Review Article

Pediatric thyroid cancer in Saudi Arabia: a literature review of current trends in management and outcomes

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Background and Objective: Pediatric thyroid cancer is on the rise, especially among adolescents. It is more aggressive than adult thyroid cancer and often presents with advanced features. This review aims to examine the current trends in the management and outcomes of pediatric thyroid cancer in Saudi Arabia.

Methods: A comprehensive literature search was conducted to identify relevant studies on pediatric thyroid cancer in Saudi Arabia. PubMed and Google Scholar were searched from inception until December 2023. Extracted information included study identifiers, patient demographics, clinicopathological features, treatment modalities, complications, surveillance practices, recurrence patterns, and survival outcomes.

Key Content and Findings: The literature search identified ten eligible studies on pediatric thyroid cancer in Saudi Arabia. Pediatric thyroid cancer in Saudi Arabia often presents with advanced features, including higher rates of lymph nodes and distant metastases at diagnosis compared to adults. Fine-needle aspiration remains accurate, correlating well with final histopathology. Treatment primarily involves surgery, with total thyroidectomy being common, followed by radioactive iodine therapy for high-risk patients or those with positive iodine uptake. Survival rates exceed 95%, indicating a generally favorable prognosis. Recurrence rates can reach up to 30% in some studies, particularly with larger tumors or distant metastases. Hypocalcemia and recurrent laryngeal nerve injury are common postoperative complications, highlighting the need for experienced surgeons and meticulous technique. Genetic alterations in pediatric thyroid cancer are being investigated, but their impact on prognosis and treatment response is unclear. Limited data on management and outcomes in other regions of Saudi Arabia calls for multicenter studies to address healthcare disparities.

Conclusions: Pediatric thyroid cancer in Saudi Arabia has unique characteristics compared to its adult counterpart, mandating specialized management approaches. More research is needed on early detection, risk stratification, personalized treatment, and addressing regional disparities to improve outcomes for this vulnerable population.

Keywords: Cancer; outcomes; pediatric; Saudi; thyroid

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Introduction

Background

Pediatric thyroid cancer, although rare, is increasing, particularly among adolescents (1,2). It shares genetic drivers with adult thyroid cancer but has unique clinical characteristics, including advanced presentation and frequent cervical lymph node involvement. Pediatric thyroid nodules carry a higher risk of malignancy compared to adults (3,4). However, a more favorable prognosis is seen for

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Table 1 The search strategy summary

Items	Specification
Date of search	20 December 2023
Databases and other sources searched	PubMed and Google Scholar
Search terms used	"thyroid cancer", "pediatric", "paediatric", "childhood", "children", and "Saudi Arabia"
Timeframe	Inception to December 2023
Inclusion and exclusion criteria	Articles published in English that reported on pediatric thyroid cancer cases in Saudi Arabia were assessed for eligibility. Exclusions were made for conference abstracts, case reports, editorials, and reviews without original data. Reference lists of eligible articles were manually screened for additional relevant studies. Observational and interventional studies were included, and various types of papers, such as original research articles and case series were considered for inclusion. Inclusion criteria required a focus on pediatric thyroid cancer in Saudi Arabia and reporting on clinical characteristics, management approaches, treatment outcomes, or prognostic factors

pediatric differentiated thyroid carcinoma (DTC) compared to adult DTC (5). The American Thyroid Association (ATA) has developed treatment guidelines for pediatric thyroid nodules, encompassing both benign and malignant cases (5).

Rationale and knowledge gap

In the United States, individuals under 20 years old account for 1.8% of diagnosed thyroid malignancies (6). Incidence rates have shown a more rapid increase from 2006 to 2013 compared to 1973 to 2006, suggesting an actual rise in pediatric thyroid cancer alongside improved detection (2). Among adolescents aged 15–19 years, thyroid cancer ranks as the eighth most common cancer and the second most common among girls (7,8). This highlights a tenfold higher risk compared to younger children, with a female-to-male predominance of 5:1 during adolescence, unlike in younger pediatric age groups (8-11). Pediatric DTC typically presents as a thyroid nodule, although papillary thyroid cancer (PTC) may manifest as a neck mass with or without a palpable thyroid lesion. Incidental detection during imaging or unrelated surgeries is not uncommon (12). In some cases, the diagnosis is only confirmed upon identification of distant metastases (13-15). The literature on pediatric thyroid cancer in Saudi Arabia is limited.

