

Thyroid cancer in South Africa — an indicator of regional iodine deficiency

W J Kalk, F Sitas, A C Patterson

Objective. Because follicular thyroid cancers predominate in iodine-deficient and papillary cancers predominate in iodine-replete populations, we have analysed national and regional (former Transvaal) incidences of these cancer types as a surrogate measure of the population iodine nutritional status in South Africa.

Design. Statistical analysis, by race and sex, of differentiated thyroid cancers reported to the South African National Cancer Registry (1988), and of the computerised histology records of the Department of Anatomical Pathology, SAIMR (January 1990 to June 1994; Transvaal data).

Main outcome measures. Relative frequencies of the two cancer types nationally and geographically in the Transvaal region.

Main results. Thyroid cancer was underdiagnosed in populations other than white. Nationally, follicular histology accounted for 55% of all differentiated primary thyroid cancers, and predominated especially in black women. Follicular morphology predominated in blacks resident in the rural regions of the former Transvaal (58%), while papillary histology predominated in urban areas (of present-day Gauteng), irrespective of race (78%; $P = 0.003$).

Conclusion. The national predominance of follicular thyroid cancer indicates that significant iodine deficiency exists in the country as a whole. The observed urban-rural differences in prevalences of follicular and papillary cancer types suggest regional differences in the severity of iodine deficiency. There is a need for a formal survey of the population iodine nutritional status in South Africa.

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There is convincing evidence that nutritional iodine status influences the morphology of thyroid cancers both within and between populations.¹⁻⁶ Papillary cancers predominate in iodine-replete areas while follicular and anaplastic cell types are commoner in iodine-deficient populations. Thyroid cancers are more frequent in women than in men, and the

Division of Endocrinology and Metabolism, University of the Witwatersrand, National Cancer Registry and Department of Anatomical Pathology, School of Pathology, SAIMR, Johannesburg

W J Kalk, MB BCh, FRCP

F Sitas, DPhil

A C Patterson, MB BCh, PhD

iodine-dependent difference in the frequency of cancer types is seen predominantly in women.⁵ Moreover, iodine deficiency may also increase the overall frequency of thyroid cancers.⁶ The introduction of iodide prophylaxis in iodine-deficient regions changes the relative proportions of the histological cancer types towards the less aggressive papillary form, with a latency period of some 25 years after the introduction of supplementary iodine.^{3,5} The relative prevalence and geographical distribution of follicular cancer may therefore be used as an indicator of iodine deficiency.

No systematic data on the racial or geographical distributions of thyroid cancers in South Africa have been published. In a small personal series of thyroid cancers in black Africans, Decker⁷ found that follicular morphology predominated, an observation which suggests that iodine deficiency was prevalent in this population. This conclusion is in keeping with a pilot survey carried out in 1954, which revealed apparently large rural 'islands' of endemic goitre seaward of the southern and eastern chain of mountains and in some north-western areas of the country.⁸ That widespread iodine deficiency probably persists in South Africa, as it does in other African countries,⁹ is supported by the identification of 3 additional goitrous populations (goitre prevalence 30 - 40%) since that time (W J Kalk — unpublished data) and by the persistence of a high goitre prevalence (34.5%) in schoolchildren in the Caprivi region of Namibia¹⁰ and in the south-eastern Transvaal (70%) (W J Kalk — unpublished data), previously identified as iodine deficient.⁸ In order to shed more light on nutritional iodine status in South Africa, we analysed national, regional and ethnic data on the incidence of papillary and follicular thyroid cancers as an indirect measure of iodine deficiency.

Methods

Two complementary data sources were used to measure the incidence and geographical distribution of thyroid cancer in South Africa. The South African National Cancer Registry (NCR) data of 1988 provided information on the ethnic but not the regional distribution of thyroid tumours. This registry records information on the incidence of all histologically diagnosed cancers via a network of all public and private histopathology, cytology and haematology laboratories ($N = 85$) in the country.¹¹ The primary site of cancer is coded using the *Systematic Nomenclature of Medicine*,¹² and the morphology is classified using the World Health Organisation's *International Classification of Diseases*.¹³ Three categories of thyroid tumour were identified — those of papillary and follicular histology, and other cancers. Crude incidence rates were obtained by dividing the number of cancers by the population at risk, estimated from national population figures obtained from the Central Statistical Services^{14,15} and adjusted to include the former 'independent' homelands.¹¹ Age-standardised rates for thyroid cancers were calculated using the 'direct' method and the 'World Standard Population'.^{15,16} Age-standardised rates were also adjusted for the proportion of thyroid cancer cases in the 'age unknown' category (13.6% of cases).

