PATTERN OF DISEASES OF THYROID: A FOUR- YEAR RETROSPECTIVE STUDY OF HISTOPATHOLOGIC DIAGNOSIS

TIKUR ANBESSA HOSPITAL, ADDIS ABABA, ETHIOPIA

Manyahelehal Solomon, MD

Department of Pathology

College of Medicine and Health Sciences

Addis Ababa University, Ethiopia

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Table of content

Abstract

***Background*: The diversity of diseases affecting the thyroid gland can be due to hormonal excess/deficiency, reactive proliferations to deficiency states, inflammation, or neoplastic conditions most of which manifest by a form of enlargement of the thyroid gland commonly called goiter.**

The distribution of these diseases depends on several factors, both environmental and individual. Simple (non toxic goiter is quiet common throughout the world and is more prevalent where iodine difficiency is prevalent. The reported prevalence of goiter in Ethiopia is in the range of 27% in the early 90s to 40% today.

***Objective:* To assess the distribution of histolpathologic types of thyroid diseases over a period of four years.**

***Setting:* Tikur Anbessa Specialized Hospital, Department of Pathology, College of Medicine and Health Sciences, Addis Ababa University**

***Methods:* Retrospective analysis of biopsy diagnoses of thyroid disease.**

***Results:* one thousand two hundred cases were included in the study. nine hundred eighty six were found to be non neoplastic(82%) and two hundred eleven were found to be neoplastic(18%). Nodular colloid goiter was the commonest, appearing in 956 cases(79.6%). Adenoma, carcinoma and thyroiditis accounted for 64(5.3%), 147(12.3%) and 16(1.3%)respectively. The female to male ratio was 5.1:1. Eighty four point five percent of thyroid diseases were found in the age group between 20 and 59 years.**

***Conclusion:* Nodular colloid goiter is the commonest of all thyroid diseases. Thyroid malignancies have become more common than adenomas. Papillary carcinoma is the commonest of thyroid cancers. Efforts need to improve to tackle the problem of iodine deficiency. Proper evaluation of thyroid swellings and early seeking of health service in case of neck swelling needs to be advocated.**

Introduction

Diseases of the thyroid gland lie in a spectrum ranging from non neoplastic simple goiter to the deadly neoplastic conditions like anaplastic carcinoma, with the additional uncommon congenital anomalies. Diseases of the thyroid are of great importance because most are amenable to medical or surgical management. They include conditions associated with excessive release of thyroid hormones (hyperthyroidism), those associated with thyroid hormone deficiency (hypothyroidism), and mass lesions of the thyroid(1). Their manifestations vary from area to area determined principally by the availability of iodine in the diet.

Almost one third of the world's population lives in areas of iodine deficiency where prevalence of goiter can be as high as 80% and risk the consequences despite major efforts to increase iodine intake primarily through iodinization of salt(2). Simple non toxic goiter is extremely common around the world and is thought to affect 200 million individuals (3).

Neoplastic diseases of the thyroid are the other face of this problem with adenomas being the commonest of the benign tumors (3). Thyroid cancers represent approximately 1% of new cancer diagnoses each year. Approximately 23500 cases of thyroid cancer are diagnosed yearly in the United States and their incidence is three times higher in women, with a peak in the third and fourth decades in life. Papillary thyroid carcinoma is the commonest of all thyroid neoplasms followed by follicular carcinoma. Medullary and anaplastic carcinomas follow in decreasing order of frequency while primary lymphomas and sarcomas are rare (4).

Radiation exposure significantly increases the risk for malignancies, particularly papillary carcinoma. Low iodine intake does not increase the incidence of cancers overall. However, populations with low iodine intake have increased proportion of follicular and anaplastic carcinoma (2,3). Other thyroid disease entities like thyrotoxicosis and hypothyroidism are not uncommon (3).