Objective

This review aims to comprehensively examine the current trends in the management and outcomes of pediatric thyroid cancer in Saudi Arabia, addressing the research gap in this area. This article is presented in accordance with the Narrative Review reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-42/rc).

Methods

A comprehensive literature search was conducted to identify relevant studies on pediatric thyroid cancer in Saudi Arabia. PubMed and Google Scholar were searched from inception until December 2023 using the following search terms individually and in combination: "thyroid cancer", "pediatric", "paediatric", "childhood", "children", and "Saudi Arabia". Titles and abstracts were screened, and full-text articles published in English that reported on pediatric thyroid cancer cases in Saudi Arabia were assessed for eligibility. Exclusions were made for conference abstracts, case reports, editorials, and reviews without original data. Reference lists of eligible articles were manually screened for additional relevant studies.

Observational and interventional studies were included, and various types of papers, such as original research articles and case series were considered for inclusion. Inclusion criteria required a focus on pediatric thyroid cancer in Saudi Arabia and reporting on clinical characteristics, management approaches, treatment outcomes, or prognostic factors. Extracted information included study identifiers, patient demographics, clinicopathological features, treatment modalities, complications, surveillance practices, recurrence patterns, and survival outcomes. The search strategy is summarized in *Table 1*.

Results

The literature search identified ten eligible studies on pediatric thyroid cancer in Saudi Arabia, summarized in *Table 2* (16-25). All studies were conducted in Riyadh on patients diagnosed between 1988 and 2019, and published from 2015 to 2023. Eight of the studies were carried out at the King Faisal Specialist Hospital and Research Center, the primary tertiary care center in Saudi Arabia where more than 90% of thyroid cancer cases are referred for management (22). Sample sizes ranged from 20 to 170 patients, with variation in the age cut-off for defining the pediatric population, but most commonly including individuals aged 18 years or younger. All studies focused on DTC, predominantly papillary thyroid carcinoma (PTC), while some also included follicular (FTC), poorly differentiated, Hurthle cell, and medullary (MTC) thyroid carcinomas. Three studies reported on post-operative complications.

The included studies provided insights into the clinical characteristics, management approaches, treatment responses, and prognostic factors of pediatric thyroid cancer in Saudi Arabia. Advanced disease stage and extrathyroidal extension were frequently observed at diagnosis in pediatric cases compared to older individuals. Surgery was the primary initial treatment, often followed by adjuvant radioactive iodine (RAI). Prognostic factors associated with worse clinical outcomes included larger tumor size, multifocality, nodal and distant metastases, and persistent/recurrent disease. Molecular profiling also revealed differences in mutations between pediatric and adult DTC.

In summary, this review examined ten studies conducted in Saudi Arabia, shedding light on the epidemiology, management, and prognosis of pediatric thyroid carcinoma. Variations in presentation, treatment approaches, and outcomes were reported.

Discussion

Epidemiology

Thyroid cancer has shown an increasing incidence globally, including in Saudi Arabia (26). A study conducted at King Faisal Specialist Hospital and Research Centre reported that thyroid cancer accounted for approximately 9% of all malignancies and 12% of all female malignancies at the institution (26).

According to the Saudi Cancer Incidence Report 2020 (27), thyroid cancer ranked as the 3rd most common cancer among Saudi nationals (7.4% of all cancers) and the 2nd most common cancer among females (10.4%). The report also highlighted geographical variations in thyroid cancer incidence within Saudi Arabia.

PTC was found to be the most prevalent type of thyroid cancer among pediatric patients (16). Pediatric thyroid cancer presents distinct differences in presentation, molecular characteristics, treatment response, and outcomes compared to adult thyroid cancer (1,28). Pediatric patients with DTC often present at advanced stages and have higher recurrence rates compared to adults (4). A study using the Global Burden of Disease databases in Saudi Arabia reported an upward trend in thyroid cancer incidence between 1990 and 2019 (29). Over this 30-year period, there was a significant increase in both incidence and mortality rates.

