Prevalence of thyroid antibodies in Nigerian patients

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Summary

Background: Thyroid antibody testing is not routinely available in developing countries, and few studies have measured thyroid antibodies in Africans. The significance of thyroid autoimmunity in an African setting is thus unclear.

Aim: To determine the prevalence of thyroid antibodies in patients attending a Nigerian teaching hospital.

Design: Prospective survey.

Methods: We measured antibodies to thyroglobulin (TgAb) and thyroid peroxidase (TPOAb) using an ELISA technique in 104 patients with various thyroid pathologies attending an endocrine referral centre in Lagos, Nigeria. Patients were clinically grouped into Graves’ disease (GD) (n = 69), simple non-toxic goitre (SNTG) (n = 21), toxic nodular goitre (TNG) (n = 8) and suspected Hashimoto’s thyroiditis (HT) (n = 6). Blood donors without thyroid disease (n = 100) acted as controls.

Results: TgAb and TPOAb were found in 4% and 7%, respectively, of healthy adult controls, 11.6 and 76.8% of patients with GD, 25% and 12.5% of patients with TNG and 9.52% and 14.29% of patients with SNTG. TPOAb testing confirmed HT in six patients, and identified two further cases that would have been misdiagnosed without antibody testing.

Discussion: Thyroid autoimmunity appears more common in these Nigerian patients than in previous reports from Africa, and TPOAb was significantly associated with auto-immune thyroid disease. The clinical utility of these antibody measurements requires further evaluation in a wider African population.

Introduction

The classic autoimmune thyroid disorders, Graves’ disease (GD) and Hashimoto’s thyroiditis (HT), are characterized by the presence of raised serum antibodies directed against thyroid antigens, namely thyroglobulin antibody (TgAb) and thyroid peroxidase antibody (TPOAb). These disorders are common in developed countries, where they form the bulk of the thyroid physician’s workload, but in Africa, such disorders are considered rare. For example, the incidence of GD in Whickham, UK was reported to be about 9/10 000 per year in females, whereas in Johannesburg, South Africa, it was at least ten times less common. HT is even rarer than GD in Black Africans, and is hardly ever diagnosed, either in the clinical setting or on examination of thyroid histopathological specimens. Studies of thyroid antibodies in African patients have been few to date, and in most instances have been performed with agglutination or immunofluorescence methods, which suffer from poor sensitivity and specificity. These methods have since been rendered obsolete by the advent of more sensitive and specific ELISA techniques. It therefore remains unclear whether autoimmune thyroid disorders are...
indeed rare in Africans, or if cases are overlooked due to the absence of appropriate diagnostic facilities. The latter possibility has implications for patient well-being, since undetected autoimmune thyroid disease carries considerable morbidity (reviewed in reference 18). In this study, we used an ELISA method to measure TgAb and TPOAb in healthy individuals and patients with various thyroid disorders seen in an endocrine referral centre in Lagos, Nigeria. Our aim was to determine the occurrence of thyroid autoimmunity in this setting.

**Methods**

**Patients and controls**

We studied 104 consecutive patients with various thyroid pathologies referred to the endocrine department of the Lagos University Teaching Hospital. This department provides an endocrine referral service for health facilities within the urban and suburban Lagos area. Each patient was independently examined by two physicians (OEO and AEO), and then placed in one of the following clinical categories: GD (n = 69), toxic nodular goitre (TNG) (n = 8), suspected HT (n = 6), and simple non-toxic goitre (SNTG) (n = 21). Inter-observer agreement between both examiners was high (κ = 0.98), and in two patients where there was discordance, a diagnosis was reached by consensus. After antibodies were tested, each patient’s case was reviewed and a final diagnosis was reached. We excluded patients with neoplastic goitres. In addition, we recruited 100 healthy blood donors aged 18–55 years (mean age 39.7 years), excluding donors who had a personal or family history of thyroid disease. Donors receiving immunomodulatory medications, e.g. corticosteroids, amiodarone or lithium were likewise excluded from the study. All participants consented to the study, and ethical approval was obtained from the local ethics committee.

