Original Research

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

OTO Open
1–5

DOI: 10.1177/2473974X18777238
http://oto-open.org
SAGE

Thyroid Cancer and Iodine Deficiency Status: A 10-Year Review at a Single Cancer Center in Tanzania

Lulu L. Sakafu, MD[1], Teddy F. Mselle, MD, PhD[2], Julius D. Mwaiselage, MD, PhD[1], Khamza K. Maunda, MD, MSc[1], Bouyoucef S. Eddin, MD, PhD[3], and Mark E. Zafereo, MD[4]

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Received December 27, 2017; revised April 4, 2018; accepted April 25, 2018.

Abstract

Objective. To highlight the magnitude and distribution of thyroid cancer at the largest cancer center in Tanzania and to correlate patient region of residence with regions of dietary iodine adequacy and deficiency in the country.

Study Design. A retrospective cross-sectional chart review to characterize patients with thyroid cancer and regions of residence.

Setting. Ocean Road Cancer Institute (ORCI), the largest cancer center in Tanzania.

Subjects and Methods. Subjects had histologically confirmed thyroid cancer and no history of cancer treatment. Between January 2006 and April 2016, the cases of 139 consecutive patients with thyroid cancer at ORCI were retrospectively reviewed. Patients were grouped into those from iodine-adequate and iodine-deficient regions, based on the Tanzania demographic and health survey.

Results. Patients' median age was 47 years (range, 17-73 years), and the male:female ratio was 1:5. The number of people with thyroid cancer seen at ORCI increased steadily during the study period, with no significant difference between papillary (46%) and follicular (45%) diagnoses. Nonpapillary cancers occurred more frequently among males and patients $\geq$45 years of age, but these did not reach statistical significance. Seventy-five percent of all thyroid cancers were from areas of iodine deficiency, and this was similar in papillary and follicular cancer subtypes.

Conclusion. The incidence of differentiated thyroid cancer is increasing at the largest cancer center in Tanzania, whereby papillary and follicular subtypes were significantly higher in regions with long-standing dietary iodine deficiency.

Keywords

thyroid cancer, iodine deficiency, Tanzania

Thyroid cancer is the leading cause of endocrine malignancy worldwide.[1] In spite of increasing incidence over the years, mortality has remained stable.[2] Histologically, the 2 most frequent subtypes of thyroid cancer are papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC),[1,3] both derived from follicular epithelial cells and collectively referred to as *differentiated thyroid cancer*.[4] The etiology for the majority of differentiated thyroid cancers is unknown, but childhood radiation exposure[2,5] and dietary iodine deficiency have been implicated as risk factors.[6] Hurthle cell carcinoma, FTC, and anaplastic thyroid cancers have been associated with dietary iodine deficiency.[6,7] Studies have reported that FTC may be particularly associated with long-standing dietary iodine deficiency on the African continent.[8]

Because of long decades of dietary iodine deficiency in Tanzania, an iodination campaign was initiated in the late 1990s.[7-9] A survey in Tanzania to establish the magnitude of dietary iodine deficiency revealed that approximately 50% of the population had endemic goiter secondary to long-term dietary iodine deficiency.[10,11] This study aims to highlight the

[1]Department of Clinical Oncology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Ubungo, Tanzania
[2]School of Medicine, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Ubungo, Tanzania
[3]Department of Nuclear Medicine, CHU Bab El Oued University, Algiers, Algeria
[4]Department of Head and Neck Surgery, MD Anderson Cancer Center, Houston, Texas, USA

Corresponding Author:
Lulu L. Sakafu, MD, Department of Clinical Oncology, School of Medicine, Muhimbili University of Health and Allied Sciences, PO Box 65001, Kwembe, Dar es Salaam, Ubungo +255, Tanzania.
Email: willymeena2007@yahoo.com

magnitude and distribution of thyroid cancer in regions with long-standing dietary iodine deficiency among patients treated at the Ocean Road Cancer Institute (ORCI) in Tanzania.

