The profile of thyroid cancer in patients undergoing thyroidectomy at Chris Hani Baragwanath Academic Hospital

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Background: The histological type of thyroid cancer in well-resourced countries is predominantly papillary. Follicular carcinoma is predisposed by iodine deficiency that was present the Black population of South Africa until salt iodination in 1995. The aim of this study was to analyse the profile of thyroid cancer in Black South Africans from January 2001 to December 2017 and to identify any temporal changes in thyroid cancer histological subtypes since salt iodination.
Method: Histopathological reports of patients who underwent thyroidectomy for cancer at Chris Hani Baragwanath Academic Hospital in Johannesburg, South Africa between January 2001 and December 2017 were retrospectively assessed. Data captured included name, age, gender, race, the date when the specimen was sent and the detailed histopathological report.
Results: Of the 143 thyroidectomies performed for malignancy, papillary thyroid cancer was the predominant type (65%) with a papillary to follicular thyroid cancer ratio of 4:1. Follicular, medullary and anaplastic cancers were 16.8%, 9.8% and 2.8% respectively. The reports were incomplete in 5 cases and there were 3 non-epithelial neoplasms.
Conclusion: There is a gradual temporal increase in the frequency of resected papillary cancer over a 16 year period while follicular has remained static. These changes may be attributable to better salt iodination.

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Background

Thyroid cancer is the most frequent endocrine malignancy, ranging from 7.3% to 15% in surgical series in Africa.[1] Thyroid cancer accounts for only 1–2% of all malignancies worldwide.[2] Well-differentiated thyroid cancer, namely papillary and follicular thyroid cancers are the most common types. Over the past three decades, there is evidence that the global incidence of thyroid cancer is increasing.[2] This apparent rise may be attributed to the increased use of imaging modalities like ultrasound, CT scan and MRI[3] with cytology, and is mainly due to the increase in the incidence of papillary thyroid micro-carcinomas.[4]

The SEER data reported an annual percent change (APC) of 2.4% to 6.6% in the USA.[2] The incidence in the African context is largely unknown due to insufficient detection and underreporting.[2]

In South Africa in 1988, 359 thyroid cancers were recorded in the South African National Cancer Registry (NCR) with a crude national annual incidence of 1.25/100 000 with a population of approximately 30 million.[5] In 2012, the NCR reported 533 cases of thyroid cancer in South Africa, with an estimated population of 52.5 million.[6] Although the exact population figures are in excess of 50 million, this number could suggest that there may have been an increase in thyroid cancer which is in line with the global experience. The reasons for this increase have been hypothesised to be two-fold. The apparent increase in the number of new cancers is thought to be due to increased diagnostic accuracy while a “true” increase is attributed to environmental and lifestyle changes[2] due to iodination of salt and its availability through urbanization.

Environmental factors may well be a significant contributor to the increased incidence of thyroid cancers in a population. In 1988, Kalk demonstrated that many areas in South Africa appeared to be iodine-deficient as evidenced by the predominance of follicular thyroid cancer (FTC), suggesting that the prevalence of FTC compared to PTC could be used as a surrogate marker for iodine deficiency in a certain area.[5]

Iodine intake in population varies and it determines the occurrence of benign thyroid disorders.[7] While this is clear with benign thyroid disorders, the role of iodine intake in thyroid cancer is not well established.[6] Populations that are iodine deficient have a high incidence of goitre and thyroid nodules, which may precede the development of thyroid cancer.[7] These areas also have the highest rate of mortality from thyroid cancer as patients typically present with more advanced tumour stages and with more aggressive subtypes like anaplastic thyroid cancer (ATC).[8]

What seems to be unclear is whether chronic TSH stimulation leads to thyroid tumours. In iodine deficiency, TSH is increased and this may lead to thyroid cell proliferation, which leads to marked thyroid hyperplasia and hypertrophy.[7] These thyroid cells are deemed more vulnerable to mutagens which include radiation, chemical carcinogens and oxidative stress.[7] Animal studies in this field suggest that transition from follicular adenoma to follicular carcinoma is a result of chronic TSH stimulation brought about by goitrogenic diets or partial thyroidectomy.[7] The same study by Kalk showed that differentiated thyroid cancer was predominantly of the follicular type and this was mainly seen in Black patients from rural areas where iodine deficiency was likely.[5] In 2001 Mulaudzi et al. reported that the predominant type of thyroid cancer in an urban black population in Durban was FTC (follicular 68%, papillary 16%), compared to the Indian population where there was a higher incidence of PTC (57%) followed by FTC (35%).[8] Sidibe and colleagues also reported that FTC in Algeria accounted for up to 55% of thyroid cancers.[7] In their observations, thyroid cancers were associated with a low socio-economic status, where a low iodine status was likely. A histopathological report from Harare in Zimbabwe noted FTC to be the commonest histological subtype (70%) and there were equal numbers of papillary and anaplastic types (14% each).[10] This was also thought to be comparable with the lack of adequate iodine intake observed in the whole sub-Saharan region.