Specifically focusing on pediatric patients aged 18 years or younger during the years 2000–2012, DTC was found to be rare but displayed more aggressive clinicopathological features compared to young adults aged 20–45 years (17). While not specific to Saudi Arabia, a recent comprehensive literature review has revealed that despite the aggressive presentation, pediatric patients with DTC typically experience an excellent long-term prognosis (4).

The management of pediatric thyroid cancer requires specialized expertise due to the complexity of the disease and the need for long-term follow-up. The age cutoff for defining the pediatric age group varies across studies (28). The ATA recommends defining pediatrics as patients aged 18 years or younger to consider the impact of growth and development-related physiological changes on tumor behavior (5).

While PTC is the most common type of pediatric thyroid cancer, limited literature is available on rarer types such as follicular, poorly differentiated, and medullary carcinomas, with most studies originating from Western countries and limited data from Asian countries, including Saudi Arabia (28).

A retrospective review by Almosallam *et al.* examined the outcomes and complications of thyroid surgery in pediatric thyroid cancer patients (23). The study analyzed medical records from a single institution covering the period from 2000 to 2014 and included data on demographic and clinical characteristics, indications for thyroidectomy, pathological findings, complications, length of stay, RAI treatment, and recurrences. The study sample comprised 103 pediatric patients who underwent a total of 112 thyroidectomy procedures, with malignancy being the most common indication for surgery in children (64% of cases).

Table 2 Summary of the included studies (arranged by publication date in ascending order)

Reference number	Publication year	Institution; study period	Age cutoff (years)	N (% female/male)	Inclusion	Cancer subtypes [%]	TNM stage	Key findings
(16)	2015	King Khalid University Hospital, King Saud University; 2003–2013	21	23 (69.6/30.4)	DTC diagnosis	PTC [95.6]; FTC [4.3]	Not reported	Extrathyroidal extension was found in 26.1% of patients and recurrence occurred in 4.7%
(17)	2015	King Fahad Medical City; 2000–2012	18	27 (74.1/25.9)	DTC diagnosis	PTC [100]	Stage I: 96.3%; stage II: 3.7%	The 10-year LRC and DMC rates were significantly lower in children (75.3% and 64.7% respectively) than young adults and adults. 18 LRs (11.5%) were observed; 6/27 in children, 9/78 in young adults and 3/52 in adults
(18)	2016	King Faisal Specialist Hospital and Research Center; 1998–2011	20	97 (81.4/18.6)	DTC diagnosis	PTC [95.8]; FTC [4.1]	Stage I: 83.5%; stage II: 16.4%	Persistent/recurrent disease at the last follow-up was 33.7%
(19)	2017	King Faisal Specialist Hospital and Research Center; 1998–2015	18	79 (86.1/13.9)	DTC diagnosis	PTC [100]	Stage I: 88.6%; stage II: 11.4%	*BRAF* V600E mutation was significantly less common compared to adult DTC, and there was no association between this mutation and the histopathological features and outcome of PTC
(20)	2016	King Faisal Specialist Hospital and Research Center; 2003–2014	18	55 (83.6/16.4)	Thyroid cancer	PTC [94.6]; FTC [3.6]; poorly differentiated [1.8]	Stage I: 85.5%; stage II: 14.5%	*TERT* promoter mutations in pediatric TC have an exceedingly low prevalence This study suggested an association of the *BRAF* V600E mutation with TC recurrence in pediatric patients
(21)	2019	King Faisal Specialist Hospital and Research Center; 2002–2018	18	20 (80/20)	Lung metastasis at diagnosis	PTC [95]; poorly differentiated [5]	Stage I: 0%; stage II: 100%	The biochemical response to iodine-131 can be substantial but resolution of structural abnormalities was rare
(22)	2020	King Faisal Specialist Hospital and Research Center; 2004–2019	18	48 (77/23)	DTC diagnosis	PTC [91.7]; Hurthle cell [8.3]	Stage I: 89.6%; stage II: 10.4%	Fusion genes were more common than single-point mutations The most common genetic alterations are *RET::PTC1, BRAF* V600E, *RET::PTC3*, and *ETV6::NTRK3* Genetic alterations did not correlate with the clinicopathological features or the outcome

