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## THYROID CANCERS IN NODULAR GOITERS IN KANO, NIGERIA

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### ABSTRACT

**Background:** Cancer is an occasional incidental finding in nodular goiter, but there has been no formal study on this disease in our locality.

**Aims and objectives:** To determine the occurrence of histologically diagnosed malignancy in patients who present with nodular goiters.

**Methodology:** This is a 7- year (2000-2006) retrospective study of all histologically diagnosed malignancies within nodular goiters at Aminu Kano Teaching Hospital, Kano

**Results:** There were 160 multinodular goiters during the study period, out of which 24 (15.0%) had histologically diagnosed cancer, and 1 out of the thirteen patients with solitary thyroid nodule (7.6%) had carcinoma. The ages of the patients with carcinoma ranged from 16 to 65 years, with a mean age of 38.8 years. Eighteen (72%) were females, and 7(28%) were males. Six out of the 25 cases of carcinoma were detected preoperatively by fine needle aspiration cytology. Well differentiated follicular carcinoma was the predominant histological type in 13(52%) cases, followed by papillary in 10(40%), medullary carcinoma in 1(4%) and anaplastic carcinoma in 1(4%) patient.

**Conclusion:** One-seventh of nodular goiters in our center harboured malignancy, and follicular carcinoma was the prevalent histological type. This is consistent with the findings elsewhere in endemic goitrous regions. Ultrasound guided fine needle aspiration would improve preoperative diagnosis and guide appropriate surgical management.

**Key Words:** thyroid, nodular goiters, malignancy, fine needle aspiration cytology. (Accepted 6 August 2009)

### INTRODUCTION

Nodular goiters are common causes of thyroid gland enlargement requiring surgical excision<sup>1-3</sup>. Although these lesions are generally benign, several studies have documented occasional malignancies within these supposedly non-neoplastic nodules. The reported frequency of cancer in nodular goiter varies widely from 4 to 20% and it is generally thought to be more common in Solitary thyroid nodule than in Multinodular goiters<sup>4-7</sup>. That cancer may arise within nodular goiter is not entirely surprising given the established epidemiological association between iodine -deficiency induced endemic goiter and follicular carcinoma<sup>8,9</sup>. Nodular goiters are derived from longstanding/ sporadic goiters due to sustained mitogenic stimulation of thyroid follicular cells by TSH<sup>8</sup>. Different subpopulations of follicular cells with variable response to TSH proliferative signals soon emerge. It is this differential growth rate of different populations of follicular cells that is largely responsible for the characteristic nodularity of the disorder<sup>8</sup>.

Several studies have demonstrated that the varied

proliferative rates of different follicular cell populations in nodular goiter are due to clonal genetic mutations particularly affecting TSH signalling<sup>8,10</sup>. Mutations in TSH signaling pathway are also known to be involved in follicular adenoma<sup>11</sup>. Thus it can be hypothesized that gradual acquisition of further mutations in cancer related genes via tumor progression can lead to malignancy in nodular goiter. RAS, PAX8, and RET are among the cancer genes that have been implicated in malignant transformation of thyroid follicular cells<sup>8</sup>. Nodular goiter may therefore be considered a neoplastic lesion.

Kano, in Northern Nigeria falls within the iodine deficiency endemic goiter zone, so it is pertinent to evaluate and ascertain the frequency of malignancy in nodular goiters in our locality, hence the relevance of this study.

### MATERIALS AND METHODS

This is a retrospective study of all surgically excised nodular goiters at Aminu Kano Teaching Hospital Kano (AKTH), Nigeria between January 2000 and 2006. The specimens were submitted to our histopathology laboratory for histodiagnosis. Biodata ( age, sex, distribution of thyroid lesions and histological type of thyroid cancer) were collated

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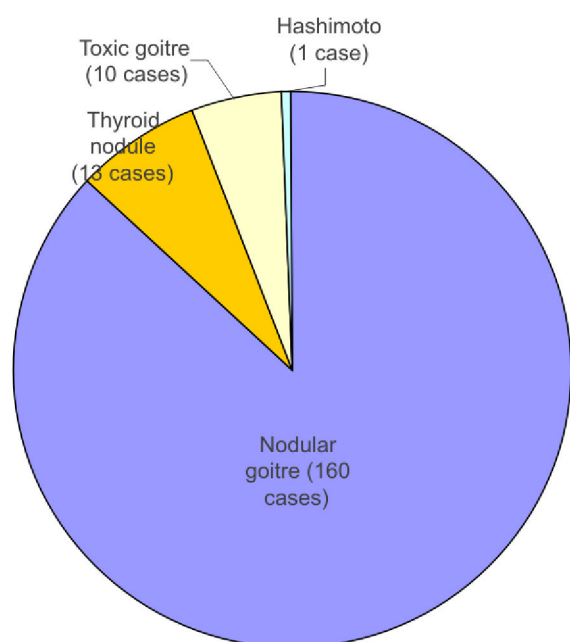
from the patients' case folders and histopathological records. All the patients were preoperatively evaluated by fine needle aspiration cytology (FNAC) and thyroid function tests. Biopsy specimens were fixed in 10% formol saline then processed into paraffin embedded sections and stained with haematoxylin and eosin. Histology slides were retrieved and reviewed by the authors. The results are presented in tables and figures.