Secondly, we reviewed the computerised records of malignant thyroid tumours histologically diagnosed between January 1990 and June 1994 by the Pathology Department

of the South African Institute of Medical Research (SAIMR), Johannesburg. This laboratory provides diagnostic facilities for the public sector hospitals in the north-eastern part of the country (the former Transvaal), which serve the great majority of poor patients, predominantly from the black population. The records of blacks are therefore likely to be representative, while those of whites are probably biased by the omission of many younger insured patients who were managed privately. These data provided information on the hospital where surgery or biopsy was performed and, by inference, the region of residence of the patients and their gender and ethnicity. Detailed histological reports permitted some additional analysis of tumours classified as being of neither papillary nor follicular histology.

The chi-square test and the *t*-test were used in the statistical analyses.

Results

In 1988, 45 570 histologically diagnosed malignant tumours were registered in the country by the NCR, of which 359 (0.79%) were thyroid cancers (74 papillary, 92 follicular, 193 other thyroid cancers), giving a crude national annual incidence of 1.25/100 000. The crude and age-adjusted incidence rates for 1988 by race and gender are shown in Table I; adjustment for the populations' age distributions resulted in considerable changes in some groups. Thyroid cancers were approximately 3 - 5 times more frequent in the white population than in the other groups ($P = 0.004 - < 0.000001$), but the female/male ratios were similar in each racial group, ranging from 2.0 to 2.4.

Table I. The crude incidence and age-standardised incidence rate (ASIR) of all histologically diagnosed thyroid cancers by race and sex in South Africa in 1988, obtained from the National Cancer Registry

Race	Thyroid cancer	Population (millions)	Incidence per 100 000	ASIR
Females				
Black	99	9.895	1.00	1.1
Europid*	127	2.488	5.10	4.3
Indian	7	0.467	1.50	1.1
Mixed	12	1.584	0.76	0.9
Males				
Black	46	10.718	0.43	0.6
Europid†	53	2.454	2.16	1.8
Indian	3	0.461	0.65	1.3
Mixed	6	1.536	0.39	0.5
Total				
Black	145	20.613	0.70	0.8
Europid	180	4.942	3.64	3.0
Indian	10	0.928	1.08	1.1
Mixed	18	3.120	0.58	0.7

Race not recorded = 6.

* v. blacks — $P < 0.00001$; v. mixed race — $P < 0.00001$; v. Indians — $P = 0.0039$.

† v. blacks — $P < 0.00001$; v. mixed race — $P = 0.000014$; v. Indians — $P = 0.05$.

Follicular histology was slightly more frequent than papillary in the group as a whole, but predominated significantly in the black patients. Among the women, the

ratio of follicular to papillary morphology was 3.7:1 in blacks and 0.68:1 in whites ($P = 0.00007$), while in men of both groups follicular cancers predominated and the ratios were similar (1.38:1 and 1.63:1, respectively). In both sexes combined, the ratios were 2.67:1 in the blacks and 0.78:1 in the Europids ($P = 0.001$). Numbers in the two other subgroups were too small for meaningful comparison (Table II).

Table II. The distribution of histologically diagnosed thyroid cancer morphology according to sex and race

Race	Tumour histology			Total
	Follicular	Papillary	Other	
Females				
Blacks*	37	10	52	99
Europid	23	34	70	127
Indian	0	4	3	7
Mixed	5	4	3	12
Unknown	0	5	0	5
Total	65	57	128	250
Males†				
Blacks	11	8	27	46
Europid	13	8	32	53
Indian	1	0	2	3
Mixed	2	1	3	6
Unknown	0	0	1	1
Total	27	17	65	109

Source: National Cancer Registry, 1988.

* Follicular/papillary cancers v. Europids — $P = 0.0002$.

† There were no significant differences in distribution of cancer types in males.