Table 2 (*continued*)

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Reference number	Publication year	Institution; study period	Age cutoff (years)	N (% female/male)	Inclusion	Cancer subtypes [%]	TNM stage	Key findings
(23)	2020	King Faisal Specialist Hospital and Research Center; 2000–2014	18	103 (78/22)	Thyroidectomy	PTC [59]; FTC [2.9]; MTC [1.9]	Stage I: 89%; stage II: 11%	Malignancy was the most common indication for thyroid surgery in children Hypocalcemia and recurrent laryngeal nerve injury were significant complications The recurrence rate of thyroid cancer was 15%
(24)	2022	King Faisal Specialist Hospital and Research Center; 1988–2018	18	88 (73.9/26.1)	DTC + surgery + RAI	PTC [95.5]; FTC [4.5]	Stage I: 86.4%; stage II: 13.6%	Primary tumor size and the presence of distant metastasis at diagnosis were the only independent prognostic risk factors for EFS in pediatric DTC in Middle Eastern ethnicity
(25)	2023	King Faisal Specialist Hospital and Research Center; 1988–2018	18	170 (74.7/25.3)	DTC	PTC [92.3]; FTC [7.7]	Stage I: 84.1%; stage II: 15.9%	Lung metastases were associated with younger age, extrathyroidal extension, bilateral tumors, LN disease, a high post-operative sTg and *NTRK3* fusions

N, sample size; TNM, tumor, node, metastasis; DTC, differentiated thyroid carcinoma; PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; LRC, locoregional control; DMC, distant metastasis control; LR, local recurrence; TC, thyroid cancer; MTC, medullary thyroid carcinoma; RAI, radioactive iodine; EFS, event-free survival; LN, lymph node; sTg, serum thyroglobulin.

Disease characteristics

A comparative study at King Faisal Specialist Hospital and Research Center investigated the clinical and pathological features, management, and long-term outcomes of DTC in children and adolescents (≤20 years) compared to young adults (18). The study included 310 DTC cases, with 97 pediatric patients and 213 young adults. Pediatric DTC showed significantly higher rates of extrathyroidal extension, lymph node involvement, and distant metastases. However, there were no significant differences in gender, tumor subtype, size, or multifocality. Pediatric patients had higher rates of persistent disease requiring additional interventions, although the rate of persistent/recurrent disease approached that of adults after 5 years. Long-term outcomes were excellent in both groups, with low mortality rates, but pediatric DTC carried a higher risk of persistent/recurrent disease, particularly within the first 5 years. Age was identified as an independent prognostic factor, with pediatric patients more likely to experience persistent/recurrent disease.

Parvathareddy *et al.* identified several risk factors for distant lung metastasis in pediatric DTC, including younger age (≤15 years), extrathyroidal extension, multifocal/bilateral tumors, lymph node involvement, and high postoperative thyroglobulin (Tg) levels (25). Alzahrani *et al.* conducted a study specifically focusing on lung metastasis in pediatric thyroid cancer patients and found that most cases presented as bilateral radioiodine-avid micrometastases, showing a substantial response to iodine-131 treatment, although complete structural resolution was rare. The study also detected rare single *PIK3CA* mutations in one tumor sample (21).

