

# Characterizing Thyroid Disease and Identifying Barriers to Care and Treatment in Uganda

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## ABSTRACT

Thyroid disease in Uganda continues to be endemic, despite national salt iodination. This study describes the local characteristics of thyroid disease and identifies potential barriers to surgical access. A prospective database was established for all patients with suspected thyroid disease who presented to the Endocrine Surgery Clinic at Mulago National Referral Hospital in Kampala, Uganda in 2008. A cross-sectional study collected and analyzed for presentation, diagnostics and the surgical plan. A total of 89 patients were included, with an average age of 40 years, and 88% were women. The most common presentation was compressive symptoms (39%, n = 35), signs and symptoms of hyperthyroidism (30%, n = 27) and cosmetic concerns (16%, n = 14). Ultrasound, which is subsidized by the hospital, was performed in 85% of patients (n = 76). Thyroid function tests (TFTs), which are less subsidized, were done in 67% (n = 60). Of these, 27% (n = 16) were hyperthyroid and 7% (n = 4) were hypothyroid. Fine needle aspiration was done in 30% (n = 27) and were suspicious for malignancy in 27% of patients (n = 7). The most common diagnosis was multinodular goiter (n = 55) and tracheal compression or deviation and/or retrosternal extension was seen on imaging in 22 of 75 patients (29%). Thyroid disease in Uganda is more advanced, involves a different population than in Western countries and includes high rates of symptomatic multinodular goiter and cancer. Resource constraints limit the care of these clinically challenging conditions. Further evaluation of these potential barriers to surgical care needs to be conducted.

**Keywords:** Thyroid, Uganda, Surgical care, Africa, Thyroidectomy.

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## INTRODUCTION

Thyroid disease is endemic in many parts of the world. Much of this is related to iodine deficiency which can result in goiter, hypothyroidism, impaired physical and intellectual development that can lead to cretinism in severe cases during childhood, and pregnancy complications. Long-standing goiter is also associated with increased risk of follicular thyroid cancer. Multiple thyroid nodules are common and fine needle aspiration (FNA) biopsy may be falsely negative. Goiter also can result in

airway and esophageal compression, and shortness of breath thus, severely affecting quality of life which is a key indication for operative intervention.

The World Health Organization (WHO) estimates that 43% of the population in the African region, or approximately 260 million people, have insufficient iodine intake and has put in place universal salt iodination as the primary strategy to address the morbidity from iodine deficiency, particularly the neurologic consequences.<sup>1</sup> In Uganda, despite public health measures, such as fortification of salt with iodine, endemic goiter continues to be a major problem. Based on a cross-sectional study published in 2002, 64% of Ugandan households were thought to have adequate iodine intake, but rates of goiters in school-aged children were still quite high at 60% suggesting that iodine availability is a persistent problem. Visible (WHO Grade II/III) goiter was noted in 30% of children who were surveyed.<sup>2</sup> Thus, the burden of thyroid disease is a significant public health problem in this setting.

Surgery is the principle treatment for symptomatic goiters and thyroid cancers, and thyroid operations constitute a significant portion of major elective surgery in developing countries with high prevalence of endemic goiter.<sup>3</sup> However, surgical treatment for thyroid disease is particularly challenging in resource-constrained settings for many reasons including advanced disease, limited supplies and equipment, little formal training in complex endocrine operations for surgeons, and determination of the appropriate extent of thyroidectomy given the limited resources for thyroid hormone replacement therapy.<sup>3-5</sup> Yet, little is known about the epidemiology of thyroid disease seen by surgeons or the barriers to providing surgical care in these settings. This study aimed to characterize thyroid disease in the Ugandan population and identify possible barriers to surgical care and treatment.

## MATERIALS AND METHODS

Uganda is a former British colony and a country of approximately 32 million people.<sup>6</sup> The annual per capita income is \$420 which places it in low-income category as defined by the World Bank's classification system.<sup>7</sup> Kampala is Uganda's capital city and has a population of 1.2 million.<sup>8</sup> Mulago Hospital and Makerere University

in Kampala is the National Referral Hospital for Uganda and as a public facility provides free or highly subsidized care to the community.

Through an existing partnership between the Departments of Surgery at the University of California, San Francisco (UCSF) and Mulago Hospital and Makerere University, a collaborative project was begun in July 2008 to study all patients with suspected thyroid disease who presented to the Endocrine Surgery Clinic at Mulago Hospital.

In order to update and standardize medical records at the Endocrine Surgery Clinic, a template used as a part

of the medical records at UCSF was tailored to the Ugandan setting and established as a part of the clinic data collection system (Supplement 1). Clinicians used this form during each weekly clinic and integrated it into the medical records as a systematic approach to thyroid patients. After Institutional Review Board approval was obtained, data from the first 8 weeks after the template was introduced, was analyzed descriptively, as a pilot cross-sectional study. Thyroid disease presentation, diagnostic work-up and surgical plan were abstracted from the new medical record system and analyzed using Microsoft Excel (Seattle, WA).

