Pattern of thyroid malignancy at a university hospital in western Saudi Arabia

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ABSTRACT

Objective: The aim is to study the incidence of thyroid cancer in surgically treated nodular thyroid disease, clinicopathological characteristics and treatment results

Methods: Retrospective review of 45 patients with thyroid malignancy at King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia during a 3-years period between January 2000 through to December 2003. Analysis of clinicopathologic characteristics, age correlation to different risk factors, outcome of surgery and radioiodine treatment.

Results: Total of 120 thyroidectomies was performed during the 3-years period between January 2000 through to December 2003 at King Abdul-Aziz University Hospital. Forty-five (37.5%) patients had histopathology confirmed diagnosis of thyroid cancer. Eighty-two point two percent cases of papillary carcinoma, 4.4 % follicular type and 6.7 % anaplastic and medullary carcinoma of thyroid. Mean age was 40.5 ± 14.8 years. Male preponderance was seen in this study with males: female's ratio is 1.1:1. Nodular goiter was the most frequent presentation, observed in 30 (66.7%) cases. Fine needle aspiration cytology was suggestive of malignancy in 76 % of cases. Ninety-seven patients with papillary carcinoma received ablative dose of radioiodine with average dose of 100-200 mCi. One female patient with follicular carcinoma of thyroid with bone, lung, and brain metastases received 4 doses of radioiodine with total dose of 800 mCi. Mortality rate was (2.2%), one patient died of complication of invasive anaplastic carcinoma with invasion of the trachea.

Conclusion: There is a lot of controversy regarding thyroid malignancy investigations and management . We recommend that thyroid cancer patients should be treated by a team of endocrinologist, pathologist, experience thyroid surgeon, nuclear medicine and external radiotherapy physician to achieve an optimum care and good prognosis

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Thyroid cancer is the most frequent endocrine malignancy. In the Kingdom of Saudi Arabia (KSA) thyroid carcinomas accounted for 5% of all newly diagnosed cancers. This cancer ranked fourteenth in males and second in females.[1,2] Although thyroid nodules are common, differentiated and undifferentiated thyroid carcinomas are relatively rare. Clinically detectable thyroid carcinomas constituted less than 1% of all cancer.[3] The median age at diagnosis was 45-50-years. The assessment of thyroid nodules has also evolved, with percutaneous fine needle aspiration cytology (FNAC) becoming the most important tool of investigation.[4] Papillary and follicular thyroid carcinomas are among the most curable cancers. However, for several decades the management of difference thyroid cancer has been controversial. For the majority of patients, standard initial management consists of thyroidectomy followed by radioiodine ablation.[5] However, there is a great controversy regarding the ablative dose of iodine ^{131} (I^{131}) and its indication; other conventional modes of neoplastic treatment; chemotherapy with external beam irradiation have much poorer results. The overall survival rate at 10-years for middle age adults with thyroid carcinoma is approximately

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80-95%. Five to twenty percent of patients have distant metastasis. The prognostic indicators of recurrent disease and death are the age at time of diagnosis, histopathology type of thyroid cancer. The relationship between these factors remains incompletely defined. However, Coburn and Wanbeo[6] concluded that the prognostic importance of age in thyroid cancer maybe due to the great prevalence of pathological risk factors in older patients. The aim of this retrospective study is to estimate the incidence of thyroid cancer in surgically treated nodular thyroid disease and to study its clinicopathologic characteristics, age correlation with risk factors as well treatment results.

