CLINICAL CHARACTERISTICS AND PROGNOSIS OF PAPILLARY THYROID CARCINOMA IN ADOLESCENT PATIENTS: A Single Center Study

ABSTRACT

Background and Objective: The management of Papillary Thyroid Carcinoma (PTC) is influenced by factors such as patient age and clinical characteristics. However, the clinical features of PTC in adolescents (ages 10-19) have not been widely studied. Adolescents may present unique biological behaviors and treatment responses compared to pediatric and adult patients. This study aims to provide an initial understanding of the clinical features, prognosis, and treatment outcomes of PTC in adolescent patients to inform more tailored management strategies for this age group. **Methods:** This is a quantitative descriptive study utilizing secondary data from medical records. The data were analyzed to assess clinical characteristics, staging, treatment responses, and recurrence rates in adolescent patients with PTC. **Results:**
The study included 7 adolescent patients with PTC, all female and at least 15 years old, with all cases classified as stage 1 (no distant metastasis). Variations were observed in tumor size, regional lymph node metastasis (based on TNM staging), treatment responses, and risk stratification according to American Thyroid Association (ATA) guidelines. Three of the seven cases experienced recurrence. These findings suggest differences in the clinical characteristics of adolescent patients compared to pediatric patients, indicating potential distinctions in biological behavior. **Conclusion:**
Despite variations in tumor characteristics and treatment responses, the prognosis for adolescents with PTC is generally favorable, similar to pediatric patients. However, recurrence in some cases highlights the need for ongoing monitoring and personalized treatment. Further research is necessary to better understand the relationship between clinical features, risk factors, and prognosis to improve management strategies for adolescent PTC patients..

Keywords: Papillary Thyroid Carcinoma (PTC), Adolescent Patients, Clinical Characteristics, Risk Stratification

1. INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy in both pediatric and adult populations. Among pediatric thyroid cancers, approximately 90% are papillary thyroid carcinoma[1]. Thyroid carcinoma in children has distinct characteristics compared to adults. It is often asymptomatic in its early stages and is typically diagnosed at a more advanced stage, particularly in children under the age of 10, when widespread metastasis is already present[2]. The diagnosis of papillary thyroid carcinoma is made based on the characteristic histological features of the tumor, including clear or grooved nuclei, papillary or follicular architectural patterns, and the presence of fibrosis and psammoma bodies.[3]

Although the prognosis for thyroid carcinoma is generally favorable, with low mortality even in metastatic cases, the management of pediatric patients with advanced disease presents significant challenges[4]. The clinical characteristics of thyroid carcinoma, specifically in adolescents aged 10 to 19 years according to the World Health Organization (WHO), have not been extensively studied. Most existing research combines data from pediatric and adolescent groups or uses age classifications that do not align with the WHO's definition of adolescence[5]. Some studies, for instance, consider patients up to 18 years old as adolescents. Given that the incidence of thyroid carcinoma increases with age, the adolescent population warrants focused investigation.[6]

This article aims to examine the clinical characteristics and prognosis of papillary thyroid carcinoma in adolescent patients to determine whether these differ from those observed in younger children (under 10 years old) or adults.

2. RESEARCH METHODOLOGY

Study Design (Quantitative Descriptive Study): A quantitative descriptive study is appropriate for exploring patterns and associations in the data. This design is useful for summarizing and analyzing the dataset's characteristics, such as variables related to thyroid cancer recurrence.

Use of Secondary Data: Using secondary data, especially a public dataset like the one from the UCI Machine Learning Repository, is a common and acceptable practice in research. However, it is essential to ensure that the dataset is appropriate for the research question and that the data was collected ethically.

Dataset Description: The dataset's 17 variables (e.g., age, gender, smoking history, pathology type, and recurrence) are relevant to the study of thyroid cancer recurrence and appear to provide comprehensive data that could help assess risk factors and prognosis.

Source of Data: The dataset from the Hamadan University of Medical Sciences and Healthcare Services Hospital in Iran is credible, but the study must ensure that the dataset is publicly available for use and that the proper permissions have been obtained if necessary.

Ethical Considerations:If the secondary data was collected from patients, ensure that it follows ethical guidelines (e.g., patient consent, data anonymization). Although the data is

publicly available, it is important to verify that the dataset was shared in accordance with relevant ethical standards.

