An Overview on Thyroid Cancer Diagnosis and Management Approach, Literature Review

Hussain Abbas Alabdrabalnabi[1], Ghadah Abdulfattah Fallatah[2], Omar Ali Bajafar[3], Marwa Fahad Alsuwaidan[4], Azzam Arshad Shaikh[3], Fatimah Abdu Alsayed[5], Yousef Talal Alshammari[6], Nawi Jabr Alshammari[7], Raed Mohammad Faraj[8], Rewaf Hesham Hariri[9]*, Ghadah Abdulfattah Fallatah[2]

[1] Faculty of Medicine, King Faisal University, Al Ahsa, KSA
[2] Faculty of Medicine, Medical University of Lublin, Lublin, Poland
[3] Faculty of Medicine, Umm Al Qura University, Makkah, KSA
[4] Faculty of Medicine, Alfarabi Medical College, Riyadh, KSA
[5] Faculty of Medicine, King Khalid University, Abha, KSA
[6] General Practitioner, Rafha Maternity and Children Hospital, Rafha, KSA
[7] Faculty of Medicine, Medical University of Silesia, Katowice, KSA
[8] Faculty of Medicine, King Saud University, Riyadh, KSA
[9] Faculty of Medicine, Ibn Sina National College of Medicine, Jeddah, KSA.

ABSTRACT

Introduction: Thyroid malignancies are not uncommon, and would often present on routine checkups as an inconspicuous neck nodule. On further investigation, these nodules are often dormant and benign in nature. Others may require further diagnostic investigation such as ultrasound, fine needle aspiration, or definitive diagnosis through biopsy by lobectomy. **Objectives:** We wanted to review the literature and discuss the thyroid malignancy approach, diagnosis, and management, and recent updates to the thyroidectomy. **Methodology:** PubMed database was used for article selection, papers were obtained and reviewed. The keys terms included: thyroid malignancy, risk factors, evaluation, management, and diagnosis. **Conclusion:** Thyroid carcinomas are one of the most common types of cancer, thus the disease risk and prevalence are increasing. As a result, patients presenting with any lumps or suspicious clinical features shall be approached well by the clinician in order to thoroughly investigate and diagnose as early as possible. Early detection will make the management options more accessible and provide the best prognostic outcome for these cases.

Key Words: *Thyroid malignancy, diagnosis, management, thyroidectomy*

eIJPPR 2020; 10(6):47-50

HOW TO CITE THIS ARTICLE: Hussain Abbas Alabdrabalnabi, Ghadah Abdulfattah Fallatah., Omar Ali Bajafar, Marwa Fahad Alsuwaidan, Azzam Arshad Shaikh, Fatimah Abdu Alsayed and *et al.* (2020). "An Overview on Thyroid Cancer Diagnosis and Management Approach, Literature Review", International Journal of Pharmaceutical and Phytopharmacological Research, 10(6), pp.47-50.

INTRODUCTION

Thyroid malignancies are not uncommon, and would often present on routine checkups as an inconspicuous neck nodule [1, 2]. The most commonly occurring thyroid malignancies in descending order are papillary, follicular, medullary, and anaplastic carcinomas. There are other types but rarely occur, including lymphomas, primary thyroid sarcomas, and Hürthle cell variant of follicular carcinomas. The Hürthle variant is of particular interest as they characteristically manifest in females in their forties. In the United States, the most commonly occurring thyroid malignancy is papillary carcinoma. While this trend has been increasing in incidence previously, recent research shows a decrement in incidence in more recent years. This has been largely ascribed to the diagnostic re-classification of malignancy [3]. In this paper, we will provide a recent research review about this disease and its causes, diagnosis, and how to manage it.

METHODOLOGY

Through PubMed database, the selection process took place in order to identify the relevant articles, and the

Corresponding author: Rewaf Hesham Hariri
Address: Faculty of Medicine, Ibn Sina National College of Medicine, Jeddah, KSA.
E-mail: rewaf.h.h @ hotmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 02 August 2020; **Revised:** 29 November 2020; **Accepted:** 07 December 2020

following keywords were used in the Mesh ((“Thyroid malignancy"[Mesh]) AND (“Diagnosis"[Mesh] OR "Management"[Mesh] OR "Risk factors"[Mesh])). The inclusion criteria were based on including one of the following phrases: thyroid malignancy, risk factors, evaluation, management, and diagnosis. Exclusion criteria were all other articles that did not meet the inclusion criteria and/or did not have any of the inclusion criteria topics.