**Clinical and biochemical examinations**

On collection, venous blood samples were immediately centrifuged, then frozen at −20°C and later transported to the UK in dry ice. FT4 and FT3 were measured with competitive labelled antibody assays, and TSH by a two-site immunochemiluminometric assay. These were analysed on an automated immunoassay analyser, the ACS-180 Plus (Chiron Diagnostics). Normal values were as follows: FT3, 3.5–6.8 pmol/l; FT4, 9.8–23 pmol/l; TSH, 0.35–5.2 mU/l. The between-batch precisions of the assays were estimated as coefficients of variation (CVs): FT4 (mean 13.6 pmol/l), 4%; FT3 (mean 5.27 pmol/l), 4.85%; TSH (mean 4.89 mU/l), 7.56%. TgAb and TPOAb were measured by an ELISA technique standardized against National Institute for Biological Standards and Control (NIBSC) reference standards, as previously described by Groves et al.19 Normal values were <98 kIU/l for TgAb and <19.4 kIU/l for TPOAb. Intra-assay variations were 4.9% for TPOAb (at a mean of 155 kIU/l) and 4.8% for TgAb (at a mean of 1350 kIU/l). Interassay variations were 7.6% for TPOAb (at a mean of 149 kIU/l) and 7.2% for TgAb (at a mean of 1387 kIU/l).

**Statistical analyses**

Values are presented as means (SD). Differences between groups were assessed by χ² test for proportions and by Mann-Whitney test and Students t test for quantitative data. Correlations between groups were assessed using Pearson’s coefficient of correlation. The level of statistical significance at which the null hypothesis was rejected was chosen as 0.05.

**Results**

**Demographic and clinical characteristics**

The age and sex distributions of patients and controls are shown in Table 1. There was a preponderance of females in patients with Graves’ disease, Hashimoto’s thyroiditis and simple non-toxic goitre. There were no significant age differences between males and females in any of the groups. In patients with GD, ophthalmopathy was present in 38 patients (55%), congestive cardiac failure in six and atrial fibrillation in two. The clinical presentation of six patients with HT is shown in Table 2.

**Serum levels of FT4, FT3 and TSH**

The results of the plasma thyroid hormone and TSH tests of the patients and controls are shown in Table 3. Five of the patients with SNTG had abnormal thyroid function tests: isolated low FT4 in two; isolated raised TSH in two; and isolated low TSH in one.

**Thyroid autoantibodies**

The prevalence of TgAb and TPOAb in various categories of patients and in healthy adults is shown in Figure 1. TgAb and TPOAb were present in 4% and 7%, respectively, of healthy adults. Of these, three were positive for TPOAb alone,
while four showed both TgAb and TPOAb activity. None was positive for TgAb without being positive for TPOAb. There was good correlation between the positivity for both antibodies in the control group $(r=0.88, p<0.05)$ but not in patients with thyroid disease $(r=0.27, p>0.05)$. TgAb and TPOAb were detected in 11.6% and 76.8%, respectively, of patients with GD, 25% and 12.5% of patients with TNG, and 9.52% and 14.29% of patients with SNTG. Two patients with SNTG had strong positive TPOAb activity; both had isolated raised TSH levels, thus raising a suspicion of autoimmune thyroid disease in these patients. Of six patients with a suspected diagnosis of HT, all tested positive for TPOAb, three were positive for both antibodies, and none was positive for TgAb alone.

### Discussion

Thyroid antibodies are an invaluable tool in the management of thyroid disorders. However, antibody testing is not widely available for routine clinical practice in Africa, and few studies have measured thyroid antibodies in African patients.\textsuperscript{8–17} The occurrence of thyroid autoimmunity, and hence the utility of antibody testing in African patients with thyroid disease, is therefore unclear. We used an ELISA method to determine the prevalence of TgAb...
and TPOAb in patients with thyroid disorders and healthy controls in Lagos, Nigeria, and found a higher prevalence of thyroid antibodies than has previously been reported in healthy Black Africans (Table 4).8–16 In Western populations, the prevalence of TgAb and/or TPOAb is estimated at about 10% of the general population,19 but the few available studies in Africans report a much lower prevalence (0–2.7%) in healthy individuals (Table 4).8–16 This seemingly reduced tendency for thyroid autoimmunity in Black populations is supported by studies in the US, in which thyroid antibodies are less prevalent in African Americans than in Caucasian Americans.20 However, the prevalence of TgAb (2.7%) and TPOAb (4.5%) reported in healthy African Americans is in excess of that generally observed in the indigenous African population, suggesting that environmental factors might contribute to the lower prevalence of thyroid autoimmunity in Africans. However, our prevalence of 4% for TgAb and 7% for TPOAb in healthy blood donors is comparable to that reported for African Americans, and greater than the reported prevalence from other African studies.