Appropriateness for Research:The variables in the dataset (including smoking history, thyroid function, TNM staging, response to therapy, and recurrence) are highly relevant to understanding the recurrence of differentiated thyroid cancer. As long as the data aligns with the research objectives and the study hypothesis, the methodology is justified.This study uses secondary data in the form of a public dataset on differentiated thyroid cancer recurrence, sourced from

https://archive.ics.uci.edu/dataset/915/differentiated+thyroid+cancer+recurrence. The dataset consists of 383 data entries and contains 17 variables, including: Age, Gender, Hx Smoking (history of smoking), Hx Radiotherapy (history of radiotherapy), Thyroid Function, Physical Examination (presence of thyroid nodule), Adenopathy (presence of lymph node enlargement), Pathology (subtype of carcinoma based on pathology results), Focality, Risk (according to the American Thyroid Association guidelines), TNM Stage (scores for T, N, M, and stage), Response (response to initial therapy), and Recurrence (thyroid cancer recurrence). The data was collected from the Hamadan University of Medical Sciences and Healthcare Services Hospital in Iran.[7]

3. RESULT

The total 383 patients in the dataset, 7 adolescent patients (1.83%) were diagnosed with differentiated thyroid carcinoma. All adolescent patients in the study were found to have Papillary Thyroid Carcinoma based on their pathological examination, with an average age of 17.42 ± 1.29 years and a minimum age of 15 years. All of these patients were female, non-smokers, had no history of radiotherapy, and had normal thyroid function (euthyroid). At the time of diagnosis, no metastasis was detected, and all patients were classified as Stage I. The variations in clinical characteristics, prognosis, and recurrence events are presented in Tables 1 and 2.

Table 1. Variations in Clinical Characteristics and Prognosis of Papillary Thyroid Carcinoma in Adolescent Patients

Case	Age	Nodul	Risk based on ATA	T	N	Response	Recurrence
1	15	Normal	Moderate	T3a	N1b	Incomplete	Yes
2	17	Solitary in right lobe	Low	T1b	N0	Good	No
3	17	Multinodular	Moderate	T2	N1b	Indeterminate	No
4	17	Solitary in right lobe	High	T2	N0	Incomplete	Yes
5	18	Solitary in right lobe	Moderate	T1b	N1b	Incomplete	Yes
6	19	Solitary in right lobe	Low	T2	N0	Good	No
7	19	Multinodular	Low	T3a	N0	Good	No

Table 2. Descriptive Analysis of Variation in Clinical Characteristics and Prognosis of Papillary Thyroid Carcinoma in Adolescent Patients

Variable	Mean	n	%
Age	17,42 ± 1,29		
Nodule			
Normal		1	14,29
Solitary in right lobe		4	57,14
Multinodular		2	28,57
	APA Risk		
Low		3	42,86
Moderate		1	14,29
High		3	42,86
T (TNM)			
T1b		2	28,57
T2		3	42,86
T3a		2	28,57
N (TNM)			
N0		4	57,14
N1b		3	42,86
Response			
Good		3	42,86
Incomplete		3	42,86
Indeterminate		2	28,57
Recurrence			
Yes		3	42,86
No		4	57,14

DISCUSSION

This study evaluates the clinical characteristics, prognosis, and recurrence of Papillary Thyroid Carcinoma (PTC) in 7 adolescent patients diagnosed with differentiated thyroid carcinoma (DTC) out of a total of 383 patients in the dataset. Here is a summary of the key findings based on the available data:

1. **Patient Demographics**: All analyzed patients were female, with an average age of 17.42 ± 1.29 years. The youngest patient was 15 years old. This age factor is important because thyroid carcinoma in adolescents has different characteristics compared to adults and children. Adolescent thyroid carcinoma, particularly papillary, generally has a better prognosis than in the adult age group.
2. **Nodule Characteristics**: Based on physical examination, most patients had nodules in the right thyroid lobe, either solitary or multinodular. Specifically, 4 patients (57.14%) had a solitary nodule in the right lobe, 2 patients (28.57%) showed multinodular growth,

and 1 patient (14.29%) had a normal nodule. The presence of these nodules is often an important marker for early detection of thyroid carcinoma in adolescents.

