechoic nodule (11 patients), hypoechoic cyst and nodule (3 patient), isoechoic nodule (6 patients), isoechoic and cystic nodule (4 patients), cystic nodule (20 patients) and micro-calcification (1 patient).

Of the patients, 21 had undergone FNAB. Results of FNAB were benign in 15 patients, 2 had lymphoid hyperplasia, 1 had atypia with unknown significance and 3 had suspected papillary carcinoma. Five patients had undergone surgery. Demographic and clinical characteristics and

pathology results of the patients who underwent surgery are presented in Table 2.

Thyroid function test results were within normal ranges in 33 (73.3%) patients, 1 patient had subclinical hypothyroidism, 11 had evident hypothyroidism and they were receiving therapy. Anti-TPO and anti-Tg antibodies were positive in Hashimoto and Graves diseases. Calcitonin and thyroglobulin values were within normal ranges in all patients.

## Discussion

In the present study, we retrospectively analyzed clinical, laboratory and USG findings, FNAB and surgical pathology results in children and adolescents who had thyroid nodules at a single center.

Thyroid nodules are rarely seen in children and its prevalence is 0.2-5% (4,5). On the other hand, some recent studies are available reporting that thyroid nodule and thyroid cancer incidence increase in children (6,7). Most of thyroid nodules are usually benign, however there is a 2-3 fold greater malignancy risk in children or adolescents as compared to adults with the estimated incidence of about 20-25% in children and 5-0% in adults (8,9). Besides, risk for lymph node and distant metastasis, and recurrence risk are higher in children (10-12). In our study, 21 out of 45 patients were performed FNAB and 5 patient underwent surgery due to various reasons and one patient was detected to have follicular carcinoma. Ratio of malignancy was found to be 2.2% in our study, lower than in literature. This difference may be explained with low number of cases.

Some studies have proposed that adolescents had a higher incidence of thyroid cancer as compared to small children (6, 13). In a study of Hodax et al., mean age at the time of diagnosis was 15.6 years in children who were detected to have thyroid cancer (14). Mean age was found to be 13.1 years in the study of Divarçı E. et al. (15). Mean age was 12.8 at the time of diagnosis of thyroid nodules in our study.

Thyroid cancer was reported to be more prevalent among females (1,6). In our study, 84.4% of the patients with thyroid nodules were girls. This female preponderance may be explained with estrogen sensitivity (16,17).

Obesity is gradually supported with more studies to be a precipitating factor in development of cancer including thyroid cancer (18). In a study, incidence of papillary thyroid cancer was reported

**Table 1.** Demographic and clinical features of patients with thyroid nodules

Parameters	n (% or SDS)
Age at diagnosis (male/female)	11.7 ± 2.7 /13.9 ± 3.5
Sex (male/female)	7 (%15.6)/38 (%84.4)
BMI at diagnosis	54.6 ± 33.2
BMI SDS at diagnosis	0.19 ± 1.33
Symptom at first visit	
Goiter (>grade 1)	15 (33.3%)
Palpable mass	0
Asymptomatic	30 (66.6%)
Family history (+)	6 (13.3%)
History of radiation exposure	1 (2.2%)
Thyroid Disease	
Graves Disease	1
Hashimoto's thyroiditis	7
Congenital Hypothyroidism	12
Multi-nodular Goiter	2
Subclinical Hypothyroidism	1
Pendred Syndrome	1
Non-thyroid Disorders	
Hearing Loss	1
Non-Hodgkin's Lymphoma	1
Ectopic Kidney	1
Type 1 Diabetes Mellitus	1
Xeroderma Pigmentosum	1
Results of FNAB	
Benign	15
Atypia with Unknown Significance	1 (Right Lobectomy)
Lymphoid hyperplasia	2
Suspected Papillary Carcinoma	3 (Total Thyroidectomy)

SDS: Standard Deviation Scores

BMI: Body Mass Index

FNAB: Fine Needle Aspiration Biopsy

to increase with increasing BMI (19). However this correlation was not clearly proven in children and adolescents. In our study, BMI was 85% and above in 11 patients (24.4%). Body mass index was within normal ranges in our patient who was detected to have follicular carcinoma. For this reason, we could not evaluate the relationship between obesity and thyroid cancer.