Conversely, Cairncross published a study that showed predominance of papillary carcinoma in an urban population in Cape Town.[11] In the study, 56 PTC were recorded vs. 30 FTC.[11] This also supports the hypothesis that South Africans in urban settings are likely to be iodine-replete.[13] Bombil also found PTC to be the most common thyroid cancer in Chris Hani Baragwanath Academic Hospital in 2014, which serves a predominantly African population in Soweto in Johannesburg.[12]

To combat iodine deficiency disorders (IDD) in South Africa, which may range from endemic goiter to cretinism, guidelines from the WHO and UNICEF universal iodination programs were implemented.[13] "Universal salt iodisation (USI) is a process where all salt for human and animal consumption is iodised according to the country's recommended levels".[14]

In South Africa, a sub-standard attempt at eliminating IDD was started in 1954 and entailed "optional" salt iodisation.[15] Thereafter, South Africa implemented mandatory iodination in response to UNICEF recommendations.[15] Mandatory iodination entails the addition of potassium iodate to table salt at 40–60 parts per million (ppm).[15] This was further revised in 2006 where the concentration of potassium iodate was increased to 35–65 ppm.[15]

Objective

The current study was undertaken to examine the histopathological profile of thyroid cancer in patients who underwent thyroidectomy for cancer at Chris Hani Baragwanath Academic Hospital (CHBAH) that mainly serves the urban Black population of Johannesburg. The study is an attempt to identify any effect that mandatory iodination of diets may have had on the profile of thyroid cancer.

Methods

This is a retrospective review of histopathology reports of patients who underwent thyroidectomy for malignancy between January 2001 and December 2017 at CHBAH.

The data was collected from theatre registries, patient files and the National Health Laboratory Services (NHLS) database using a Systematized Nomenclature of Medicine (SNOMED) extract. This database records patients' demographic details (name, age, gender, race) and the date on which the biopsy was taken. The coded database identifies the site of the biopsy and the histopathological result of a specified patient. Where race was missing, it was inferred from the patient name. Race was also used as a proxy for access to iodination because of social and economic disadvantage historically assigned by racial category.

Thyroidectomies done for benign disease were excluded. Stata and Excel were used to analyse the data.

Results

The results are depicted in Tables 1 and 2.

Table 1: Description of patient profiles

Characteristics	Number and percentages (mean ± std deviation)
Total	143
Gender	
Males	25 (17.5)
Females	118 (82.5)
Age mean (SD)	47 (15.5)
Race	
Black	106 (74.1)
Coloured	5 (3.5)
Indian	1 (0.7)
Not specified*	31 (21.7)
Histology results	
Papillary thyroid carcinoma	93 (65.0)
Follicular thyroid carcinoma	24 (16.8)
Medullary thyroid carcinoma	14 (9.8)
Anaplastic thyroid (undifferentiated) carcinoma	4 (2.8)
Other (sarcoma, lymphoma)	8 (5.6)

SD= standard deviation

Not specified*: the patients reported as unspecified predominantly had African names

Table 2. Distribution of age ranges in 140 patients. Age was not specified in three (3) patients						
	Age					
Histology	15–24	25–34	35–44	45–54	> 55	Total
PTC	4	18	26	16	27	91
FTC	0	5	4	7	7	23
MTC	2	2	7	3	0	14
ATC	0	0	1	0	3	4
Other	0	1	1	3	3	8
Total	6	26	39	29	40	140

PTC = papillary thyroid cancer FTC = follicular thyroid cancer
MTC = medullary thyroid cancer ATC= anaplastic thyroid cancer

Figure 1 demonstrates an undulating pattern in the incidence of PTC and an overall widening gap between PTC and FTC. The incidence of FTC has been constant, with a slight increase in 2016 and 2017. The net result is that the papillary to follicular ratio has increased to 4:1 at the end of the study (2017) from an almost 1:1 ratio in the early phase of the study (2002). The current preponderance of PTC is best evidenced by comparison between the 1988 results to the findings of this study (Figure 2).