3. **Risk Stratification According to ATA Guidelines**: Patient risk according to the American Thyroid Association (ATA) guidelines varied. Three patients (42.86%) were classified as low risk, 1 patient (14.29%) as moderate risk, and 3 patients (42.86%) as high risk. This risk stratification helps determine the optimal treatment approach and long-term monitoring, as higher-risk patients are more likely to require more aggressive therapy and closer surveillance.
4. **T (Tumor) and N (Lymph Node) Stage**: According to the TNM staging, the majority of patients had tumors classified as T2 (42.86%), followed by T1b (28.57%) and T3a (28.57%). Lymph node involvement (N1b) was found in 3 patients (42.86%), while 4 patients (57.14%) had no lymph node involvement (N0). Although there were no distant metastases at diagnosis, lymph node involvement indicates that the prognosis for PTC in adolescents still requires careful attention, especially in terms of treatment and monitoring.
5. **Response to Therapy**: The response to therapy varied among patients. Three patients (42.86%) showed a good response to treatment, three others (42.86%) showed an incomplete response, and two patients (28.57%) had an indeterminate response. Incomplete responses were commonly observed in patients with moderate or high risk, who may require further treatment or more aggressive therapy.
6. **Recurrence**: Of the 7 patients, 3 (42.86%) experienced recurrence after initial therapy, while 4 patients (57.14%) did not experience recurrence. Recurrence occurred in patients with moderate and high risks, as well as in those with larger tumors or lymph node involvement. This indicates that, although the overall prognosis is favorable, long-term monitoring is essential for early detection of recurrence.
7. **Clinical Characteristics and Prognosis**: Despite variability in clinical characteristics and responses to therapy, adolescent patients with PTC generally have a favorable prognosis, with a relatively low recurrence rate. However, for some patients, recurrence can occur, especially in those with moderate to high risk factors. This underscores the importance of long-term monitoring and adjusting treatment strategies based on individual risk profiles.

This study highlights that although PTC in adolescents generally has better outcomes than in adults, attention must be given to the risk of recurrence, especially in those with higher-risk factors. It also emphasizes the need for a more individualized treatment approach for adolescent patients.

Wang X, Wang XL (2020) The standard treatment for pediatric differentiated thyroid carcinoma (DTC) remains uncertain due to limited clinical evidence. This study aims to review clinical experiences and investigate postoperative recurrence risk factors through a retrospective analysis to develop more effective clinical strategies for managing pediatric DTC[8]. Kim K, Lee CR, Kang SW, Lee J, Jeong JJ, Nam KH, Chung WY. (2020) This

study evaluates recurrence risk factors in pediatric patients with differentiated thyroid carcinoma (DTC) treated with thyroidectomy. The average age was 16.6 years, and 14 patients experienced recurrence. Tumor size >2 cm and positive lymph nodes were significant risk factors for disease-free survival (DFS). Kaplan-Meier analysis showed significant DFS differences based on tumor size, but DFS did not differ significantly between total bilateral thyroidectomy and less extensive surgery[9].

Guille JT, Opoku-Boateng A, Thibeault SL, Chen (2015) The incidence of thyroid cancer is higher in pediatric thyroid nodules, requiring more extensive surgical intervention compared to adults. The goal of this review is to summarize new concepts in the management of nodular thyroid disease in the pediatric population, including patient history, medical examination, and diagnosis.[10]. A thyroid nodule is a discrete lesion in the thyroid gland that can be detected through palpation or medical imaging such as ultrasound (US), CT, MRI, or PET scan. In children, thyroid tumors tend to be larger, have a higher rate of metastasis to lymph nodes and lungs, and exhibit higher recurrence rates. However, the prognosis for cancer-related mortality is better in children. The ATA guidelines define the upper pediatric age limit as ≤ 18 years, as most children have completed their development by this age.[11]

George et al. (2018) found that the incidence of PTC was higher in patients over 45 years of age (54.13%), with 60.55% of the patients being female. Among 109 patients, 35.78% had lymph node metastasis, 15.60% had extrathyroid extension, and 18.35% had distant metastasis. Of the distant metastasis, 45% were detected at an early stage, while 55% were detected during follow-up. According to the ATA staging, 64.2% of patients were in stages 1 and 2, while 35.8% were in stages 3 and 4. The ATA 2009 risk classification showed that 38.53% of patients were at low risk, 15.60% at intermediate risk, and 45.87% at high risk. [12]

Tehzeeb H, et al. (2024) included a total of 60 cases of OSCC, with a mean age of 50.81 years and a standard deviation of 13.20 years (ranging from 25 to 81 years). In terms of gender, the majority of cases were male, comprising 55 patients (84.62%). Regarding clinical staging, most patients were in stage IV A (30.77%), followed by stage II (29.23%), stage III (18.46%), stage IV B (13.85%), and only five cases were in stage I (7.69%)[13]. Response to therapy in PTC patients varies, with incomplete responses common in intermediate or high-risk cases (heterogeneity of treatment effects). Risk stratification is performed after thyroid surgery and reassessed after 6 months to 1 year based on ATA 2009 guidelines. Therapy responses are categorized as: a) **Excellent**: No disease (negative imaging, Tg<0.1 ng/mL or stimulated Tg<1 ng/mL without anti-Tg antibodies). b) **Biochemical incomplete**: Elevated Tg or anti-Tg without radiological evidence of disease. c) **Structural incomplete**: Evidence of disease at any Tg level. d) **Indeterminate**: Elevated Tg or anti-Tg without structural disease..[14]