In Ethiopia, diseases of the thyroid are not uncommon, particularly in the highlands owing to the iodine deficiency which is common in these areas (5). A school based cross sectional study done in Kaffa zone in south western Ethiopia showed the prevalence of goiter to be 27.4 %(6). According to a situational analysis carried out by Ministry of Health (MOH) and the /United Nations Children's Fund (UNICEF) in 1993, 78% of the total population of Ethiopia are exposed to iodine deficiency, 62% are iodine deficient, 26% have goiter(7). Another document published by Micronutrient Initiative states this rate has increased to become 40% today and iodized salt consumption has decreased to below 5% after the early 1990s(8)

Regarding neoplastic diseases in Ethiopia, a previous study done in Tikur Anbessa hospital(the setting of the current study) in the department of pathology had indicated that 21% of all thyroid diseases were found to be neoplastic with a predominance of benign adenomas overall, and papillary thyroid carcinoma from among the malignant neoplasms(3). Another study done in the same hospital in the department of surgery showed papillary carcinoma to be the commonest of malignant lesions (9).

This study aims at assessing the histopathologic patterns of thyroid diseases retrospectively, along with their age and sex distributions as seen in the Department of Pathology, College of Medicine and Health Sciences, Addis Ababa University, over a period of four years (2009-2012).

This study will be only the second of its kind in assessing the histopathologic patterns of thyroid disease in recent times, in a country where the diseases of thyoid are not rare at all.

Literature Review

In a retrospective study done on histopathologic patterns of thyroid diseases in this hospital in 2003, a total of 792 cases were reviewed out of which nodular colloid goiter was found to be by far the commonest lesion(76.9%). Neoplastic conditions accounted for 21% of cases. From among the latter, the commonest of benign tumors, i.e. adenomas were found to be 12.8% while malignancies were 8.2%. Thyroidtis consisted of only 2.1% of cases. In this study, 85.7% of cases were found in the age group of 20-59 years. Females were more affected by thyroid diseases compared to males, i.e., 80.5% versus 19.5%, making the female to male ratio 4.5:1. From among the malignant lesions, papillary carcinoma was found to be the commonest (76.6%) while only 1.5% were medullary carcinoma- even less common than anaplastic carcinoma which in this study comprised 6.3 %(3)

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In a study done to assess the five-year distribution of thyroid diseases in the same hospital in 2004, in the department of surgery, it was found that the mean age of patients was 35 with a range of 15-73 years and a female to male ratio of 3.8:1. Nodular colloid goiter was still found to be the commonest lesion (5).

Another study done on distribution of thyroid neoplasms in the same hospital had shown a mean age of 37 and a female to male ratio of 1.7:1. Papillary carcinoma was found to be the commonest neoplasm in this study comprising 72% of all neoplasms(9).

A five-year retrospective study done in zewditu hospital located in the same city as this hospital, reviewing data obtained in the period between 1996 to 2000 showed a female to male ratio of 6.6:1 and 73.6% of patients were in the age group between 20 and 50. Multinodular goiter constituted 54.2% of all thyroid lesions followed by solitary nodules,23.1%. Malignancy consisted of 2.7% of all thyroid lesions in this study.this study used histopathologic as well as clinical diagnosis as a ground for classification of cases(10).

A five-year retrospective study of thyroid disease in an Uganda hospital showed that about 67% of cases are due to goitrous hyperplasia, with colloid diffuse goiter twice as common as nodular goiter. The rising incidence of thyrotoxicosis (11.4%) is in keeping with its increasing frequency elsewhere in Africa. The incidence of neoplastic diseases of the thyroid is low. Chronic thyroiditis was not seen (11).

A histopathological analysis of thyroid diseases in Ile-Ife, Nigeria, a review of 274 cases which is a retrospective study of thyroid lesions seen at the OAUTHC Histopathology Department during a 10-year period between 1988 and 1997 showed there to be 85.8% females and (14.2% male cases in the study giving a female: male ratio of 6:1. Colloid goiter accounted for about 75% of cases with an average age of occurrence of 40.7 years. The adenomas constituted about 6% while carcinomas constituted about 11% of cases. Adenomas occurred almost a decade earlier than carcinomas. Follicular carcinoma was the commonest thyroid cancer seen in this study (12).