Thyroid function test is one of the essential assessment methods for thyroid disorders. Some studies have evaluated TFT in thyroid cancer, tried to predict thyroid cancer and some researchers proposed that serum TSH level increased in thyroid cancer. In some studies conducted in adults, TSH concentration was found to be higher in patients with malignant nodules as compared to the ones with benign

nodules (20,21). A clear association could not be shown between TSH and thyroid cancer in the studies carried out with children (22,23). In our study, TSH was within normal ranges in the patient with thyroid cancer however our patient population is not large enough to make a comment about this issue. However we may state that the rate of nodule detection would be higher as more ultrasonographies are done in patients with abnormal TFTs.

In our study, TSH elevation was detected particularly in the patients with Hashimoto's thyroiditis. The relationship between anti-Tg antibody and anti-TPO antibody which are high in HT, and thyroid cancer is still of debate. In previous studies, a relationship was reported between thyroid cancer and HT in children and

**Table 2.** Demographic, clinical features and pathology results of patients who underwent surgery due to thyroid nodules

Patient no	Age (years)	Gender	Symptom / Physical Exam	Thyroid Nodule Size (mm)	USG Findings	Results of FNAB	Surgery	Surgical Pathology
1	17	K	None/Thyroid nonpalpable	18x10	Isoechoic	Suspected Papillary Carcinoma	Total Thyroidectomy	Follicular Carcinoma
2	15.8	K	None/Stage 3 goiter	37x25	Isoechoic, cystic	Suspected Papillary Carcinoma	Total Thyroidectomy	Nodules Hyperplasia
3	14.9	K	Difficulty to swallow / Stage 3 goiter	40x30	Isoechoic, cystic	Suspected Papillary Carcinoma	Total Thyroidectomy	Non-invasive Follicular tumor
4	16	K	None/Thyroid nonpalpable	11x8	Cystic	Atypia with Unknown Significance	Right Lobectomy	Chronic Thyroiditis
5	16	K	Difficulty to swallow / Stage 3 goiter	30x26	Cystic	Benign	Right Lobectomy	Benign

adolescents. Corrias et al. reported the incidence of thyroid nodules and thyroid cancer as 31.5% and 3.0% in patients with auto-immune thyroiditis (23). Keskin et al. investigated the incidence of nodule in children with HT and reported the ratio of thyroid nodule as 13% and ratio of malignant thyroid cancer as 0.67% (24). In our study, 7 (15.5%) of our patients had HT and malignancy was not detected in these patients.

Echogeneity of thyroid nodules is among the prominent characteristics particularly for hypoechoic nodules that were reported to have a malignant nature (20,25). While most of mixed echoic nodules and cystic nodules are benign, solid nodules were proven to be usually malignant (25,26). In our study, pathology result was benign in 15 patients who were performed FNAB and USG was reported to be cystic in all. The patient who was detected to have malignancy was reported to have an isoechoic nodule.

In our study, in the non-thyroid disorder group, the patient with hearing loss was diagnosed with Pendred syndrome.

Another patient with non-thyroid disease had xeroderma pigmentosum, coexistence of this condition and thyroid cancer/thyroid nodule was not encountered in literature.

Our study has some limitations. First is its retrospective design and thereby the data's having been evaluated by different radiologists and pathologists, and this condition could have resulted in various results. Another limitation is the small number of patients.

In conclusion, we evaluated the management of thyroid nodules in children. 46.6% of the patients with thyroid nodule underwent FNAB and malignancy ratio was detected to be 2.2% in the study sample. Female gender was seen to be prominent. Since we have a patient with malignancy, we could not comment on the relationship between risk factors and malignancy. For evaluation of pediatric thyroid nodules, a meticulous physical examination, a comprehensive assessment of radiation history, family history, laboratory tests and most importantly, USG findings are required. Prospective studies conducted with larger patient populations are required for investigating pediatric thyroid nodules.

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