Despite a standard incidence of 0.54 cases per 100,000 people, differentiated thyroid cancer (DTC) is a rare disease in children and adolescents, accounting for only about 1.4% of all pediatric malignancies. Moreover, its incidence is increasing. Due to its rarity and the long

survival of pediatric DTC patients, there is limited evidence in most areas of treatment. As a result, the management of pediatric DTC is filled with controversy, and many questions remain unresolved regarding the optimal management of pediatric papillary thyroid cancer (PTC), with numerous challenges yet to be addressed [15]

This descriptive study explores the characteristics of papillary thyroid carcinoma in adolescents. The incidence of well-differentiated thyroid carcinoma in adolescents in this dataset is 1.83%, with the incidence of papillary thyroid carcinoma specifically at 2.44% among patients with papillary thyroid carcinoma across all age groups. In this study, there were no patients under the age of 10. This figure is lower than that reported in previous studies. (5)This difference may be due to variations in policies across the countries where the research was conducted. The incidence of subclinical papillary thyroid carcinoma has significantly increased in countries that perform screening to detect subclinical papillary thyroid carcinoma. This practice remains controversial, as some experts argue that early detection and screening for subclinical papillary thyroid carcinoma may lead to overdiagnosis. Furthermore, in this study, all adolescent patients with papillary thyroid carcinoma had no history of radiotherapy. Radiation exposure, such as from radiotherapy, is considered a significant factor in the development of papillary thyroid carcinoma at a young age, with a latency period of 5-10 years. This group of patients may carry BRAF mutations, which are commonly found, or less frequently, RET/PTC fusions, but confirming the diagnosis would require genetic testing to confirm the presence of genetic alterations[16] The absence of a history of radiotherapy may also explain the very low incidence in this study compared to previous research, especially studies conducted in areas with radiation exposure.[5][17]

All adolescent patients with papillary thyroid carcinoma in this study were female, which is consistent with previous research[18] and existing literature, which states that papillary thyroid carcinoma is found three times more often in females than in males[19] although according to the WHO, this carcinoma subtype can occur in both males and females (1). The small sample size may explain the absence of male adolescent patients with papillary thyroid carcinoma in this study. Several efforts have been made to determine the prognosis of patients with papillary thyroid carcinoma. The staging system by the American Joint Committee on Cancer (AJCC) 8th edition uses the TNM system to predict the survival of cancer patients, while risk stratification based on the American Thyroid Association (ATA) classification is used to predict recurrence. According to the AJCC 8th edition staging system, tumor size categories are as follows: T1a for tumors 1 cm or smaller and confined to the thyroid; T1b for tumors larger than 1 cm but not exceeding 2 cm, confined to the thyroid; T2 for tumors larger than 2 cm but not exceeding 4 cm, confined to the thyroid; T3a for tumors larger than 4 cm, confined to the thyroid; T3b for tumors with macroscopic extrathyroidal extension to any of the sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles, regardless of tumor size; T4a for tumors with macroscopic extrathyroidal extension to subcutaneous soft tissue, the larynx, trachea, esophagus, or recurrent laryngeal nerve,

regardless of tumor size; and T4b for tumors with macroscopic extrathyroidal extension to the prevertebral fascia or encasing the carotid artery or mediastinal blood vessels, regardless of tumor size. The regional lymph node categories (N) include N0a, N0b, N1a, and N1b. N0a means at least one lymph node is free of malignant cells, both cytologically and histologically. N0b means no regional lymph node metastasis is detected either radiologically or clinically. N1a indicates metastasis to lymph nodes at levels VI or VII (pretracheal, paratracheal, prelaryngeal, and superior mediastinal), either unilaterally or bilaterally. N1b indicates metastasis to lateral cervical lymph nodes (levels I, II, III, IV, or V) or retropharyngeal nodes, either unilaterally, bilaterally, or contralaterally[20].

Based on tumor size, the patients in this study's dataset fall into a range between minimal T1b and maximal T3a categories. There were two patients classified as T1b, one with N0 and the other with N1b. The patient in case 2, with T1bN0M0 (stage 1), showed a good treatment response and did not experience recurrence, while the patient in case 5, with T1bN1bM0 (stage 1), showed an incomplete response and experienced recurrence. Although two out of three patients with recurrence had regional lymph node metastasis (N1b), the lymph node category alone does not guarantee recurrence, as seen in case 3, where the patient with T2N1bM0 (stage 1) did not experience recurrence. The minimum category found was T1b, suggesting that early detection or screening for subclinical thyroid tumors was likely not conducted in this study.