Another retrospective review of 75 cases of thyroid gland diseases seen and managed at Aminu Kano Teaching hospital, Kano, Nigeria over a 5-year period showed 69(92%)of all patients were females. Simple non-toxic goiter was the most common histologic type accounting for 51 (68.0%) of cases while 5.4% were follicular adenoma and 10 (13.3%) other patients had proven carcinoma. Well-differentiated follicular carcinoma was the most common malignant type (13).

A study done on thyroid gland diseases in sub-Saharan Africa showed that, the diseases are influenced by population isolation and the absence of food self-sufficiency, both factors affecting the onset and persistence of iodine-deficiency goiters. Women are mainly affected (94.2%), most often with euthyroid goiters (54.7%), followed by Graves disease (13.1%), hypothyroidism (8.8%), thyroiditis (6.6%), toxic multinodular goiters (6.6 %) and unclassified goiters (10%) [Gabon]. Very recent surveys show a prevalence of endemic goiters of 28.6% in the community of Sekota, Ethiopia, 64-70% in Sahel-Sudan (population aged 10-20 years), 20-29% in KwaZulu-Natal (school children), 14.3-30.2% in Namibia (school children), 0.21% (congenital hypothyroidism or cretinism) in Plateau State, Nigeria, 55.2% at Zitenga, Burkina Faso (210 persons 0-45 years), and 10% in Hararé and Wedza, Zimbabwe The prevalence of goiters is 43.6% in children emigrating from Ethiopia to Israel. Single-nodule tumors were assessed in 89 patients in Khartoum: they were found to be simple goiters in 72% of cases, follicular adenoma in 13.5%, cancer in 13.5% (with 6 of the 12 cases follicular, 5 papillary, and 1 anaplastic). The sex ratio for thyroid cancer in Ouagadougou is 0.22, thus mainly women. It affects mainly women in their 30s. Thyroid cancer at Ibadan was found to be papillary carcinoma in 45.3% of cases; follicular forms

were seen in 44.5% and this series includes 5% of medullary cancers (7 cases), with a mean age of 34 years.

An extensive retrospective study of five decades done in Sao Polo, Brazil indicated non-neoplastic lesions comprised 86.68% of the cases, and most of them were nodular goiter(91.4%). Of 1072 primary neoplasms, 49.4% were benign and 50.5% were malignant. Of the malignant neoplasms, papillary and follicular were the most frequent types (37 and 34.5%, respectively), followed by undifferentiated (15.8%), Hürthle (8.4%), medullary (2.9%)(15).

A retrospective study done in Barcelona, Spain of nine years data showed average age was 56.5 +/- 15.6 years. Women presented thyroid pathology more often: 88.7% against 11.3%(ratio 8:1) Among morphological disorders, 19 cases of thyroid nodule 3 carcinomas(15.7%): 2 papillary(10.5%) and 1 follicular(5.2%) and 16 cases of non-toxic diffuse goiter(84.2%) were recorded(16)

Objectives

- *General objective*: to assess the distribution of thyroid diseases over a period of four years(2009-2012) in the Department of Pathology, Tikur Anbessa Specialized Hospital, College of Medicine and Health Sciences, Addis Ababa University
- *Specific objectives*:
    - To determine the pattern of non neoplastic diseases of the thyroid along with age and sex related features
    - To determine the distribution of neoplastic diseases of the thyroid and assess the age and sex distribution
    - To compare these features with results of studies done previously in the same department, local hospitals and international data