Review:

Thyroid malignancies arise from different cell lines, two of them being directly in thyroid tissue. Endodermal mutation results in the common carcinomas of papillary, follicular, and anaplastic carcinomas. Medullary carcinomas are often syndromic and as with other neuroendocrine tumors appear to arise from neuroendocrine calcitonin releasing cells, termed C-cells. Finally, lymphomas and sarcomas arose from lymphoid and connective thyroid tissue, respectively.

Etiology

Many aetiological risk factors are suspected to cause thyroid malignancy, these include nuclear radiation exposure. Radiation exposure is significantly associated with aggressive forms of papillary carcinomas. This was evidently seen in the children from Fukushima, Japan, where the nuclear bomb was dropped nearly a century ago. [4] There is rising evidence of genetic predisposition when it comes to papillary carcinoma development at a young age. [5] Exposure to nuclear radiation results in aggressive papillary carcinoma, while sporadic cases occur in a less aggressive manner, both decrease in incidence with age. [6-8]. There is, however, rising evidence that the propensity of Fukushima residents to develop thyroid carcinoma is unrelated to radiation exposure.[9] On the other hand, people who have an insufficient dietary intake of iodine do not have an increased incidence of developing thyroid carcinomas. It is, however, in these groups that follicular and anaplastic carcinomas are more likely than other forms of thyroid carcinomas.

Clinical Features

Patients with a thyroid swelling would present early in their fourth decade or later seventh to eighth decade of life, with a painless, single nodule that is palpable on examination. While many of these growths are nodular, they are not necessarily malignant. As males are more susceptible to this form of endocrine organ carcinoma, a history of the rapid growth of the nodule should alert the surgeon to the possibility of an underlying malignancy. On the contrary, the presence of tenderness is not ominous and would indicate a more benign course of the disease. The reason malignant nodules are found incidentally is that they are commonly painless. Possible aetiological factors for a painful nodule include bleeding into a nodular cyst or, in patients with a history of upper respiratory tract infection, subacute viral thyroiditis. The surgeon should always thoroughly examine neck swellings, treating each case with the utmost meticulousness. This includes examining the whole head and neck for any other nodules, and lymph swellings. Some patients may require an indirect laryngoscopy, such as those with recent vocal changes. If the vocal folds are seen to be paralyzed, then the surgeon should suspect a malignant spread to the recurrent laryngeal nerves. Rarely, bilateral cord paralysis may close the airway, requiring emergency securing of the airway.

Diagnostic Modalities

In addition to meticulous clinical examination, specific laboratory investigations may be required. These depend on the clinical presentation of the nodule, for example in solitary nodules measuring the thyroid-stimulating hormone levels in the serum would be suitable. Thyroid-stimulating hormone levels are first-line investigations in pregnant women, and only if they are abnormal the surgeon should proceed to fine-needle aspiration biopsy. [10, 11] In patients with suspected multiple neuroendocrine neoplasms, a test for serum calcitonin or pentagastrin-stimulated calcitonin levels would be needed for detecting medullary thyroid carcinomas. Further investigation for genetic mutations by polymerase chain reaction is required for patients with familial history of neuroendocrine tumors. The ultrasonographic features of the common thyroid malignancies are of particular importance, as follicular malignancy is often confused with its benign follicular form. [12] While ultrasonography is valuable and commonly used in thyroid nodule investigation, it is limited by operator experience and its inability to differentiate benign from malignant nodules. When the surgeon suspects a thyroid nodule to be malignant, then the next best step is to perform a fine-needle aspiration biopsy (Table 1). Medullary carcinomas require further workup with calcitonin levels and DNA analysis, as these patients could be having multiple endocrine neoplasia syndromes.

Table 1: Ultrasonographic features of suspicious Thyroid Nodules

	Indications	Best Next Step
Papillary malignancy	Hypoechoic, microcalcifications, infiltrative irregular margins	Fine needle aspiration biopsy
Follicular malignancy	Isoechoic, thick irregular ring-like margin	Fine needle aspiration biopsy
Medullary malignancy	Spiculated margin, small nodules, ovoid shape	Fine needle aspiration biopsy

Follicular adenoma	Cystic nodules or spongiform	Not required to biopsy

With the advent of improved imaging techniques, more patients are investigated for incidental thyroid nodules. In suspicious nodules, the approach is constituent of thyroid function tests and ultrasonography followed by fine-needle aspiration biopsy. This method is central to differentiating between benign and malignant thyroid nodules. [13] Fine needle aspiration biopsy has four interpretations: benign, malignant, inconclusive, and non-diagnostic.

