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October 2004

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L M. Zuberi

*Aga Khan University*

A Yawar

*Aga Khan University*

N Islam

*Aga Khan University, najmul.islam@aku.edu*

A Jabbar

*Aga Khan University*

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## Recommended Citation

Zuberi, L. M., Yawar, A., Islam, N., Jabbar, A. (2004). Clinical presentation of thyroid cancer patients in Pakistan--AKUH experience. *Journal of Pakistan Medical Association*, 54(10), 526-528.

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# Clinical Presentation of Thyroid Cancer Patients in Pakistan - AKUH Experience

L. M. Zuberi, A. Yawar, N. Islam, A. Jabbar  
Department of Medicine, Aga Khan University Hospital, Karachi.

## Abstract

**Objective:** To assess the clinical presentation of patients with thyroid cancer, their preferred diagnostic work-up and preferred surgical procedure.

**Methods:** A retrospective chart review of patients that underwent partial or total thyroidectomy for thyroid cancer at AKUH between 1989 and 2002. SPSS was used to analyze data. Pearson's chi square and likelihood ratios used to calculate tests of significance.

**Results:** A total of 97 patients were included in this review. Solitary thyroid nodule was the initial presentation in three. Majority (58.7%) presented with "neck swelling" or enlarging goiter. One out of every 3 patients showed evidence of lymph node involvement and 20% had distant metastases. The aggressiveness of the disease did not correlate with age, sex or histological subtype. There was no correlation between the size of the tumor and presence of local or distant metastases.

**Conclusion:** Thyroid cancer is a more aggressive disease in Pakistan, with majority of patients presenting with multinodular goiters, and a significant number have lymph node metastases. A higher degree of vigilance and a lower threshold for fine needle aspiration (FNA) is needed while evaluating patients with thyroid goiter (JPMA 54: 526;2004).

## Introduction

Clinical thyroid cancer is uncommon, with an estimated incidence in various parts of the world of 0.5 to 10 cases per 100,000 persons.<sup>1</sup> It accounts roughly for about 0.5% of all cancers in men and 1.5% of all cancers in women.<sup>2</sup> It is however the most common endocrine tumor and may present either as a solitary nodule in the setting of an entirely normal thyroid gland or, as a dominant nodule in the setting of a multinodular goiter. Five to 6.5% of nodular thyroid are found to be neoplastic.<sup>3-5</sup>

In Pakistan thyroid cancer is responsible for 1.2% cases of all malignant tumors.<sup>6</sup> Previous reports from this region show papillary thyroid cancer to constitute 57 to 89% of all thyroid malignancies.<sup>6-8</sup> The female to male ratio in this part of the world is noted to be between 2.5 to 4:1, which is comparable to international data. No information is available regarding its mode of presentation and clinical characteristics in Pakistan.

## Patients and Methods

A retrospective chart review was conducted of all those patients that underwent partial or total thyroidectomy between 1989 and 2002 at Aga Khan University Hospital (AKUH), Karachi. These patients were operated upon by either general or ENT surgeons. All those found to have thyroid cancer proven on pre-operative cytology and/or post operative histopathology were included in the study. The patients who underwent thyroidectomy for Graves disease or toxic multinodular goiter were excluded, unless the histopathology showed presence of incidental thyroid carcinoma. Information regarding demographic characteristics,

presenting symptoms, past history of radiation exposure, family history of thyroid cancer, preferred initial diagnostic work-up, histopathology, presence of local and/or distant metastases and initial surgical procedure was gathered. The clinical description of the thyroid was noted from pre-operative physical examination notes. The thyroid gland was noted to have a "single nodule" when this notation was recorded as such. Multiple nodules bilaterally or "large goiter" was noted as a multinodular gland. Thyroid "mass" was deemed to indicate a large lobe that was asymmetric, and therefore recorded as an asymmetric "goiter". An attempt was also made to access post-operative follow-up care; however this data was scanty and therefore not included in the final analysis. SPSS was used to analyze the data and Pearson's chi-square and likelihood ratios used to calculate significance.

## Results

A total of 97 patients were included in this review. The peak incidence was seen in 30 to 60 year age group, with a female to male ratio of 2.2:1. The symptoms at presentation are shown in Figure.

Majority of the patients presented either with a "thyroid mass" in the anterior neck (31%) or with an increase in the size of a long standing goiter (27.8%). Solitary thyroid nodule was the presentation in only 3 patients, and hyperthyroidism was an associated presentation in 2 others. Hoarseness, dysphagia and shortness of breath were seen in less than 5% at the time of presentation. Size of the tumor was documented in two thirds of the patients either at the time of clinical evaluation or pathologic reporting. Of these 58 patients, 42 (72%) had a primary tumor of over 3 cm in

shortness of breath.

Majority of the patients (76%) underwent at least one pre-operative diagnostic procedure. This included a fine needle aspiration cytology (FNAC) in 48 patients, ultrasound of the thyroid in 3, technetium scan of the thyroid in 3, CT scan of the neck in 2 and a combination of two or more procedures in 13 patients.