Methods

The study was approved by the Institutional Review Board of Muhimbili University of Health and Allied Sciences, Dar Es Salaam, Tanzania, and granted permission from the Research Review Board of ORCI. The medical records of 139 consecutive patients with a histopathologic diagnosis of thyroid cancer between January 2006 and April 2016 at ORCI in Dar es Salaam, Tanzania, were retrospectively reviewed. Information extracted included demographics, region of residence, and histopathology. Six patients with follicular variant PTC were included in the papillary thyroid subgroup analysis. Regions of residence were grouped on the basis of iodine status (adequate vs deficient), according to data published in the Tanzania demographic and health survey from the Tanzanian National Bureau of Statistics.[12] During regional iodine status analysis, 51 patients were omitted from further analysis due to inadequate data with regard to region of residence. Specifically, patients who did not have data indicating that they had lived in a particular region of residence for at least 10 years were excluded from this analysis. Excluding these patients, the regional iodine status evaluation included 88 patients.

Data was entered into SPSS 20 (IBM, Chicago, Illinois) for analysis. Descriptive statistics, such as frequencies, percentages, mean, range, and standard deviation, were calculated with SPSS software. Univariate and multivariate analysis were performed. The multivariate logistic regression model was a poor fit for the data and unstable. Therefore, to control for false discovery, we used a Bonferroni correction and used an adjusted significance threshold of 0.17 (0.05 divided by 3, since there were 3 tests).

Results

Demographics

A total of 139 patients with thyroid cancer met inclusion criteria (**Table 1**). The median age was 47 years (range, 17-73 years), and most patients were female. The majority of patients presented with either PTC (46%) or FTC (45%), while 9% patients had anaplastic, Hurthle cell, or medullary thyroid carcinoma. There was a steady increase in the number of cases of thyroid malignancy over the 10-year period from 2006 to 2015, with the total yearly number of patients with diagnosed thyroid malignancies more than doubling during that period (**Figure 1**).

Association between Thyroid Cancer and Dietary Iodine

Among 88 patients with residence status available, 22 patients with thyroid cancer had residence in iodine-adequate regions, while 66 (75%) with thyroid cancer had residence in iodine-deficient regions. Furthermore, PTC incidence and FTC incidence were higher in dietary iodine–deficient areas as compared with regions with adequate dietary iodine, while there was no difference in distribution of thyroid cancer according to dietary iodine between these subtypes (**Figure 2**, **Table 2**).

Table 1. Demographics and Pathology for 139 Patients with Thyroid Carcinoma in Tanzania.

Characteristics	n	%
Age, y		
<45	76	55
≥45	63	45
Sex		
Male	22	16
Female	117	84
Histopathology		
Papillary[a]	64	46
Follicular	62	45
Others (anaplastic, medullary)	13	9

[a]Includes 6 patients with follicular variant papillary thyroid cancer.

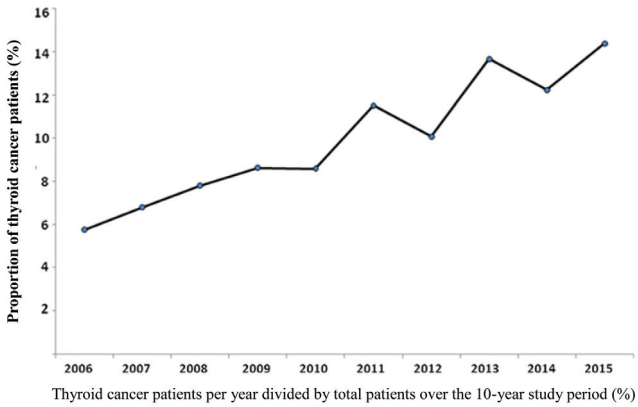

Figure 1. Thyroid cancer diagnosis trend, 2006-2015 (N = 139). The number of patients with thyroid cancer per year divided by the total number of patients over the 10-year study period (%).