Materials and Methods

A retrospective record review of histopathologic diagnoses of thyroid diseases was done. The diagnoses were reached via histopathologic examination of thyroidectomy specimens to the Department of Pathology in Tikur Anbessa Specialized Hospital, College of Medicine Health Sciences, Addis Ababa University. The department which is located in this tertiary care and teaching hospital, the largest health care center in the country, receives biopsies from all over the country and provides histopathologic diagnostic services. All casesof patients who had undergone surgery for thyroid diseases in the period between 2009 and 2012 were included in this study. All biopsy specimens were fixed in 10% formalin upon submission and tissue was processed with paraffin embedding and staining with eosin and hematoxylin(H&E). The diagnostic reports, paraffin blocks and slides are kept in the department archives for all cases. All cases were studied by pathology trainees and finally diagnosed and reported by pathologists. The information collected consisted of patient sex, age and histopathologic diagnosis. The slides were not retrieved for review, the index diagnosis was accepted as a final diagnosis. Histologic classifications of thyroid diseases were used: nodular colloid goiter(colloid and adenomatous), follicular adenoma, hurthle cell adenoma, different types of thyroiditis, and carcinomas of all subtypes(papillary, follicular, hurthle cell, medullary, poorly differentiated and anaplastic). Twenty six report forms with incomplete data were removed from the study. Duplications were excluded to the possible extent. The data was entered into Microsoft excel worksheets and analysed.

Results

A total of 24867 biopsies were received by the department and processed for diagnosis in the four years period between 2009 and 2012. Out of these, 1200 (4.8%) were thyroid tissue specimens. Female patients constituted 1007(82.5%) of the total thyroid cases with a female to male ratio of 5.2:1. The most commonly affected age group by thyroid diseases was between ages 20 and 59(84.5%)
Non neoplastic diseases of the thyroid consisted of 986(82.1%) of all thyroid cases while the neoplastic diseases were 211(17.6%). Thyroid diseases occurred in patients with an age range between 4 and 80 years. The mean and median ages of these patients were 36.3 and 35 respectively. Nodular colloid goiter was by far the commonest thyroid disease constituting 956 cases (79.6%)(table 1.) with an age range beween 4 and 80 years, mean and median ages of 35.6 and 34 respectively(table 2). The female to male ratio of this disease was 5.3:1. Other non neoplastic conditions include the thyroiditis: six cases of Hashimoto's thyroiditis(0.5%), seven cases of lymphocytic thyroiditis(0.6%), and one case of De Quervain's and two of Reidel's thyroiditis. There were 14 cases of thyroid cysts (1.2% of total). There was also only one case of diffuse colloid goiter.

Neoplastic conditions of the thyroid were found to be 211(17.8%), out of which the benign lesions were 78(6.5%) with follicular adenoma accounting for 50 cases(4.2%), cysts 14(1.2%) and Hurthle cell adenoma, 11(0.9%) of total thyroid cases. The malignant lesions were 147 (12.3% of total and 69.7% of the neoplastic lesions). Papillary thyroid carcinoma was the commonest malignancy with 105 cases(71.4% of the malignant and 8.8% of total) including 14 cases of follicular variant, 3 cases with lymphnode secondaries and 1 case with dedifferentiated component and another with mixed follicular counterpart. This is followed by follicular carcinoma with 23 cases (15.6% of malignancy). The other less common malignant lesions were medullary thyroid carcinoma of 6(4.1% of malignant), anaplastic carcinoma with 5 cases(3.4%) poorly differentiated carcinoma of 2 cases(1.6%) and 2 cases of Hurthle cell carcinoma and 1 case of unspecified NHL, plus one case of MALTOMA. (table 4)
The majority of cases were seen in the age group between 20 and 59 years (84.5%)(table 3)