Genetic alterations

Multiple studies have explored genetic alterations in pediatric thyroid cancer in Saudi Arabia. One study analyzed 48 cases of pediatric DTC using a comprehensive childhood cancer gene panel (22). The study identified prevalent genetic alterations, including the single-point mutation *BRAF* V600E (19%), and several fusion genes, such as *RET*::*PTC1* (19%), *RET*::*PTC3* (8%), and *ETV6*::*NTRK3* (8%). Fusion genes were more commonly observed than single-point mutations. However, no correlation was found between genetic alterations and clinicopathological features or outcomes. In a retrospective study by Alzahrani *et al.*, 89 cases of pediatric DTC were examined to analyze mutations in *BRAF*, *HRAS*, *KRAS*, *NRAS*, *PIK3CA*, *PTEN*, and *TERT* (19). The prevalence of the *BRAF* V600E mutation was significantly lower in pediatric DTC (26.4%) compared to adult DTC. This mutation was not associated with histopathological features or outcomes. Other mutations identified included *TERT C228T* (1.3%), *NRAS 61* (2.5%), *PIK3CA* exon 9 (1.4%), *PIK3CA* exon 20 (1.3%), and *PTEN* exon 5 (1.4%). The study supported the notion that pediatric DTC has distinct clinical, histopathological, molecular, and biological profiles compared to adult DTC. The lower prevalence of certain mutations in pediatric DTC may contribute to better response to RAI treatment and less disease progression. Kong *et al.* observed a correlation between *NTRK* fusions and pediatric PTC, lymph node metastasis, and *BRAF* wild-type tumors (30). This finding suggested the potential use of immunohistochemistry (IHC) as a screening tool for PTC patients with *NTRK* fusions. Such patients could benefit from TRK inhibitors, and *NTRK* fusion may be a prognostic factor. Another study involving 55 cases of pediatric DTC found *TERT* promoter mutations in 23.6% of cases, compared to 31.9% in 210 adult DTC cases (20). The coexistence of *TERT* and *BRAF* V600E mutations was more common in adults (33%) than in pediatric cases (11.1%). *TERT* mutations were associated with aggressive tumor behavior and advanced stage in pediatric DTC. Additionally, the study demonstrated an association between the *BRAF* V600E mutation and thyroid cancer recurrence in pediatric patients.

Diagnosis and management

Effective management of pediatric DTC requires a careful and tailored approach to diagnosis and treatment. This section explores the current practices and trends in diagnosing and managing pediatric DTC in Saudi Arabia, drawing from relevant studies included in this review.

Diagnosis

Pediatric DTC often presents a more aggressive profile than its adult counterpart, necessitating efficient diagnostic strategies. Ultrasound (US) plays a pivotal role in identifying and characterizing thyroid nodules in pediatric patients. Across the studies included in this review, US emerged as the primary imaging modality used for all patients. Upon clinical suspicion or detection of a thyroid nodule, a dedicated thyroid and neck US examination is recommended (5). This evaluation should encompass a

detailed description of various features, including nodule composition, echogenicity, margins, presence or absence of calcifications, shape, and vascularity (4). While scoring systems such as the Thyroid Imaging Reporting and Data System (TI-RADS) and the ATA nodule sonographic patterns system are commonly employed to select thyroid nodules for fine needle aspiration (FNA) in adults, their applicability to children is limited due to the higher incidence of DTC in pediatric nodules (4). Furthermore, US guidance proves invaluable for FNA procedures targeting suspicious lesions or lymph nodes in the thyroid bed or lateral neck. The aspirated material can be evaluated with routine cytology and Tg immunoassay of the needle washout, particularly beneficial when cytopathology results are inconclusive or non-diagnostic (5). FNA remains the cornerstone of diagnosis for thyroid nodules in pediatric patients, with a diagnostic accuracy of over 94% (23). This minimally invasive procedure provides timely and accurate diagnosis by closely correlating with final histopathology. In addition to FNA, shear wave elastography shows promise as a tool for differentiating between malignant and benign thyroid nodules in children (31). While molecular testing has the potential to enhance diagnostic capabilities, its use in pediatric cases is limited (19,20,22,30).

Surgical management

Al-Qahtani *et al.*'s work highlights the increased prevalence of lymph node metastasis and extrathyroidal extension in children with DTC, emphasizing the need for personalized management approaches (17). Surgery is the primary treatment for pediatric DTC, followed by RAI therapy for residual or metastatic disease after resection, as recommended by the ATA guidelines (5). Total thyroidectomy has traditionally been the preferred surgical approach for most children with DTC in Saudi Arabia (16-18,23). However, a growing body of evidence supports a more conservative approach in certain cases, such as solitary unifocal classical PTC ≤1 cm or minimally invasive FTC <4 cm in size without locoregional or distant metastases or unusual histological features (18). The decision between total and conservative surgery should consider individual risk factors and tumor characteristics.