Other Risk Factors

Table 2 delineates that PTC was the most common thyroid cancer (57%) among patients <45 years of age. However, patients aged ≥45 years were more commonly diagnosed with FTC (50%) or other thyroid cancers (13%; $P = .03$, univariate analysis). While this distribution of thyroid cancers was significant on univariate analysis, the multivariate logistic regression model was a poor fit and unstable; therefore, we determined that this distribution did not maintain statistical significance when we incorporated a Bonferroni correction with an adjusted significance threshold of 0.17. Female sex was highly associated with all types of thyroid malignancy; however, there was no statistically significant difference in the distribution of subtype of thyroid cancer according to sex.

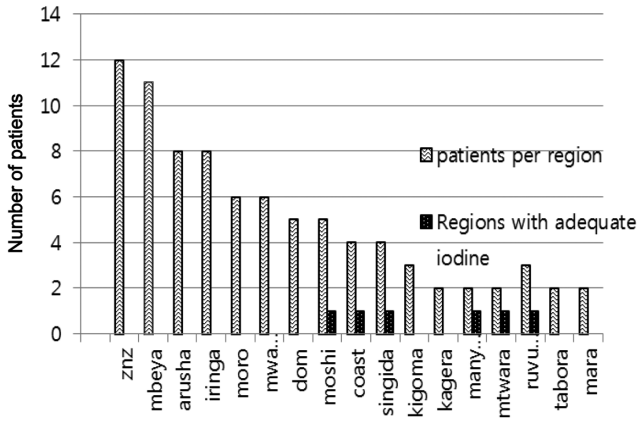

Figure 2. Thyroid cancer distribution per region of residence (n = 88). Patients with thyroid cancer according to region of residence, with region iodine status per the Tanzania demographic survey.[12]

Table 2. Risk Factors for Thyroid Cancer.

Category	Papillary	Follicular	Others	Total	*P* Value
Age, y					
<45	36	24	3	63	
≥45	28	38	10	76	.03[a]
Sex					
Female	56	50	11	117	
Male	8	12	2	22	.55
Regional iodine status[b]					
Adequate	10	11	1	22	
Deficient	30	33	3	66	≥.99

[a]After control for false discovery via Bonferroni correlation (0.05 divided by 3, given 3 tests), adjusted significance threshold was 0.017. Therefore, this analysis did not reach statistical significance.
[b]Patients with regional iodine residence data (ie, must have lived in region for at least 10 years), n = 88.

Discussion

This retrospective study over a 10-year period at ORCI, the largest national referral cancer hospital in Tanzania, contributes to an understanding of the demographics and distribution of thyroid cancer in Tanzania according to histopathologic subtype and dietary iodine. This is the first such study to be conducted in Tanzania, where there is a unique opportunity to study thyroid cancer in the setting of regions with adequate dietary iodine and iodine deficiency. Approximately 75% of patients diagnosed with thyroid cancer resided in areas of dietary iodine deficiency, whereas approximately 50% of the Tanzanian population lives in these areas. Follicular and other nonpapillary pathologies were relatively more common among older patients, while PTCs had relative predominance among younger patients and a trend for predominance in females. This relatively high distribution of diagnoses of non-PTCs among older patients is in contrast to epidemiologic studies in more developed countries, which report much higher relative rates of PTC versus FTC among all patient age groups.[3]

Previous studies have suggested that FTCs may be associated with dietary iodine deficiency.[7,13] In the natural history of the potential development of thyroid cancer from endemic goiter due to long-standing dietary iodine deficiency, the transformation to malignancy may require many years,[14] a theory that may explain a later age of presentation of FTC versus PTC in an iodine-deficient population.