Discussion

In this study the commonest thyroid lesion was found to be nodular colloid goiter as seen in 956 of the 1200 cases (79.6%). This finding is consistent , though slightly higher, with a previous retrospective study done in the same setting in 2003which had revealed that NCG was the predominant lesion(76.9%) of all thyroid lesions(3). This shows after a decade, the predominance of nodular colloid goiter has not declined even with measures which have been introduced to reduce iodine deficiency in the community, thereby resulting in an increment in the prevalence of goiter to 40% (8). The slight increase of the proportion of NCG in this study can be explained by a larger number of thyroid cases overall.
This finding is also consistent with a study done in Zewditu hospital previously which had showed NCG was the most common thyroid lesion (54.2) of all (10).
This picture is also found to be a consistent finding when compared to similar studies done in Ile Ife and Kano, Nigeria that showed NCG to be the commonest consisting of 75%, and simple nontoxic goiter rate of 68% respectively(12,13).
A study assessing thyroid diseases in sub-Saharan Africa has shown that euthyroid goiters were the commonest and their occurrence is influenced by the prevailing iodine deficiency in the region (14).
Studies done in other continents have also shown a consistent finding with this study stating that NCG was the predominant lesion: 91.4% in Sao Polo, Brazil. The higher figure in the later can be explained by the more exensive nature of this study which reviewed material of six decades (15).

Regarding the sex distribution of NCG, this study has found that NCG more commonly seen in women than in men with a female to male ratio of 5.3:1. This is a consistent finding with the study done by Drs B.Tsegaye and W.Ergete in the same hospital. The slightly raised ratio can be due to differences in the number of cases reviewed but does not change the general fact, which is also a reflection of the predominant nature of thyroid lesions in general in women compared to men. This predominance of NCG in women has also been reflected in various studies done in the same hospital as well as Nigeria, Sub Saharan Africa, and Spain with variable ratios which can be due to different study populations (5, 9, 10,12,14,16).
The commonest age group affected by thyroid diseases in general was found to be between 20 and 59 years(84.5%), a similar finding to the study previously done in the same department of this hospital indicating that the age distribution of thyroid diseases has not changed(3).

Inflammatory conditions were found to be 16 cases (1.3% of thyroid lesions and 1.6% of non neoplastic lesions) similar to the number of cases detected by the previous study from the same department (3). This figure is lower than one

reported in the sub Saharan Africa study (6.6%) probably owing to differences in the number of cases studied in the two studies.

Neoplastic diseases of the thyroid were found to be 211(17.6%), constituting the second commonest thyroid lesion in this study- a figure lower than the study done by B.Tsegaye and W.Ergete,(21%) probably owing to a larger number of non neoplatic diseases in the current study because of larger study population(3). The findings are, however consistent with findings in the two studies from Nigeria which were 17% and 18.7% of neoplastic(12,13), but higher than findings of the Brazil study which showed 13.3% of cases to be neoplastic. In spite of these variations, the overall picture is in agreement with the fact that neoplastic conditions are lower in proportion compared to the non neoplastic ones.
Adenomas were found to be 61 in this study(5.1% of all thyroid and 28.9% of neoplastic, which when compared to findings of the study by B.Tsegaye and W.Ergete(12.8% of thyroid and 61% of neoplastic)(3) shows a lower rate of benign lesions. There is also an apparent shift in the proportion of malignancy which is the dominant neoplastic disease in the current study. This can be an indicator of the fact that thyroid malignancies become increasingly more common in the past decade. It can also be a variation caused by differences in the management options for neoplastic conditions in this hospital over this period of time. The current findings are, however, consistent with the two studies from Nigeria which show malignant lesions to be more common than benign ones (12,13).

Among the malignant neoplasms of the thyroid, papillary carcinoma was found to be the commonest with 105 cases(71.4% of malignancies) consistent with the 76.6% found in the study by B.Tsegaye and W.Ergete(3), a study done in the surgical department of same hospital(9), and studies done in Brazil and Spain(15,16) while there is a discrepancy in proportion with studies done in Nigeria(12,13) and sub-Saharan Africa(14) all showing follicular carcinoma to be the more common type. This discrepancy could be due to variations in the study population.