Prophylactic central lymph node dissection (CLND) is reported in some cases (24), but it is not routinely performed due to limited evidence of its benefits and the potential for complications (18,23). However, therapeutic CLND is routinely conducted for all patients with pre-operative or intra-operative evidence of lymph node involvement.

RAI therapy

RAI therapy is vital for managing high-risk patients and those with radioiodine-avid disease that cannot be surgically removed or have distant metastases (17,25). The decision to use RAI should be personalized, taking into account risk assessment and potential long-term side effects (19,20). To optimize treatment outcomes, careful consideration of dosage and timing is crucial.

For most patients at risk, RAI remnant ablation is routinely administered. One study specified that RAI was not given to patients with very low-risk tumors (microcarcinomas <1 cm without locoregional or distant metastases and no significant extrathyroidal extension or aggressive histopathological subtypes) (18).

In the case of metastatic thyroid cancer, RAI was given at activities adjusted for body weight, considering the extent of lung involvement found on diagnostic imaging. One study reported initial I-131 therapies given every 6 to 12 months (25). These patients are monitored regularly (every 3 to 9 months) for thyroid stimulating hormone (TSH), FT4, free T4 (FT4), Tg, and anti-Tg antibodies. Another study highlighted the use of repeated RAI doses every 6–12 months for patients with evidence of small or metastatic radioiodine-avid persistent/recurrent disease until achieving remission, reaching a cumulative activity of around 1,000 mCi, or encountering radioiodine refractoriness (18). Surgically treatable macroscopic persistent/recurrent disease is treated with surgical resection.

Molecular targeted therapies

The use of molecular targeted therapies in pediatric DTC is limited in Saudi Arabia, with only one reported case in the literature (21). In this case, sorafenib was used as a last resort in a patient with inoperable, progressive, radioiodine-refractory, and metastatic poorly DTC. Unfortunately, the patient's disease progressed, leading to death within 1.5 months of starting treatment.

Though limited in scope, the study by Kong *et al.* suggests the potential usefulness of *NTRK* fusion screening in PTC patients through IHC, as this alteration appears to be more common in the pediatric population and may provide a target for TRK inhibitors (30).

Complications

Thyroid surgery in pediatric patients can lead to various

Table 3 Rates of surgical complications

Reference number	Paper	Authors	Transient hypocalcemia	Permanent hypocalcemia	Temporary RLN injury	Permanent RLN injury
(16)	Differentiated thyroid carcinoma in paediatric and adolescent age group: 10-year experience in a university hospital in Saudi Arabia	Alsaif	30.4%	4.3%	21.7%	–
(17)	Clinicopathological features and treatment outcomes of differentiated thyroid cancer in Saudi children and adults	AL-Qahtani *et al.*	14.8%	3.7%	3.7%	–
(23)	Thyroid surgery in 103 children in a single institution from 2000-2014	Almosallam *et al.*	22%	3%	3% (unilateral)	3% (unilateral)

RLN, recurrent laryngeal nerve.

complications. In a study conducted by Almosallam *et al.* (23), hypocalcemia occurred in 22% of patients, with 3% experiencing permanent hypocalcemia. Unilateral recurrent laryngeal nerve injury was observed in 5.8% of patients, of which 3% had permanent nerve damage. No cases of postoperative bleeding, wound infection, or tracheal injury were reported. Overall, complications were observed in 19.6% of patients, but no cases of mortality were reported.

Al-Qahtani *et al.* (17) also reported on surgical complications and their respective rates. They found that the incidence of permanent hypocalcemia was significantly higher in children and young adults (P=0.043) compared to adults. Specifically, the rates of permanent hypocalcemia were 3.7% in children, 2.6% in young adults, and 1.9% in adults. Recurrent laryngeal nerve damage was observed in 1 patient (3.7%) in the children's group, 1 patient (1.3%) in the young adults' group, and 1 patient (1.9%) in the adults' group. Acute complications of RAI ablation were more frequent in children (59.3%) compared to young adults (46.1%) and adults (34.6%). These acute complications included sialadenitis, acute sickness (nausea, vomiting), and neck pain. Late complications of RAI ablation occurred in a smaller percentage of patients overall but were still more common in children (7.4%) compared to young adults (3.8%) and adults (1.9%). These late complications included sicca syndrome and nasolacrimal duct obstruction.