Methods. King Abdul-Aziz University Hospital (KAUH) is a teaching government hospital providing health care to a multinational population of mixed socioeconomic status. A total of 120 thyroidectomy were performed in the Surgical department during the period January 2001 through to December 2003. All patients was presented with single nodule or multinodular goiter was included in the study. The medical notes were reviewed for age, sex, nationality, radiation history, family history of thyroid disease, clinical presentation, physical examination of neck included goiter and cervical lymph nodes. The data included thyroid function test; thyroid scan which was carried out routinely in most of the patient to confirm the solitary nature of nodule or otherwise. Results of fine needle aspiration of thyroid nodule or any palpable cervical nodes at presentation before surgery as well froze section results if carried out before thyroidectomy. In attempts to identify the possible correlation between the age of the patients at presentation and other risk factors, the study group was analyzed in 3 age group. Group A included patients younger than 30-years, group B included those ranging between 30-45-years. Group C included those between 45-60-year and group D included patients older than 60-years. Almost all patients had total thyroidectomy included those patients had found to have conservative surgery; he was referred for completion near total thyroidectomy. Six week after surgery, when thyrotrophin (TSH) level > 30 iu/ml, diagnostic whole body scan was performed thereafter radioiodine ^{131} therapeutic doses was given by the nuclear medicine physician. One hundred to two hundred mCi for remnant ablation, 200-300 mCi for lymph nodes metastases or distant metastases. After radioiodine therapy patients with gross residual disease received external beam radiotherapy (whole neck irradiation of total dose of 50-60 Gy over 4-6 weeks). All patients were put on a suppressive dose of L-thyroxin and kept under regular follow up for TNM (tumor, node, metastases) system recommendation[7,8] 1. For PT1,NO, M0 disease the serum TSH concentration should be in the lower half of the normal range (0.5-2.0 Mu/L) 2. For PT2, PT3 , N0, M0, disease the serum TSH should be between 0.1 and 0.5 Mu/l 3. For PT2, PT3 , N1, M0, disease the serum TSH should be between 0.05 and 0.1 Mu/l 4. For PT2-PT3, or MI disease the serum TSH should be below 0.05 Mu/l. Then 6-12 months after first dose radioiodine therapy. Patients were followed in nuclear medicine clinic where second whole body scan in each patient was performed. If there were persistent abnormal radioiodine uptake, a second or third dose of 131 was given. Results were expressed as a mean ± SD (standard division). Results were considered significant if the *p* value is less than 0.005. All analyses were performed with excel program.

Results. ***Clinical characteristics.*** Out of total 120 thyriodectomies performed during the 3-year period between January 2001 through to December 2003 at King Abdul-Aziz University hospital, 45 (37.5%) patients with a histopathologically confirmed diagnosis of thyroid cancer were included in the study. Nineteen (42.2%) were Saudi, where various other nationals comprised 26 (57.8%) cases with Saudi: Expatriate ratio of 0.7:1 Twenty-four (53.3%) were males and 21 (46.7%) were females , with males to females ratio of 1.1 :1. Mean age of all patients was 40.5 ± 14.8 years. Mean age of females was 38.4 ± 11.64 years and of males was 42.5 ± 16.9 years with a *p* value 0.004. None of the patients in this study gave history of radiation exposure in the past. Family history of goiter and thyroid disease was available in 10 (22.2%) cases; however, there was no family history of thyroid cancer in our patients.

Histopathological classifications. Among 45 patients with thyroid neoplasms, there were 37 (82.2%) cases of papillary carcinoma, 2 cases (4.4%) with follicular carcinomas. Anaplastic and medullary carcinomas had an equal distribution of 3 cases (6.7%) each. Fifteen patients (33.3%) presented with a clinically solitary nodule, 30 (66.6%) patients had multinodular goiter. Two patients presented with huge goiter with multiple cervical lymph nodes, which was confirmed to be anaplatic carcinoma of thyroid on histopathology. Pressure symptoms were observed in 7 cases, mainly in patients with ana plastic, follicular carcinomas and one with medullary carcinoma of thyroid. **(Table 1)**

Age of the patient and other risk factors. In an attempt to identify the correlation of the age of the patient at presentation. In addition, other risk factors, the study group was divided to 4 groups. Group A included 15 patients younger than 30

years, group B included 13 patients ranging between 30-45-year, group C included 12 patients ranging 45-60-years and group D included 8 patients older than 60-years. Analysis of the clinico-pathologic characteristics showed that papillary carcinoma is commoner in age group below 45-years, whereas follicular, anaplastic and medullary carcinoma were commoner after 45-years of age. Patients older than 45-years had statistically higher incidence of cervical lymph nodal involvement and higher incidence of distance metastases **(Table 2)**.