The SAIMR pathology records provided information on 154 patients with thyroid cancer — 75 with papillary and 35 with follicular histology (71%); the remaining patients had anaplastic (13 cases), Hürthle cell (6), medullary (5), lymphoma (6), or metastatic (14) tumour morphology. This proportion (29%) of 'non-papillary' and 'non-follicular' morphology is substantially lower than in the National Cancer Registry, suggesting probable misclassification of some tumours in the NCR. The characteristics of the black and combined other races with papillary and follicular thyroid cancers are shown in Table III. The overall female/male ratio was 4.0:1 in each group, higher than in the NCR populations, and the blacks were younger than the other patients — 10 white patients were older than 70 years indicating probable selection bias. Of these patients, 74 (67%) underwent surgery at hospitals in the large towns and cities of the industrialised southern Transvaal, most in Johannesburg itself, and 36 (35 blacks) in smaller rural towns of the eastern (28 patients), western and northern Transvaal. Twenty-one of the 36 (58%) patients diagnosed in rural hospitals had follicular tumours compared with 16 of 74 (22%) patients diagnosed in urban hospitals ($\chi^2 = 13.1$; $P = 0.0003$). Among the black patients, 21 of 35 (60%) rural subjects exhibited follicular histology, compared with 10 of 40 (25%) urban patients ($\chi^2 = 8.0$; $P = 0.005$). The follicular/papillary cancer ratio in the urban blacks (1:4.0) was similar to that of the white patients (1:4.2), all of whom resided in urban centres.

Table III. Characteristics of patients of black and other ethnic origins with follicular and papillary thyroid cancers in the former Transvaal

	Blacks	Other groups*	
No.	75	35	
Age	44.3 (15.0)	55.8 (22.9)	$P = 0.001$
F/M	60:15	28:7	
Follicular/papillary	31:44	6:29	$P = 0.02$

Source: School of Pathology, SAIMR.

* Europids, Indians and mixed ethnic origins.

Discussion

Thyroid malignancies comprised only 0.8% of all recorded cancers in the country, with a national incidence of 1.35/100 000 in 1988, in keeping with the rarity of these tumours seen internationally.¹⁷ While the incidence was expectedly higher in women in each ethnic division, and the sex ratios were comparable, the incidence was significantly higher in whites than in other races. The most likely explanation for these apparent differences between population groups lies in unequal ascertainment — underdiagnosis, especially in blacks — due to lower levels of awareness¹⁸ and the uneven geographical distribution of health facilities in the country. About half of the black population resides in underdeveloped rural regions with poor health service provision. For example, in one hospital serving a black rural population some 40% of clinically diagnosed cancers were not histologically verified.¹⁹ In contrast most people of European and Indian origins live in industrial towns and cities with easily accessible public and private hospitals. These findings apply primarily to the black population, but they also apply to those of mixed race.

On the other hand, the observed differences in ethnic incidences of follicular and papillary thyroid cancers could be genuine. The incidence of each histological type in the whites — predominance of papillary neoplasms — was similar to that reported from iodine-replete Europe,⁵ while the predominance of follicular tumours in blacks strongly suggests that much of this population is iodine-deficient.^{5,6} This interpretation is supported by the regional data on thyroid cancers in the former Transvaal province. Here a female preponderance of thyroid cancers persisted, and in the blacks follicular cancers occurred significantly more frequently than in the other groups, although they were not the predominant histological type. Moreover, most patients with follicular neoplasms originated in the south-eastern and western parts of the province, areas identified some 40 years ago as iodine-deficient.⁵ In these areas papillary tumours were in the minority. These observations strongly suggest that the population living in the north-eastern regions of the country remain iodine-deficient. In contrast, papillary tumours were more frequent in the urban patients, whether black or white, evidence which suggests that these urban populations are likely to be iodine-replete.^{5,6} If this interpretation is extrapolated to the data from the National Cancer Registry, which indicated an almost threefold greater frequency of follicular cancers in blacks than in whites, it may be concluded that many rural areas in the country remain iodine-deficient. Moreover, the national ratio of papillary to follicular cancers in whites (predominantly urban)

was 1.2:1, suggesting that some white urban centres in the country may be iodine-deficient as well.

Weaknesses of this study are the incomplete ascertainment of thyroid cancer cases in the black population and the lack of precise data on the actual places of long-term residence of the black patients. In rural settings the hospitals where surgery was performed were probably close to the places of residence. Among apparently urban blacks the duration of residence in the major towns is obviously important but uncertain in the light of recent rapid urban migration.

In summary, the data presented show an overall predominance of follicular thyroid cancer in South Africa, especially in some populated rural areas and perhaps some towns. This indicates probable past and current widespread iodine deficiency in this country, as in many others in Africa.⁹ The data support the need for formal population studies on the prevalence and geographical distribution of iodine deficiency in South Africa, as well as a more accurate assessment of the incidence of the different types of thyroid cancer.

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