In another study (16), the rate of postoperative complications in a series of 23 patients was reported. Temporary hoarseness of voice was observed in five patients (21.7%), temporary hypocalcemia in seven patients (30.4%), and one patient (4.3%) required permanent hypocalcemia management with calcium and vitamin D replacement therapy. No cases of postoperative bleeding or wound infection were reported. Reported complications are summarized in *Table 3* (16,17,23).

Outcomes and prognosis

The prognosis for pediatric DTC is generally favorable, but long-term follow-up is crucial due to the risk of late recurrence (5). A retrospective study conducted at King Faisal Specialist Hospital (24) investigated prognostic factors for event-free survival (EFS) in 88 pediatric DTC patients aged 18 years or younger, with a median age of 15 years and a male-to-female ratio of 1:3. The majority of tumors were PTC. Lymph node metastasis was present in 70.5% of cases, and distant metastasis was observed in 13.6%. The patients underwent surgery and RAI therapy. This study identified several important outcomes. Events, including locoregional recurrence, pulmonary metastasis, and persistent disease, occurred in 32.9% of cases. The 10-year overall survival (OS) rate was 98.4%, and the 10-year EFS rate was 79.2%. Tumor size larger than 4 cm and synchronous distant metastasis were negative predictors of EFS. The risk stratification system proposed by the ATA did not impact EFS.

Another study (23) analyzed outcome data of thyroid surgery in a pediatric population, with a specific focus on demographic and clinical factors, indications for surgery, thyroid pathology, complications, length of stay, and recurrence rates, with a mean follow-up duration of 71.7 months. Two-thirds of the patients received postoperative RAI, and the recurrence rate was 15%. Lymph node metastasis was observed in 67.6% of cases, with 11% having distant metastases to the lung.

In Parvathareddy's study (25) of patients with distant metastasis treated with RAI, only one patient (3.7%)

achieved an excellent response after 12.1 years. Despite structural persistent disease, the OS was excellent at 96.3%. The study concluded that tumor size larger than 4 cm and distant metastasis negatively impact EFS. Close monitoring and risk-adapted therapy are warranted due to the risks of recurrence and metastasis, especially in larger/metastatic tumors. This study also concluded that genetic profiling may not necessarily predict outcomes.

Al-Qahtani *et al.* (17) reported that the 10-year disease-free survival (DFS) rates were 67.3% in children, 82.4% in young adults, and 90.1% in adults. The DFS rates were significantly lower in children compared to young adults and adults (P=0.021). The 10-year locoregional control (LRC) and distant metastasis control (DMC) rates for the entire cohort were 87.2% and 84.2%, respectively. However, the 10-year LRC and DMC rates were significantly lower in children (75.3% and 64.7%, respectively) compared to young adults and adults. There was no statistically significant difference in the 10-year OS rates among all age groups (P=0.075).

In another study (22), researchers analyzed the response to therapy status at the last follow-up visits, DFS, and the relationship between genetic alterations and clinicopathological features. At the last follow-up visits, the majority of patients (66.7%) had an excellent response to therapy. However, 16.7% had an indeterminate response, 4.2% were biochemically incomplete, 8.3% were structurally incomplete, and 4.2% were lost to follow-up with an unclear status. The study found no significant difference in the probability of DFS between patients with tumors harboring genetic alterations and those without mutations. Furthermore, the study reported that there were no differences in clinical and pathological features and outcomes over time among patients with single-point mutations, fusion gene alterations, or no mutations. The study also found that 71% of pediatric patients with DTC had lymph node metastasis, and 10.4% had distant metastasis to the lungs.

Another study (16) stated that all 21 patients in the series (excluding 2 who failed to follow up) were alive, asymptomatic, and disease-free at the time of writing the paper. The average follow-up duration was 6.6 years, and there was only one instance of disease recurrence, which occurred 3 years after the initial surgery. The recurrence was observed in the lateral neck group of lymph nodes in a 16-year-old boy. In this study, all patients underwent total thyroidectomy with appropriate cervical lymph node dissection, followed by radioiodine ablation therapy and TSH-suppressant thyroxine replacement therapy.