Lobectomy and isthmusectomy was the preferred surgical procedure in 32.6% of the patients, followed by near total thyroidectomy in 30.4%. One-tenth had a subtotal thyroidectomy. The remainder were not offered thyroid surgery, either due to the advanced nature of the disease or concomitant significant comorbid conditions.

The aggressiveness of the disease did not correlate with age, sex or histologic subtype. We found no correlation between the size of the tumor and presence of local invasion, lymph node involvement or distant metastases.

## Discussion

The demographic characteristics of our patients with thyroid cancer are comparable to western literature, however clinical presentation is somewhat different and more aggressive.

Nodular thyroid disease, which encompasses both solitary nodules of the thyroid and multinodular thyroid gland, is a fairly common condition. Population based surveys show a prevalence of 4 to 7%<sup>9</sup>, but ultrasound and autopsy studies show this prevalence to be close to 50%.<sup>10</sup> Thyroid cancer occurs at a frequency of 5 to 6.5 % in nodular thyroid gland<sup>3,4</sup> and is generally detected as part of an evaluation of solitary thyroid nodule with fine needle aspiration cytology. Solitary nodule of the thyroid was a relatively infrequent mode of presentation in our series. Majority (59%) had a nodular goiter that was longstanding or of recent origin. A series from Riyadh, Saudi Arabia reports similar findings of nodular goiter as the most frequent presentation in patients with differentiated thyroid cancer. It was present in three-quarters of their patients.<sup>7</sup> This difference in the mode of presentation is multifactorial. Given the relatively expensive cost of medical care, which in most instances is borne directly by the patient, thyroid nodules and goiters are often left uninvestigated, until they become symptomatic (i.e., patients either develop obstructive symptoms, or develop hyperfunction), enlarge rapidly, or cause considerable cosmetic disfigurement. This is compounded by the misconception among health care professionals that multinodular goiters are caused by iodine insufficiency and usually remain benign, and are therefore incapable of neoplastic transformation. It has been proven that the prevalence of thyroid cancer is similar in multinodular goiters as it is for solitary thyroid nodules.<sup>11,12</sup>

Figure. Symptoms at presentation.

a primary tumor of over 3 cm in size. One-third had evidence of metastasis to the lymph nodes. There was ipsilateral cervical lymph node involvement in 60% and bilateral cervical involvement in 20%. Distant metastases to the lung, bones, brain and distant lymph nodes were present in 19 patients (lungs in 7 patients, bone only in 3 and a combination of more than one organ involvement in the rest).

Of the differentiated thyroid cancers originating from the follicular epithelium, papillary thyroid cancer constituted two thirds and follicular thyroid cancer one third; 40% of the patients with papillary thyroid cancer and 15% of patients with follicular cancer had local or regional lymph node involvement. Distant spread at the time of presentation was seen in 9% of papillary and 23% of the follicular cancers (Table).

Anaplastic and poorly differentiated variety com-

Table. Frequency of metastasis in differentiated thyroid cancer.

Type of differentiated cancer (# of patients)	Local metastases No. of patients (%)	Distant metastases No. of patients (%)
Papillary thyroid cancer (55)	25 (40 %)	5 (9%)
Follicular thyroid cancer (30)	5 (15%)	7 (23%)

prised 7.4% (n = 7). Five of these seven patients had a long standing goiter, and presented for clinical care when they developed obstructive symptoms such as dysphagia (2 patients), dyspnea (3 patients) and a superior vena cava syndrome (one patient). One other had both dysphagia and

The histopathologic distribution of differentiated thyroid cancer is comparable to international literature, and has been reported previously from Pakistan by other authors.<sup>6</sup> Series from iodine deficient regions report a relatively higher frequency of thyroid cancer. This trend is visible in our group of patients, and though only a small percentage originates from the northern iodine deficient parts of Pakistan<sup>13</sup>, majority has multinodular goiters. There was a relatively higher proportion of patients who had poorly differentiated or anaplastic thyroid carcinoma.

Papillary thyroid cancer (PTC) has a propensity to metastasize through lymphatics as apposed to follicular thyroid cancer (FTC) which spreads through blood vessels. Mayo clinic series showed that 38% of patients with papillary thyroid cancer present with nodal involvement, compared with 5% of those with follicular.<sup>15</sup> One to 7% of PTC patients have distant metastases diagnosed before or within 30 days of primary treatment compared to 5 to 20 % of FTC patients. Our data though comparable for local spread, shows a more aggressive disease in terms of distant metastases. This could be related to larger size of the primary lesion, or late presentation when the disease has already advanced.

An appropriate work-up was offered to majority of the patients with FNAC being the pre-operative procedure of choice, used either alone or in combination with other pre-operative imaging studies. There seems to be no preference for either lobectomy/isthmusectomy or total thyroidectomy, as both procedures were used with similar frequency.

Majority of the cases of thyroid cancer in Pakistan present as multinodular goiters rather than as solitary thyroid nodules. A higher percentage of these patients have dis-

tant metastases at the time of presentation to medical care, thereby reducing the chances of favorable outcome. The perception amongst the health care professional that multinodular goiter is a benign thyroid disease maybe one reason. A lower threshold for evaluating nodular thyroid for cancer is recommended, even if there is a history of long standing goiter.

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