The high proportion of patients diagnosed with FTC seen at ORCI in Tanzania is in keeping with what is seen elsewhere in areas with inadequate dietary iodine intake.[5] Furthermore, anaplastic and Hurthle cell subtypes have been reported to be more prevalent in areas with long-standing deficient dietary iodine.[7,13] The majority of patients with FTC seen at ORCI resided in areas associated with dietary iodine deficiency, as also reported in South Africa.[8] However, it is noteworthy that patients diagnosed with PTC in the current study were similarly more commonly from areas with inadequate dietary iodine according to the Tanzanian demographic micronutrient survey done in 2010.[12] These areas also had a high prevalence of goiter according to a goiter survey among schoolchildren.[10] Previous studies have shown significant reduction in disorders associated with iodine deficiency in countries with successful dietary iodination programs.[15] Interruption of iodine supply has been associated with a rapid relapse of iodide-deficiency disorders.[16] Future studies may elucidate whether dietary iodination programs have any impact on the rate of thyroid cancer development in iodine-deficient areas of Tanzania.

Among thyroid cancer cases, there were 5 times more females than males. This sex disparity is higher than that in studies from more developed countries, reporting ratios of 2-3:1 between females and males.[16,17] In Tanzania and other developing countries, a higher proportion of patients with hypothyroidism and endemic goiter during pregnancy or soon postdelivery could explain a potentially higher overall proportion of thyroid cancer occurrence among females.[11] In fact, the study by Rahbari et al showed that reproductive factors may have an association with hypothyroidism state and ultimately goiter formation and, if unattended to, may predispose to the development of thyroid cancer.[18] Pellegriti et al reported thyroid cancer as the fifth-most frequent cancer among women,[2] while World Health Organization data show thyroid cancer to be the eighth-most frequent among women worldwide.[19] In Tanzania, projected data from the International Agency for Research in Cancer indicate that each year there are about 34 new cases of thyroid cancer in Tanzania.[20] However, accurate assessment of country-wide thyroid cancer data in Tanzania is challenging, with limited resources for the diagnosis and treatment for thyroid cancer in many regions of the country and with the absence of a national cancer registry.

Finally, results of the current study indicate a steady increase in the number of new cases of thyroid cancer seen

at ORCI in Tanzania over the past decade, which corresponds to global data,[21] where it is projected that by 2030 thyroid malignancies could be more common than colorectal cancers. Whether this increase in thyroid cancer diagnoses represents an actual increase in thyroid cancer incidence or advances in technology on a global level has been a subject of much debate.[2,5] Similarly, the increase in thyroid cancer diagnoses at a single institution in Tanzania could be attributed to improvements in technology and access to medical care. Although ORCI is currently the only specialized cancer hospital in Tanzania, this institution would be expected to see a relatively small fraction of potential thyroid malignancies in the country, and there may be selection bias in the demographics and pathologies of patients presenting to this institution.

Another limitation of the iodine deficiency analysis was the exclusion of 51 patients (37% of the study population) due to inadequate data with regard to region of residence. We applied a very stringent criterion to region of residence, requiring that a patient must have lived in a region for 10 years to be included in this analysis, so that we would minimize bias from patients having moved from one region to another. While this study is subject to the inherent limitations and selection bias associated with a retrospective review, as the largest study of thyroid cancer in Tanzania to date, it adds valuable insight to potential differences in demographics and histopathology of thyroid cancers in iodine-deficient areas of the world. Future studies should continue to focus efforts on prospective evaluation of thyroid cancer and control data across multiple centers throughout the country, to more precisely understand the potential role of iodine deficiency on the development of thyroid malignancy.

Conclusion

Thyroid cancer diagnoses have steadily increased over the last decade at a tertiary referral cancer center in Tanzania, with the majority of these cancers arising in patients residing in areas with long-standing dietary iodine deficiency. Future studies will be required to assess the impact of an iodination program in Tanzania that may affect the demographics and histopathology of thyroid cancer in this country.

Acknowledgment

We acknowledge the COSTECH for financial support and the ORCI registry and nuclear medicine staff for their help in accessing patients' records.