In 1988, there were 74 cases of PTC and the number increased to more than 90 in 2017 as shown in Figure 2. FTC was very high with 92 cases in 1988 but the number decreased to 24 cases in 2017.

Table 3 compares PTC and FTC between 1988 and 2017. A large proportion of patients with PTC (65%) were recorded in 2017 compared to 20.6% in 1988 with statistically significant differences in proportion ($p < 0.0001$).

Overall, the number of PTC has been increasing as shown in Figure 3. From 2010 to 2013, there appeared to be a steady decline in PTC, followed by a sharp increase in 2014.

Discussion

In this study, the larger proportions of female to male ratio is in line with global findings, although the age of the patients with papillary carcinoma is slightly higher than similar cases reported in Western countries. Papillary thyroid cancer is most commonly seen in individuals in the third to fifth decade of life, which is also consistent with the findings in this study. More than 75% of cases occur in women, making this the fifth most

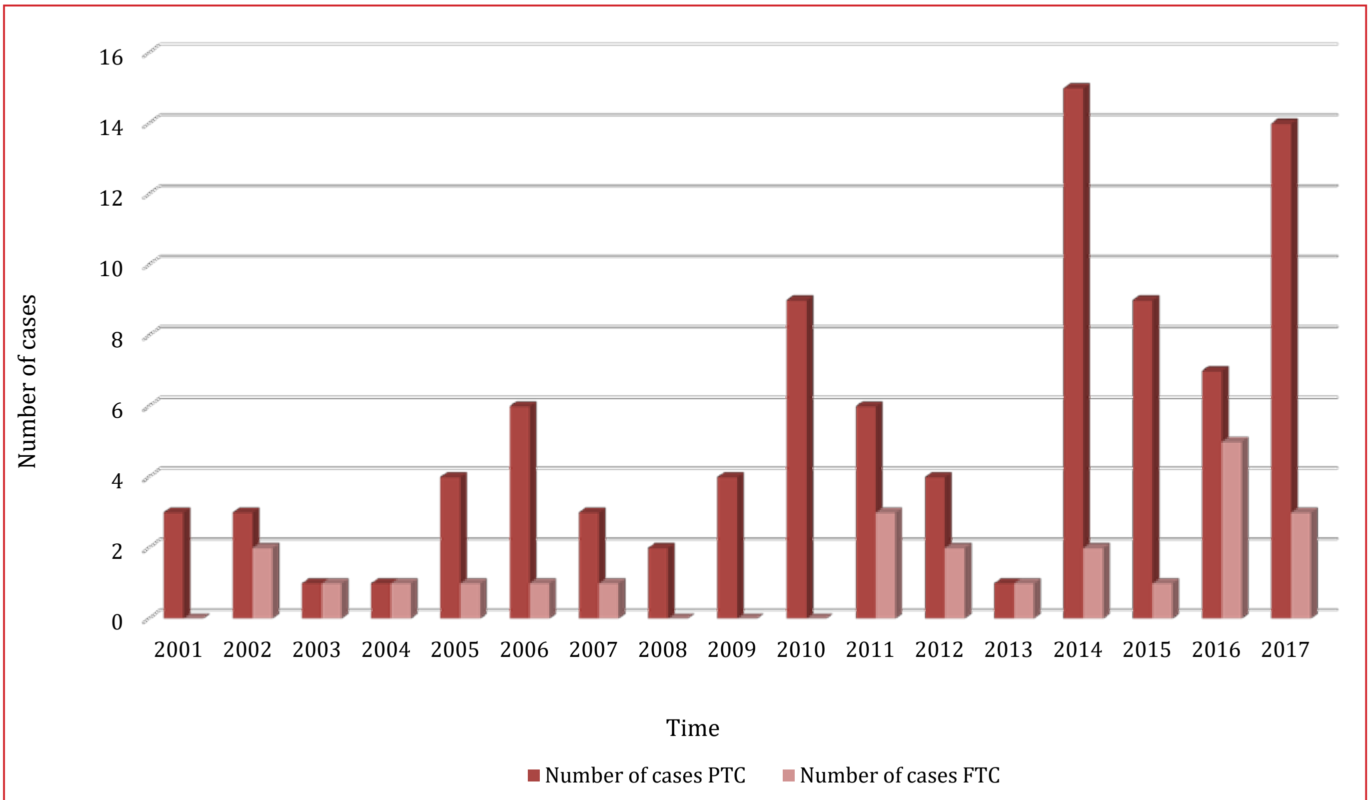

Figure 1. Incidence of papillary (PTC) and follicular thyroid cancer (FTC) from 2001–2017