A study (18) comparing DTC in children and adolescents with young adults discovered that pediatric DTC patients had a higher risk of persistent/recurrent disease compared to young adults, particularly within the first 5 years after diagnosis. Age was determined to be an independent prognostic factor for the rate of persistent/recurrent disease, with the pediatric group having a higher likelihood compared to adults. The study proposes that pediatric DTC is clinically distinct from DTC in young adults, exhibiting a higher rate of extrathyroidal extension, lymph node and distant metastases, and an increased risk of persistent/recurrent disease. In the initial follow-up evaluation, 60% of pediatric patients exhibited signs of persistent disease, while this figure was 39% for adult patients. However, in the final follow-up visit, there was no significant difference in the rate of persistent or recurrent disease between the two groups. The study found no instances of mortality due to DTC in both the pediatric and adult groups. Furthermore, according to the Kaplan-Meier analysis, the probability of DFS was lower in the pediatric group compared to the adult group during the follow-up period. Additionally, the study revealed that pediatric DTC patients required a higher number of additional interventions compared to young adults, with 43.3% of pediatric patients undergoing such interventions compared to 30% of adult patients.

Limitations

While this literature review aimed to provide a comprehensive overview of current trends in the management and outcomes of pediatric thyroid cancer in Saudi Arabia, several limitations should be acknowledged. Firstly, the limited number of eligible studies identified through the literature search (n=10) raises concerns about the breadth and depth of available literature on this topic. The scarcity of research in this area may impact the generalizability of findings and hinder a more exhaustive understanding of pediatric thyroid cancer in the Saudi context. Furthermore, the geographical concentration of the included studies in Riyadh, conducted mostly at the King Faisal Specialist Hospital and Research Center, introduces potential selection bias. This concentration in a single geographic location limits the generalizability of the results to the broader Saudi population. All the identified studies being retrospective in nature is another notable limitation. Retrospective studies are susceptible to biases and may not provide a comprehensive view of the temporal evolution of pediatric

thyroid cancer management and outcomes.

The limited scope of post-operative complications reported in only three studies underscores a critical gap in the available literature. Post-operative complications are crucial for understanding the holistic impact of interventions on pediatric thyroid cancer patients. The scarcity of information in this regard impedes a thorough assessment of the safety and efficacy of current management practices.

Additionally, the uniform focus on DTC, predominantly PTC, while including other subtypes such as FTC, poorly differentiated thyroid carcinoma, Hurthle cell thyroid carcinoma, and MTC, introduces a potential bias towards more prevalent subtypes. This may neglect less common but equally significant subtypes and their distinct management and outcome considerations.

Finally, the temporal scope of the included studies, conducted on patients diagnosed between 1988 and 2019 and published from 2015 to 2023, may not fully capture the most recent developments and advancements in the management of pediatric thyroid cancer. The evolving landscape of healthcare practices over the years underscores the need for more up-to-date research to inform current clinical practices.

Conclusions

Despite the limitations, the studies reviewed in this manuscript provide valuable insights into pediatric thyroid cancer in Saudi Arabia, highlighting the clinical differences from adult cases and emphasizing the need for individualized management approaches based on age. These investigations have identified disparities in clinicopathological features and highlighted potential complications after surgery, such as hypocalcemia and recurrent laryngeal nerve injury. Meticulous perioperative care is crucial for pediatric patients with thyroid cancer. The emergence of genetic profiling research offers opportunities for risk stratification strategies guided by biomarkers and personalized treatment approaches. Identification of predictive risk factors for outcomes like distant metastasis enables closer monitoring of high-risk pediatric patients. However, further large-scale, prospective studies are needed to fully understand the epidemiology and clinical course of pediatric thyroid cancer in Saudi Arabia. Collaborative efforts among institutions will be essential in overcoming the challenges posed by the rarity of this disease in children and adolescents, enhancing our understanding, and improving outcomes for affected children.

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Footnote

Reporting Checklist: The author has completed the Narrative Review reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-42/rc

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