Extent of surgery. Fine needle aspiration (FNA) was performed in 42 patients, 32 (76%) confirmed the diagnosis of cancer before surgery. When there was suspicion of malignancy frozen section was carried out during the operation.[9]

Table 1 - Pathological characteristics of 45 patients with thyroid malignancy.

Variable Pathological diagnosis	n	(%)
Papillary	37	(82.2)
Follicular	2	(4.4)
Anaplastic	3	(6.7)
Medullary	3	(6.7)
Cervical lymphadenopathy		
Absent	30	(66.7)
Present	15	(33.3)
Distant metastasis		
Absent	40	(89)
Lungs	2	(4.4)
Bone	2	(4.4)
Brain	1	(2.2)

Table 2 - Clinicopathological characteristics in different age group with differentiated thyroid carcinoma.

Clinicopathological characteristics	Group (A) ≤ 30 years	Group (B) 30-≤45 years	Group (C) 45-≤60 years	Group (D) ≥60
n of patients	15 (33.3)	17 (37.8)	7 (15.6)	6 (13.3)
Sex male: female	8M: 7F	8M: 9F	4M: 3F	4M: 2F
M:F ratio	1.1:11	0.9:1	1.3:1	2:1
Saudi: Expatriate ratio	6:9	5:12	4:3	4:2
S: EP ratio histopatholgic subtype	0.7:1	0.4:1	1.3:1	2:1
Papillary	11	13	7	6
Follicular			2	
Anaplastic			2	1
Medullary	1		1	1
Cervical lymph nodes involvement	4	2	4	5
Distant metastasis		1	2	2

M - male, F - female

Almost all patients underwent total or total near thyroidectomy. Cervical lymph nodes dissection was performed in 6 (13.6%) patients, 2 with anaplastic carcinoma, 3 with papillary and one with medullary carcinoma.[10]

Radioiodine therapy. High dose radioiodine 131 for thyroid remnant ablation or for distant metastases was given to 38 cases (84.4%). Thirty-six (97%) patients with papillary thyroid carcinoma received radioactive iodine ablation dose of 100-200 mCi. One female patient with papillary carcinoma did not receive ablation dose of radioiodine, as she was pregnant. Twenty-six patients received single dose radioiodine treatment 100-200mCi, 5 patients received 2 doses of RAI 300-500 mCi as of disease recurrence or metastases. Two patients received 3 doses of 600 mCi, one patient with follicular carcinoma was already had metastases to the bones, lungs and brain received 4 doses of RAI with a total dose of 800 mCi. Patients were hospitalized for an average of 3 days (3-7 days).[11] Radioiodine therapy was tolerated well in all patients, however, acute and sub acute morbidity was reported in some patients such as nauseas,

gastric upset, vomiting and pain in salivary glands due to sialoadenitises which was relieved by course of prednisolone. Follow up complications attributed to radioiodine therapy was not available in the files of patients who received high dose of radioiodine therapy. Radioiodine therapy was not given to patients with anaplastic or medullary carcinoma.[12]

External beam radiotherapy. Following radio iodine therapy, 2 patients with gross residual extra thyroid tissues and lymph nodes in the neck received external beam radiotherapy (Whole neck radiation up to 60 Gy over 5-6 weeks).[13,14] One patient with follicular carcinoma who had metastases to the brain received external beam radiotherapy to brain that improved her upper limb paralysis. All 3 patients with anaplastic carcinoma received external beam radiotherapy .

Thyroxin therapy. All patients with differentiated carcinoma of thyroid were treated with suppressive dose of thyroxin with mean 178.5 ± 40 mg/day

Survival and mortality rate. Eight patients (17%) were lost to follow up after thyroidectomy and ablation dose of radioiodine therapy. Two of them with medullary carcinoma of thyroid. Only one patient with extensive ana plastic carcinoma of thyroid where invaded her trachea and metastases to the lungs died after external beam radiotherapy?