Papillary thyroid carcinoma is classified as a well-differentiated thyroid carcinoma. The 8th edition of the AJCC introduces a new classification specifically for patients under the age of 55. [20][21]Thus, adolescent patients can use this classification. All T and N categories will be included in stage 1 if no distant metastasis is found, as observed in the data of this study.

Papillary thyroid carcinoma has an overall good prognosis, with a 5-year survival rate approaching 90%. The presence of metastasis in the lymph nodes does not alter the prognosis. The prognosis becomes poor if malignant cells have spread and metastasized to distant site [19][22] The patients in this study all had no distant metastasis (M0), with a good prognosis and high survival rate, as no mortality was observed during the 15-year data collection period..

The pediatric and adolescent patients with well-differentiated thyroid cancer, including papillary thyroid carcinoma, the risk classification is divided into the same categories: low, moderate, and high risk. According to the ATA classification for children and adolescents, low risk is defined as disease limited to the thyroid macroscopically with N0/Nx status, or patients with small N1a. Moderate risk is assigned when extensive N1a status or minimal N1b is found. High risk is identified when there is extensive N1b status, accompanied by extrathyroidal extension, with or without distant metastasis..[23]Sapuppo et al. proposed that small N1a be defined as low risk, which occurs when the number of lymph nodes containing metastatic cancer cells is 5 or fewer. High risk is defined when N1b involves more than 5

lymph nodes with metastasis greater than 3 cm. Moderate risk applies to cases where the status falls between low and high risk. [18][24]

The data of this study, no adolescent patients experienced metastasis. This finding is somewhat inconsistent with other studies, which have stated that, compared to papillary thyroid carcinoma in adults, papillary thyroid carcinoma in children tends to be more extensive, with spread including metastasis to regional lymph nodes or distant metastasis[18][25] This may also be a factor contributing to the high survival rate observed in this study.

The limitation of the TNM system from the 8th edition of the AJCC is that it does not account for histological subtypes or treatment response, and it is unable to predict recurrence. Meanwhile, the ATA system only considers histopathological data without factoring in treatment response. Another classification system that can be utilized is Dynamic Risk Stratification (DRS). This system categorizes patient responses to treatment into four categories: good, biochemically incomplete, structurally incomplete, and indeterminate [23][18]The data was obtained from radiological results and thyroid markers (TSH, Thyroglobulin, and anti-Thyroglobulin antibodies) (18). In this study's data, the incomplete data refers to structural incompleteness, which may be due to the small sample size..

Recurrence occurred in 3 patients out of a total of 7 adolescent patients with papillary thyroid carcinoma. The risk of recurrence tends to be low in patients with N0 status, but increases in those with N1a and N1b status. Lymph node status-related recurrence risk is an important factor to consider in the treatment of patients.[18].One limitation of this study is the very small number of cases. Additionally, the data used is secondary data, which may contain variations in characteristics due to factors such as location-related management policies, availability of facilities, and environmental factors like radiation exposure. Early detection and thyroid tumor screening in children and adolescents, including the use of ultrasonography in asymptomatic adolescent patients, are not recommended due to the risk of radiation exposure for diagnostic and therapeutic purposes. The effects of such exposure are considered more harmful compared to waiting until clinical symptoms appear, as papillary thyroid carcinoma is usually indolent. Therefore, diagnosis in young adulthood still provides a good prognosis.[16][5]

CONCLUSION AND SUGGESTIONS

The characteristics of papillary thyroid carcinoma in adolescents show slight differences compared to those in children under 10 years old and adults. In this study, only a few adolescent patients with papillary thyroid carcinoma experienced extensive spread, with a good survival rate; however, recurrence occurred in some cases. Further research is needed with an adequate sample size to better understand the relationship between each variable, including clinical and histopathological characteristics such as stage, as well as treatment response, in predicting recurrence and mortality. This will help optimize the management of papillary thyroid carcinoma in adolescents**.**

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The authors hereby state that no generative AI tools such as large language models (ChatGPT, COPILOT, etc.) or text-to-image generators were utilized in the creation or editing of this work.

DATA AVAILABILITY

All relevant data are included in the paper and its supporting information files. This study will assist researchers in identifying critical areas for Clinical Characteristics and Prognosis of Papillary Thyroid Carcinoma in Adolescent Patients.

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