In cases of non-diagnostic and inconclusive results, a repeat biopsy is indicated. If the result remains the same, then it would be suitable to opt for a lobectomy (Table 2). An expert review of the histopathological findings is often beneficial and necessary in such cases. [14] In children, a hemi-thyroidectomy is preferred over repeating the biopsy. [15, 16] Thereafter, a radioiodine scan may aid in monitoring the treatment of these patients, and check for any recurrence. Furthermore, thyroid radioiodine scans may also be required to determine hyperactive or hypoactive nodules, but they are not suitable for excluding malignancy per se.

Table 2: Thyroid Surgery Approach to Malignancy

	Indications	Removed	Remaining
Lobectomy	Biopsy, Cosmetic surgery	Specific part of the gland	Majority of the thyroid gland, Parathyroid glands
Total thyroidectomy	Thyroid malignancy, Medullary carcinoma, Lymphoma, Obstructive goiter not suitable for subtotal thyroidectomy	Entire gland	Parathyroid glands

Computerized tomography is often avoided in the early stages of the investigation, with particular contraindication to iodinated contrast when a CT scan is necessary. Important indications for CT scans include malignant spread to the trachea, vocal cords, and the esophagus. Patients who are found to have enlarged thyroid masses compressing the trachea or lymph node involvement are suited for CT scan preoperatively. CT scan and magnetic resonance imaging are excellent alternatives for diagnosis in cases where ultrasound expertise is unavailable or results are inconclusive.

Management Approach

The approach to surgical intervention in thyroid malignancy depends on the pathological type of disease. Sub-total or hemi-thyroidectomy is often preferred to total thyroidectomy, as it preserves both thyroid tissue and spares the risk of injury to recurrent laryngeal nerves. Pregnant patients with suspicious thyroid nodules should have their surgery deferred until after delivery after considerable discussion with the patient. [11] In children with multiple endocrine neoplasia types 2 and 3, having high medullary carcinoma risk, a prophylactic total thyroidectomy with central neck compartment dissection is recommended.

Table 3: Thyroid Surgery Approach by Histopathology

	Preferred Management
Follicular carcinoma	Lobectomy for biopsy, thyroidectomy if confirmed
Papillary carcinoma	Thyroidectomy
Hürthle cell subtype	Lobectomy and isthmectomy for biopsy, thyroidectomy upon confirmation
Medullary neuroendocrine malignancy	Thyroidectomy and lymphatic dissection of anterior neck compartment
Anaplastic	Total or sub-total thyroidectomy
Sarcomas	Total thyroidectomy and adjuvant radiation ablation
Thyroid lymphoma stage IE	Total thyroidectomy and postoperative radiation ablation
Thyroid lymphoma stage IIE	Combined chemo-radiotherapy
Cervical metastasis	en-bloc lymphatic dissection, radioactive iodine ablation

In patients who undergo total thyroidectomy, they may require radioiodine scanning to diagnose metastatic spread of thyroid tissue seeding. This is followed-up with aggressive ablation to prevent recurrence of the disease. Patients of total thyroidectomy, as previously mentioned, would require thyroxine hormone replacement therapy.

Not all thyroid malignancies are treated with thyroidectomy alone (Table 3), in patients with anaplastic carcinoma, it is necessary to provide combined chemotherapy and radiotherapy in the postoperative follow-up period. The chemotherapeutic intervention is mainly for palliative purposes. Moreover, radiotherapeutic ablation is targeted at a local disease in order to prevent the recurrence of missed malignant tissue postoperatively.

CONCLUSION

Thyroid carcinomas are one of the most common cancers and their associations are many, thus the disease risk and prevalence are increasing. As a result, patients presenting with any lumps or suspicious clinical features shall be approached well by the clinician in order to thoroughly

investigate and diagnose as early as possible. Early detection will make the management options more accessible and provide the best prognostic outcome for these cases. New breakthroughs in medical therapies may provide new guidelines about the adjacent therapy and may offer new hope for cases where surgery is difficult. However, these will need larger studies, and to be investigated fully before being approved internationally for patients.