Medullary thyroid carcinoma has increased in number(6 cases) compared to a single case in the previous study done in the same department(3) probably due to the increased number of total number of cases reviewed, while it is similar to the 7 cases found in the sub Saharan study(14).
Poorly differentiated and anaplastic carcinomas are still the rare forms of thyroid malignancies (3,14,15)

Conclusion

- Nodular colloid goiter is still by far the commonest disease of the thyroid owing to the rampant iodine deficiency in the country which is not adequately addressed
- Neoplastic diseases of the thyroid are not rare entities and their occurrence is similar to international patterns regarding sex and age distribution
- Thyroid malignancies have become more common than benign lesions

Recommendations

1. More needs to be done to address the issue of iodine deficiency in this country by increasing efforts to provide adequate micronutrient supplement in the community and awareness on the use of iodized salt
2. The commonness of thyroid malignancies mandates a proper evaluation of all goiters and that diagnosis should be cautious not to overlook malignancies.
3. Public health campaigns need to be carried out to raise public awareness about the benefit of early health service seeking once a neck mass has been noticed.
4. Further more extensive studies need to be conducted in the area of thyroid malignancies to reveal the factors behind the newly found predominance of these lesions over benign ones.

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Table 1: Histopathologic patterns of all thyroid diseases as seen at the department of pathology, Addis Ababa University, 2009-2012

Histologic type	no.	%
Nodular colloid goiter	956	79.8
Thyroid carcinoma	147	12.2
Thyroid adenoma	64	5.3
Thyroiditis	16	1
Thyroid cysts	14	1.2
Total	1197*	100

*Remaining three cases are the single cases mentioned in the result.

Table 2: The age range, mean age, median age and sex ratios of all thyroid lesions as seen at the department of pathology, Addis Ababa University, 2009-2012

Type	Age range	Mean age	Median age	F:M ratio
NCG	10-80	35.6	34	5.3:1
Hashimoto Thyroiditis	30-50	46.8	48.5	All female
Lymphocytic thyroiditis	20-50	37	37.5	All female
Follicular adenoma	16-60	36	30	2.3:1
Hurthle cell adnoma	18-46	37.6	36	10:1
Papillary carcinoma	11-75	37.9	32	4.5:1
Follicular carcinoma	22-73	45.3	48	1.3:1
Hurthle cell carcinoma	50-55	51.6	50	All female
Medullary carcinoma	30-55	42.8	44	1:1
Anaplastic carcinoma	29-65	51.6	55	4:1
Poorly differentiated ca.	40-75	56	53	2:1

Table 3: Distribution of the histological types of thyroid diseases by age as seen at the department of pathology, Addis Ababa University, 2009-2012

Age	**NCG(%)**	**Adenomas(follicular and hurthle cell)(%)**	**Carcinomas** (%)	**Thyroiditis** (%)
0-9	1(0.1)		0	0
10-19	88(9.2)	2(3.2)	8(5.5)	0
20-29	225(23.5)	20(32.7)	26(17.9)	3(18.7)
30-39	367(38.3)	20(32.7)	42(28.9)	6(37.5)
40-49	138(14.4)	15(24.5)	20(13.7)	3(18.7)
50-59	95(9.9)	2(3.2)	24(16.5)	3(18.7)
60-69	35(3.66)	1(1.6)	18(12.4)	1(6.25)
70-79	7(0.7)	1(1.6)	7(4.8)	0
Total	956(100)	61(100)	145**(100)	16(100)

**Two cases: one of unspecified NHL and one of MALTOMA not included.

Table 4: The distribution of histologic subtypes of thyroid malignancies as seen at the department of pathology, Addis Ababa University, 2009-2012

Carcinoma type	**No.**	**%**
Papillary	105	72.4
Follicular	23	15.9
Hurthle cell	2	1.4
Poorly differentiated	3	2.1
Anaplastic	5	3.4
Medullary	6	4.13
Total	145	100