## RESULTS

During the study period, 184 patients had thyroidectomy for various thyroid diseases. Based on intra-operative and histopathological findings, the lesions were classified as simple multinodular goiter in 160 (87.0%) patients, solitary thyroid nodule in 13 (7.1%), toxic goiters in 10 (5.4%), and Hashimoto's thyroiditis in 1(0.5%), as shown in figure 1. Thyroid carcinoma was detected in 25 (13.5%) out of the 184 thyroid lesions; twenty four of these was found in the 160 cases of multinodular goiters (15%), and 1 out of the 13 cases of solitary thyroid nodule (7.6%) had a focus of cancer. Carcinoma was detected preoperatively in 6 out the 25 cases (24.0%) by fine needle aspiration cytology. Of the patients with carcinoma, 18 (72%) were females and 7 (28%) males with ages ranging from 16 to 65 years with a mean of 38.8 years.

The histological types of the thyroid carcinoma are shown in table 1. Well differentiated follicular carcinoma of the thyroid was the predominant type in 13(52.0%) of cases, papillary carcinoma in 10(40.0%), medullary carcinoma in 1(4.0%), and anaplastic carcinoma in 1(4.0%). No lymphoma was recorded in this study. The mean age+sd of the patients with follicular carcinoma was 42+14.5 years while it was 38+16.0 years for papillary carcinoma.

Figure 1: Thyroid Diseases in Kano, Nigeria.



Males had more papillary carcinoma in 57.1% (4 out of 7 cases), and out of the 18 females 11 (61.1%) had follicular carcinoma, 6(33.3%) papillary carcinoma, and 1(5.6%) had medullary carcinoma (table 2).

Table 1: Thyroid Carcinomas in Kano.

Histological type	No. of cases	%
Follicular	13	52.0
Papillary	10	40.0
Medullary	1	4.0
Anaplastic	1	4.0
<b>Total (%)</b>	<b>25</b>	<b>100</b>

Table 2: Sex Distribution of Thyroid Carcinoma.

Histological type	Male	Female	Total (%)
Follicular	2	11	13(72.0)
Papillary	4	6	10(40.0)
Medullary	-	1	1(4.0)
Anaplastic	1	-	1(4.0)
<b>Total(%)</b>	<b>7</b>	<b>18</b>	<b>25(100)</b>

## DISCUSSION

The overwhelming majority of multinodular goiters(MNGs) are benign and the diagnosis is mainly clinical. However the primary challenge in the management of non functioning thyroid nodules is the exclusion of malignancy preoperatively by fine needle aspiration cytology (FNAC) with or without ultrasonography<sup>12</sup>. This procedure is limited by sampling error and expertise in the interpretation of cytological findings<sup>13</sup>. Sampling errors occasioned by the huge size of goiters seen in our center could explain the inability to preoperatively detect clinically unsuspected malignancy by FNAC in majority of cases. Moreover the predominant histological type which is follicular carcinoma is difficult to differentiate from follicular adenoma by cytological means. FNAC under ultrasound guidance or use of ultrasound guided core needle biopsy of a dominant nodule could enhance diagnosis and efficacy of the procedure<sup>12,14</sup>. Despite negative FNAC, nodular goiters can still harbor carcinoma as found in this study<sup>1-7</sup>. Therefore the key to diagnosis is careful definitive histopathological examination of resected thyroid tissues.

The risk of cancer in MNG is thought to be low compared to Solitary thyroid nodules(STN)<sup>15</sup>; but this is debatable<sup>7,16</sup>. The prevalence of cancer in published series varies widely from 4%-17% in MNG<sup>5</sup> and 9%-25% in STN<sup>6</sup>. The findings in this study are comparable

To other published reports<sup>2,4,6,7</sup>. The reasons for the marked variation in nodular goiter cancer rates are not always clear. Epidemiological studies have demonstrated that the incidence of cancer in MNG is higher than in general population<sup>4</sup>. Therefore the risk of malignancy in multinodular goiters should not be underestimated. Our findings are also in agreement with the assertion that in African zones of endemic goiter, the risk of cancer is much higher in MNG than in solitary thyroid nodules<sup>2</sup>.

There is regional variation in the incidence rates and histopathological types of thyroid cancers. The incidence of thyroid malignancy recorded in this study is comparable to others<sup>2,3,17</sup> but much lower figures have been reported elsewhere<sup>18</sup>. Majority of our patients are middle aged females, which is in keeping with others reports from our geographical area<sup>17,19</sup>, but in Caucasians it occurs in the 4<sup>th</sup> to 5<sup>th</sup> decade<sup>5</sup>. This lower age is probably related to endemicity of nodular goiters in our subregion<sup>17,19</sup>. The most frequently encountered malignant thyroid tumor is papillary carcinoma especially in areas where iodine intake is adequate<sup>4-7, 17</sup>, however in endemic goiter zones, the follicular variant is more common, due most probably to persisting iodine deficiency<sup>2,3</sup>. In contrast to a previous study from this center<sup>1</sup>, more cases of papillary carcinoma have been recorded. This changing pattern may be related to socioeconomic and environmental factors<sup>17</sup>. Thyroid lymphoma was not recorded, while medullary and anaplastic carcinomas are uncommon in this report as in others.<sup>2,3,17,19</sup> It was not known whether the case of medullary carcinoma in this study was sporadic or familial as the patient was lost to follow up after surgery.

This study has shown that the risk of malignancy in MNG is significant and the predominant histological type in our subregion remains the follicular variant.

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