The discrepancy between our findings and other African studies may in part be due to differences in methodology. Some of the studies in Africans measured thyroid antibodies using agglutination methods, which are less sensitive than more recent ELISA and radioimmunoassay techniques (Table 4).10,11,13,14,17 However, it is unlikely that methodological factors alone account for these differences. For example, a recent study, using an ELISA method found a low prevalence of thyroid antibodies in healthy adults from Cameroon,8 and interestingly, an earlier study in Lagos, with similar demographics to ours, reported thyroid antibodies in only 1.4% of healthy controls.9

These differences may therefore reflect regional as well as temporal differences between the groups studied. Thyroid autoimmunity is uncommon in

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**Table 4** Thyroid antibody prevalence (%) in healthy Africans in previous studies

<table>
<thead>
<tr>
<th>Assay method</th>
<th>Location</th>
<th>TPOAb</th>
<th>TMAb</th>
<th>TgAb</th>
<th>Study size (n)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA</td>
<td>Cameroon</td>
<td>0</td>
<td>–</td>
<td>0</td>
<td>36</td>
<td>8</td>
</tr>
<tr>
<td>RIA</td>
<td>Lagos, Nigeria</td>
<td>–</td>
<td>1.4</td>
<td>0</td>
<td>70</td>
<td>9</td>
</tr>
<tr>
<td>TRCH</td>
<td>Kenya</td>
<td>–</td>
<td>0</td>
<td>1</td>
<td>99</td>
<td>10</td>
</tr>
<tr>
<td>TRCH</td>
<td>Cameroon</td>
<td>0</td>
<td>–</td>
<td>0</td>
<td>152</td>
<td>11</td>
</tr>
<tr>
<td>IF</td>
<td>Zimbabwe</td>
<td>0</td>
<td>–</td>
<td>0</td>
<td>230</td>
<td>12</td>
</tr>
<tr>
<td>TRCH</td>
<td>Sudan</td>
<td>–</td>
<td>1.2</td>
<td>1.2</td>
<td>83</td>
<td>13</td>
</tr>
<tr>
<td>TRCH</td>
<td>Ille-Ife, Nigeria</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>50</td>
<td>14</td>
</tr>
<tr>
<td>IF</td>
<td>South Africa</td>
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<td>0</td>
<td>2.7</td>
<td>37</td>
<td>15</td>
</tr>
<tr>
<td>TRCH</td>
<td>Somalia</td>
<td>–</td>
<td>1.2</td>
<td>0.9</td>
<td>338</td>
<td>16</td>
</tr>
</tbody>
</table>

TMAb, thyroid microsomal antibody; TRCH, tanned red cell haemagglutination method; IF, immunofluorescence.

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**Figure 1.** Percentage of subjects with positive TPOAb and TgAb in the various clinical groups. Asterisks indicate differences from control group: *p<0.05, **p<0.001, χ² test.
iodine-deficient areas but becomes more prevalent with improvements in iodine nutrition.\textsuperscript{21,22} The majority of participants in our study were resident in Lagos, a cosmopolitan city with improving salt iodization, diversified diets, and coastal access to sea foods. The soil iodine content in Lagos is higher than in the hinterlands, and endemic goitre is not as common as in iodine-deficient areas.\textsuperscript{23} Thus the prevalence of thyroid antibodies in the patients we have studied, rather than being typical of iodine deficiency, may reflect ongoing transition towards iodine sufficiency.

From the clinical perspective, thyroid antibodies were significantly more prevalent in patients with clinically diagnosed autoimmune thyroid disease than in non-autoimmune thyroid disease. In agreement with studies in Western populations, TPOAb was the more discriminatory of the two antibodies for diagnosing autoimmune thyroid disease.\textsuperscript{24} However, we observed a disproportionately low prevalence of TgAb in patients with autoimmune thyroid disease. A similar pattern has been noted in other African studies,\textsuperscript{10,17} and further studies will be required to clarify the dissociation between the two antibodies. In our patients with thyroid disease, GD was clinically recognizable in most instances, and TPOAb positivity supported this impression in the majority of cases. On the other hand, a diagnosis of HT was difficult to establish on clinical grounds alone, and antibody testing played a greater role in confidently distinguishing HT from cases of SNTG. Two patients who were clinically classified as SNTG had strong positive antibody activity, making it likely that these patients had HT.

One limitation of our study is the relatively small number of patients in the HT and TNG categories. However, HT is rarely diagnosed in Black Africans, and recruitment of large numbers of HT patients will be difficult to achieve in any sub-Saharan African setting. With respect to TNG, its relative rarity in this study may have been influenced by referral bias, since ours is a non-surgical unit and some patients with TNG might have been referred to primary surgical centres. The role of TPOAb in distinguishing autoimmune from non-autoimmune thyroid disease will therefore require clarification in a larger study of African patients with thyroid disease.

In conclusion, thyroid autoimmunity appears common in the African patients that we have studied. TPOAb was significantly associated with autoimmune thyroid disease, and identified cases of autoimmune thyroid disease which would otherwise have been misdiagnosed. With improvements in iodine nutrition, autoimmune disorders may become more frequently encountered by clinicians in Africa. The clinical utility of thyroid antibodies in African patients requires further evaluation in a wider population.

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**References**