Table 3: Comparison of PTC and FTC between 1988[2] and 2017

	1988 (n=359)	2017 (n=143)	P values
PTC	74 (20.6%)	93 (65.0%)	<0.0001
FTC	92 (25.6%)	24 (16.8%)	0.363
MTC	-	14 (9.8%)	
Other	193 (53.7%)	12 (8.4%)	

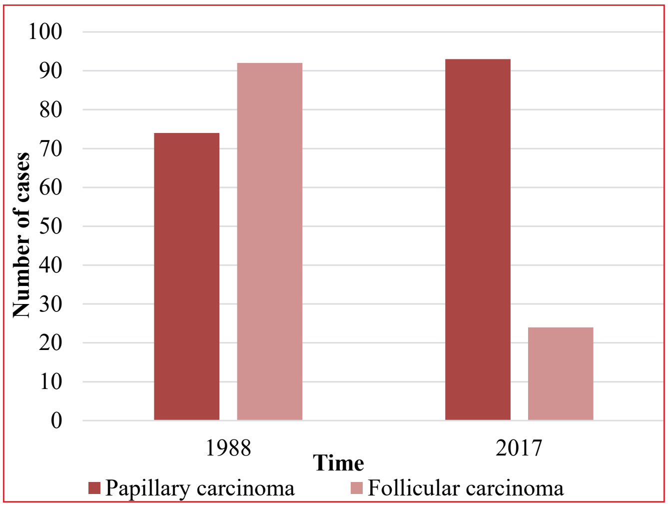

Figure 2: Comparison of PTC and FTC between 1988[2] and 2017

common malignancy in women.[12] In the current series, 82.5% were women. Age is an important prognostic factor in well-differentiated thyroid cancers.[13] Diagnosis at an age younger than 55 and older than 20 infers excellent survival. Two thirds of our patients (Table 2) were between age 20 and 55 years. The increase in the incidence of papillary thyroid cancers in this study is clear and mirrors that in iodine-rich areas. Globally the detection of papillary micro-carcinomas has contributed to an increased incidence of PTC in well-resourced countries. The WHO classifies papillary thyroid micro-carcinomas as cancers that measure 1 cm or less. In the USA, papillary thyroid micro-carcinomas have become the most common PTC detected in patients older than 45 years with an excellent prognosis.[11] In the current series, the size of the papillary thyroid cancers was not consistently recorded. PTC accounts for 80% of all thyroid malignancies in the developed world[16] and accounted for 65% in this series. Although cervical lymph node metastases are common, PTC has a good prognosis with a 5-year survival rate of up to 98%.[13] FTC is less common, accounting for up to 15% of thyroid cancers globally, and 16.7% in this series. FTC is the more aggressive subtype of differentiated thyroid cancers with a less favourable prognosis than PTC. The 5-year survival rate reported by the American Cancer Society ranged from 98–100% for early stage cancer. However for stage III PTC, the 5-year survival rate is 93% while FTC has a 5-year survival rate of 71%.[14] ATC is very uncommon, accounting for 2.8% of cases in this series: these are uniformly fatal.[18] An increased rate of ATC has been recorded in areas with an increased prevalence of FTC, suggesting that FTC may more readily de-differentiate to the anaplastic subtype than PTC.[19] FTC is more often identified in iodine-deficient areas leading to raised levels of TSH and areas of hyperplasia in the thyroid gland. The continuing stimulus by TSH may initiate a sequence of hyperplasia, dysplasia and finally thyroid tumorigenesis.[15,17] This sequence has been suggested as the explanation for the association of iodine-deficiency with follicular thyroid carcinoma. Over the past thirty years more and more of the Black population has moved from rural areas to urban centres in search of employment, better healthcare and better