Author Contributions

Lulu L. Sakafu, designed the study, collected data, did the analysis, wrote the manuscript; **Teddy F. Mselle**, supervised study designing, data collection, data analysis and manuscript writing; **Julius D. Mwaiselage**, assisted in study designing, data analysis and critical review; **Khamza K. Maunda**, supervised study designing, data collection, data analysis and manuscript writing; **Bouyoucef S. Eddin**, supervised study designing, data collection, data analysis and manuscript writing; **Mark E. Zafereo**, study design, data analysis, manuscript writing.

Disclosures

Competing interests: None.

Sponsorships: COSTECH—Tanzania Commission for Science and Technology.

Funding source: COSTECH—Tanzania Commission for Science and Technology.

References

1. Adam MA, Pura J, Goffredo P, et al. Impact of extent of surgery on survival for papillary thyroid cancer patients younger than 45 years. *J Clin Endocrinol Metab*. 2015;100:115-121.
2. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. *J Cancer Epidemiol*. 2013; 2013:965212.
3. Brown RL, de Souza JA, Cohen EEW. Thyroid cancer: burden of illness and management of disease. *J Cancer*. 2011;2:193-199.
4. Chen AY, Jemal A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1988-2005. *Cancer*. 2009;115:3801-3807.
5. Figge JJ. Epidemiology of thyroid cancer. In: *Thyroid Cancer: A Comprehensive Guide to Clinical Management*. 2nd ed. New York, NY: Springer; 2006:9-13.
6. Rahman GA. Extent of surgery for differentiated thyroid cancer: recommended guideline. *Oman Med J*. 2011;26:56-58.
7. Knobel M, Medeiros-Neto G. Relevance of iodine intake as a reputed predisposing factor for thyroid cancer. *Arq Bras Endocrinol Metabol*. 2007;51:701-712.
8. Kalk WJ, Sitas F, Patterson AC. Thyroid cancer in South Africa—an indicator of regional iodine deficiency. *S Afr Med J*. 1997;87:735-738.
9. Assey VD, Peterson S, Kimboka S, et al. Tanzania national survey on iodine deficiency: impact after twelve years of salt iodation. *BMC Public Health*. 2009;9:319.
10. Wächter W, Mvungi M, König A, Pickardt CR, Scriba PC. Prevalence of goitre and hypothyroidism in Southern Tanzania: effect of iodised oil on thyroid hormone deficiency. *J Epidemiol Community Health*. 1986;40:86-91.
11. Wächter W, Mvungi MG, Triebel E, et al. Iodine deficiency, hypothyroidism, and endemic goitre in southern Tanzania: a survey showing the positive effects of iodised oil injections by TSH determination in dried blood spots. *J Epidemiol Community Health*. 1985;39:263-270.
12. Tanzania Bureau of Statistics and Macro International. *Micronutrients: Results of the 2010 Tanzania Demographic and Health Survey*. Calverton, MD: ICF Macro; 2010.
13. Choi WJ, Kim J. Dietary factors and the risk of thyroid cancer: a review. *Clin Nutr Res*. 2014;3:75-88.
14. Mathai V, Idikula J, Fenn AS, Nair A. Do long-standing nodular goitres result in malignancies? *Aust N Z J Surg*. 1994;64:180-182.
15. Okosieme OE. Impact of iodination on thyroid pathology in Africa. *J R Soc Med*. 2006;99:396-401.

16. Zimmermann MB, Jooste PL, Pandav CS. Iodine-deficiency disorders. *Lancet*. 2008;372:1251-1262.
17. Mazzaferri EL, Massoll N. Management of papillary and follicular (differentiated) thyroid cancer: new paradigms using recombinant human thyrotropin. *Endocr Relat Cancer*. 2002;9: 227-247.
18. Rahbari R, Zhang L, Kebebew E. Thyroid cancer gender disparity. *Future Oncol*. 2010;6:1771-1779.
19. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *Int J Cancer*. 2013;132:1133-1145.
20. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. *GLOBOCAN 2008 v2.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10*. Lyon, France: International Agency for Research on Cancer; 2010.
21. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res*. 2014;74:2913-2921.