REFERENCES

[1] Ghamri KA, Ghamri RA. Evaluation of Thyroid Dysfunction and Thyroid Antibodies Among Subjects with Gestational and Pre-Gestational Diabetes at King Abdulaziz University Hospital, Jeddah: A Retrospective Analysis (2014-2018). Int. j. pharm. res. Allied sci. 2020;9(1):168-75.

[2] El-kordy M, Attia SG, Anwar HW, Mohamed IA, Elgamal ER, Shalamesh MI, Moghazy AB, Elewasy EA. Lateral backdoor approach versus conventional anterior approach in recurrent Thyroid surgery. J. Adv. Pharm. Educ. Res. 2019;9(1):6-10.

[3] Kitahara CM, Sosa JA, Shiels MS. Influence of Nomenclature Changes on Trends in Papillary Thyroid Cancer Incidence in the United States, 2000 to 2017. J Clin Endocrinol Metab. 2020;105(12):dgaa690.

[4] Iwadate M, Mitsutake N, Matsuse M, Fukushima T, Suzuki S, Matsumoto Y, Ookouchi C, Mizunuma H, Nakamura I, Nakano K, Sakamoto A. The Clinicopathological Results of Thyroid Cancer With BRAF V600E Mutation in the Young Population of Fukushima. The Journal of Clinical Endocrinology & Metabolism. 2020;105(12):dgaa573.

[5] Kure S, Wada R, Naito Z. Relationship between genetic alterations and clinicopathological characteristics of papillary thyroid carcinoma. Med Mol Morphol. 2019;52(4):181-6.

[6] Bogdanova TI, Saenko VA, Brenner AV, Zurnadzhy LY, Rogounovitch TI, Likhtarov IA, Masiuk SV, Kovgan LM, Shpak VM, Thomas GA, Chanock SJ. Comparative histopathologic analysis of "radiogenic" and "sporadic" papillary thyroid carcinoma: patients born before and after the Chernobyl accident. Thyroid. 2018;28(7):880-90.

[7] AlDossari HM, Aldossari A, AlRashed A. Assessing the Level of Knowledge About Radiation Dose in Common Radiological Examinations Among Physicians in Riyadh. Surgery. Int. j. pharm. res. Allied sci. 2018;8(1):114-8.

[8] Alhazmi HA, Alsirwani AS, Aldaadi MN, Alharthy FA, Tashkandi MA, Jahri EA. Occupational Radiation Dose for Medical Workers in Diagnostic Radiology and Nuclear Medicine in Makkah Hospitals. Pharmacophore. 2019;10(6):62-73.

[9] Bogdanova TI, Saenko VA, Hashimoto Y, Hirokawa M, Zurnadzhy LY, Hayashi T, Ito M, Iwadate M, Mitsutake N, Rogounovitch TI, Sakamoto A. Papillary thyroid carcinoma in Ukraine after Chernobyl and in Japan after Fukushima: different histopathological scenarios. Thyroid. 2020.

[10] Choe W, McDougall IR. Thyroid cancer in pregnant women: diagnostic and therapeutic management. Thyroid. 1994;4(4):433-5.

[11] Galofré JC, Riesco-Eizaguirre G, Alvarez-Escolá C. Clinical guidelines for management of thyroid nodule and cancer during pregnancy. Endocrinol Nutr. 2014;61(3):130-8.

[12] Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26(1):1-33.

[13] Bailey S, Wallwork B. Differentiating between benign and malignant thyroid nodules. Australian Journal for General Practitioners. 2018;47(11):770-4.

[14] Hescot S, Sheikh-Alard H, Kordahi M, Hartl D, Hadoux J, Terroir M, Breuskin I, Baudin E, Scoazec JY, Schlumberger M, Al Ghuzlan A. Impact of expert review of histological diagnosis of papillary and follicular thyroid cancer. Endocrine. 2020:1-7.

[15] Al Maawali A, Matheson C, Baird R, Blair G. The thyroid nodules in kids study (ThyNK study): An evaluation of clinical practice variation. J Pediatr Surg. 2020;55(5):950-3.

[16] Almosallam OI, Aseeri A, Alhumaid A, AlZahrani AS, Alsobhi S, AlShanafey S. Thyroid surgery in 103 children in a single institution from 2000-2014. Ann Saudi Med. 2020;40(4):316-20.