Discussion. Thyroid cancer is regarded as the most frequent endocrine malignancy with a variable geographic and ethnic incidence around the world.[1,16] The overall incidence is reported to be increasing worldwide with changing characteristics. In most series; papillary carcinoma is the predominant cancer, whereas follicular and ana plastic tumors are becoming less frequent. Radiation exposure[17] and endemic goiter have been suggested as strong etiological factors. In KSA, thyroid carcinomas have accounted for 5% of all newly diagnosed cancers and ranked fourteenth in males and second in females.[2] In our series papillary, carcinoma was the most frequent variety (82.2%) followed by anaplastic (6.7%) and follicular cancer (4.4%), of all thyroid malignancies. Incidence of follicular thyroid cancer in our study is much lower than what is reported from other reports of KSA[15] or other geographical areas.[18] Medullary carcinoma constituted 6.7% of all thyroid malignancies in this series. This is comparable to most other reports. It is not known whether cases of medullary carcinoma in this series are familial or sporadic cases as most of the **s** were patient lost to follow up after total thyroidectomy.[19] No known etiological factors (radiation exposure, endemic goiter, cancer thyroid among family) could be confirmed in any of the patients in this study. Male preponderance in this study was different than various local and international reports where thyroid cancer was commoner in females. This could be related to the fact that most of our patients were expatriates as KAUH is a teaching governmental hospital providing health care to saudis and expatriates population equally. As well it could be due to the demographic pattern in gulf countries where most expatriates were males. The mean age was 40.5 which was years is younger than 45-48-years-old reported from other international studies; however, it is similar to studies reported from KSA.[20,21] This reflects the changing clinic epidemiological behavior of the disease in different parts of this world.[22] The mean age of females was 38.4-years, which was younger than males 42.5- years and is similar to various other reports. Prognostic factors associated with differentiated thyroid cancer included the age of the patient at the time of diagnosis, tumor size, extra thyroid extension, nodal status, distant metastases, operative procedures, sex and histopathology. Multivariate analysis showed that distant metastases, age, tumor size were the most significant prognostic factors.[23,24] However, Coburn and Wanebo[6] suggested that the prognostic importance of age of thyroid cancer maybe due to the greater prevalence of pathological factors in older patients. In our study, there was a statistically significant association between older age and pathology of cancer, follicular and anaplastia carcinoma was commoner in the older than 45-years age group. Higher incidence of lymph nodes and distant metastases were encountered in older patients.[25,26] Thyroid cancer presents most frequently as solitary thyroid nodule. This was not the case on patients in this series, where 30 (66.7%) presented as multinodular goiter. This was probably due to the late presentation of these patients.[27] Fine needle aspiration cytology of thyroid is now considered as an important diagnostic aid in the investigations of solitary nodules and goiter. This is particularly useful in screening and selection of patients presenting with solitary or mulinodular goiter. In the current study, FNA confirmed the diagnosis of thyroid carcinoma in 76% of our patients, so that they were subjected directly to near total thyroidectomy. The positive FNA in range of 70-79% is similar to what is described in the local and international series.[28] The post-operative treatment of patients with well differentiated thyroid cancer; particularly relating to radioiodine therapy is controversial.[29] The dose of 1^{131} for ablation is not standardized. Some recommend low dose ablation with less than 30 mCi given as out patient with the successful ablation rate ranging between 27-83% with this method repeated doses are usually required for ablation. Higher ablative doses ranging from 100-200 mCi should be used for older high risk patients particularly known to have incomplete resection of the primary tumor. an invasive ablative

rate of 87%. Doses may be calculated using one of the several dosimetric approaches or standard fixed doses may be used for all patients.[30,31] In the current study, the ablative dose used by nuclear medicine was relatively higher than standard doses especially in recurrence of thyroid malignancy or metastases. The nuclear medicine physicians' policy is that this therapeutic approach might be effective in improving prognosis and survival of such patients.[32]

In conclusion, the current study as many others, concludes that thyroid cancer is one of the more important endocrine cancers with increasing incidence worldwide with changing characteristics especially in different ethnic groups like in our series. Although little doubt exists regarding the role of FNA biopsy in pre-operative diagnosis of thyroid cancer, each step in the subsequent management gives rise to controversy and debate regarding extent of primary surgical resection, the need for extensive regional lymph node dissection and the role of external irradiation and radiotherapy. We recommend that thyroid cancer patients showed has to be treated by a team of endocrinologist, pathologist, experienced thyroid surgeon, nuclear medicine and external radiotherapy physician to achieve a good care and prognosis of patients.

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