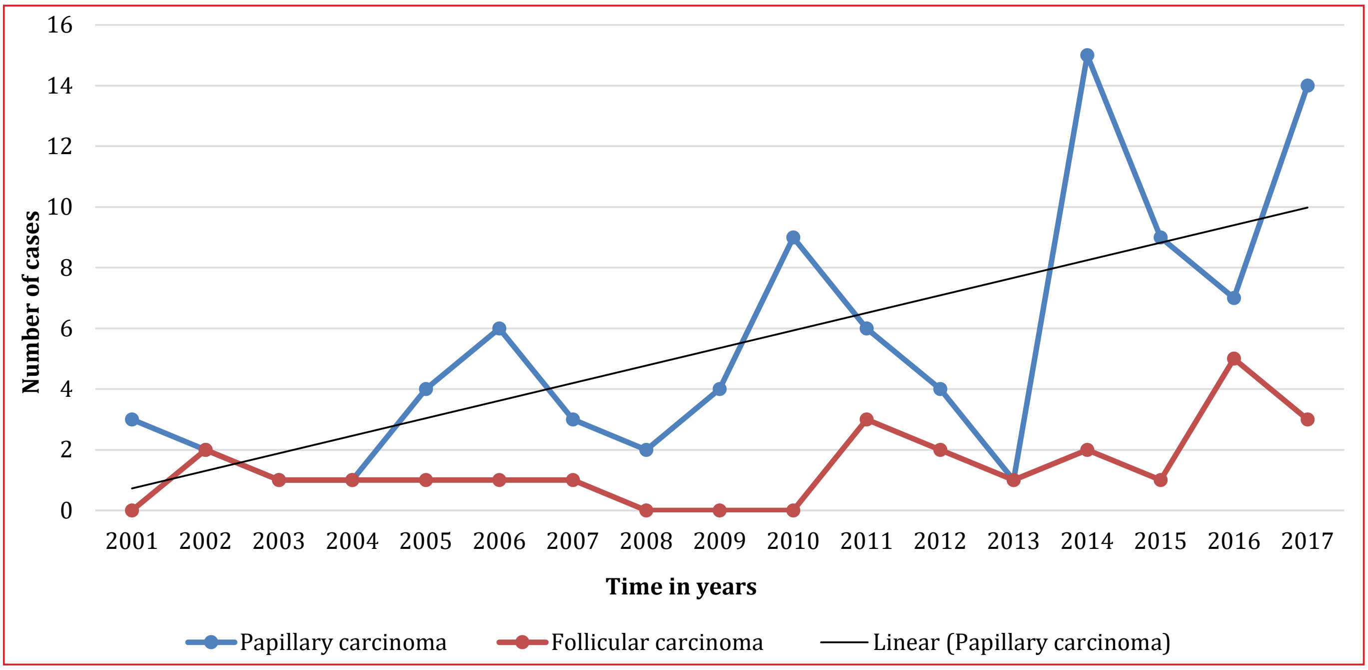

Figure 3: Trends in occurrences of PTC and FTC from 2001 to 2017

educational facilities. The result is that most of Gauteng province has been reclassified as urban.[12] Part of the reason why "optional iodination" implemented in 1954 failed to eliminate iodine deficiency disorders was the availability of cheaper salt and bread that did not contain iodine.[11] The rural population was most affected by this, while their urban counterparts who consumed processed foods (with a high iodine content) were less affected. Once iodination was made mandatory by the South African government in 1995, individuals who may have been iodine-deficient now had access to salt and bread that was adequately iodized.[11] Sufficient iodination was demonstrated in surveys conducted in four communities in the Langkloof area and in children in the Northern Cape Province in 1988.[9] These surveys were done by measuring median urinary iodine concentration in primary school children in these areas.[7] The current study, having been conducted more than two decades after mandatory iodination was implemented, serves to infer that Black South Africans in urban areas have become iodine-replete. The communities that seek healthcare at CHBAH are predominantly Black and urbanised as determined by Statistics South Africa in the census in 2001. CHBAH also receives patients from remote areas in the province that could still be iodine deficient which may account for the relatively lower PTC (65%) compared with 80% from the literature in iodine rich areas. However, residential information of patients undergoing thyroidectomy was not documented. Although names are often associated with race (with some exceptions), identifying race by patient name is an inaccurate method of determining race. However, CHBAH serves the population of Soweto, an almost exclusively Black township on the outskirts of Johannesburg. It is therefore not unexpected that almost all patients in this series had African names

This study has some limitations. These include its retrospective nature, missing data and the failure to record race accurately. Another limiting factor is the fact that iodination could not be directly measured in the study, therefore race and urban/rural location were used as proxy.

Conclusion

An overall increase in incidence of thyroid cancer and significant relative increase in the proportion of papillary to follicular carcinoma has been demonstrated in this study. This serves as indirect evidence that the urban Black population in Soweto, Johannesburg, which may have been iodine-deficient prior to mandatory iodination of table salt and bread, is now iodine replete.

Recommendation

A nationwide study that directly measures the iodine level in the urine is likely to confirm that South Africa is an iodine replete country.

Ethics approval

Ethics approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand and the Research Review Board at CHBAH (M160538).

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