**Supplement 1:** Thyroid intake form

<p><b>MULAGO Hospital</b>  <b>Breast and Endocrine Surgical Unit</b>  <b>Thyroid Intake Form</b></p>	<p>Patient Name: _____                  Birth Date: _____                  Patient Number: _____                  Date of Intake: _____</p>
<p>Gender: _____ Age: _____ Tribe: _____ Education: <input type="checkbox"/> None <input type="checkbox"/> Any Primary <input type="checkbox"/> Any Secondary <input type="checkbox"/> Any Advanced                  Birthplace (District): _____ Region: <input type="checkbox"/> North <input type="checkbox"/> South <input type="checkbox"/> East <input type="checkbox"/> West <input type="checkbox"/> Central</p>	
<p><b>Chief Complaint:</b> <input type="checkbox"/> Swelling/Mass in Neck <input type="checkbox"/> Dysphasia <input type="checkbox"/> Pain/Tenderness in Neck <input type="checkbox"/> Other (Specify) _____                  Duration of acute/presenting symptoms: _____</p>	
<p><b>Clinical Presentation:</b> <input type="checkbox"/> Pressure <input type="checkbox"/> Toxicity <input type="checkbox"/> Malignancy <input type="checkbox"/> Cosmetic <input type="checkbox"/> Other _____                  Specify all symptoms: _____                  Duration of symptoms: _____</p>	
<p><b>Risk Factors:</b> Hx of endocrine disease? <input type="checkbox"/> No <input type="checkbox"/> DM _____ <input type="checkbox"/> Thyroid _____ <input type="checkbox"/> Other _____                  Familial endocrine disease? <input type="checkbox"/> No <input type="checkbox"/> DM _____ <input type="checkbox"/> Thyroid <input type="checkbox"/> Other _____                  Hx of cancer: <input type="checkbox"/> No <input type="checkbox"/> Breast _____ <input type="checkbox"/> Ovarian _____ <input type="checkbox"/> Other _____                  Hx of treatment with radiation to neck or head? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Specify: _____                  Hx of traditional therapy? <input type="checkbox"/> Yes <input type="checkbox"/> No Specify: _____                  Number of Children: (deliveries) _____                  Dietary Intake: Cassava _____ Cabbage _____ Soya Beans _____ Others (specify): _____</p>	
<p><b>PMHx:</b> (RAI Ablation and other treatments, specify) _____</p>	<p><b>PSHx:</b> _____</p>
<p><b>Medications:</b> _____</p>	<p><b>Allergies:</b> _____</p>
<p><b>Thyroid Function Tests</b></p> <p>1. Date _____ TSH _____ nl value _____ T4 _____ nl value _____ T3 _____ nl values _____ Summary _____                  2. Date _____ TSH _____ nl value _____ T4 _____ nl value _____ T3 _____ nl values _____ Summary _____                  3. Date _____ TSH _____ nl value _____ T4 _____ nl value _____ T3 _____ nl values _____ Summary _____</p>	
<p><b>Imaging</b></p> <p>U/S: _____                  Thoracic Inlet: _____                  X-ray: _____</p>	<p>FNA: (reviewed at Mulago)                  Thyroid uptake T-99 _____                  IDL: <input type="checkbox"/> Normal <input type="checkbox"/> Abnormal: _____</p>
<p><b>Physical Exam:</b> Thyroid (lobes involved) _____</p>	<p>Lymphodes (specify) _____ Other _____</p>
<p><b>Diagnosis:</b> _____</p>	
<p><b>Treatment Plan:</b> _____</p>	

## RESULTS

### Demographics

A total of 89 patients were entered into the database. The average age was 40 years (range: 8 to >82). Women represented 88% of the patients. The most common clinical symptoms at presentation were related to compression of the trachea or esophagus, such as dyspnea on exertion and dysphagia, and signs and symptoms associated with hyperthyroidism, such as palpitations and hyperhidrosis. Twenty percent of patients reported one or more symptoms (n = 18; Table 1).

### Clinical Evaluation

During the initial presentation, the standard clinical evaluation included a detailed history of present illness, medical, surgical and family history, details regarding medication use, physical examination as well as thyroid function tests, ultrasound imaging and FNA biopsy as indicated in every patient with a thyroid nodule. However, many studies were not available through the hospital without cost or wait-time. Ultrasound imaging which costs \$6 is fully subsidized by the hospital. Thyroid function tests, which cost between \$25 and 45, are subsidized by 30 to 40%. FNA biopsy is fully subsidized but it has a wait-time of 1 to 2 weeks. Radioisotope scans using Technetium 99 are available but expensive and, therefore, not routinely used in patients with hyperthyroidism.

Sixty patients had thyroid function tests done which included serum levels of thyroid-stimulating hormone, triiodothyronine and thyroxine. The tests indicated that 66.6% of those undergoing testing were euthyroid (n = 40), while 26.7% were hyperthyroid (n = 16) and 6.7% were hypothyroid (n = 4). The laboratory values resulted in treatment changes in 75% of patients with hyperthyroidism. Two of the chemically hypothyroid patients received supplementation as of the time of this analysis.

Radiographic imaging obtained by patients included chest X-ray (n = 5), thoracic inlet view X-ray (n = 20) and neck ultrasound (n = 76). While advanced disease, such as tracheal compression or deviation and/or retrosternal extension are not typically diagnosed on X-ray or ultrasound, 22 of our 75 patients (29%) had these findings documented by a radiologist on such imaging studies. On plain radiography, 14 patients were noted to have advanced disease due to evidence of tracheal compression and/or deviation. Ten (13.2%) had ultrasonographic evidence of retrosternal extension of thyroid masses, with or without airway obstruction. One patient had superior

vena cava syndrome on physical examination (i.e. Pemberton's sign).

FNA biopsies, which are typically done by palpation because the nodules tend to be very large, were performed in 27 patients and 26% (n = 7) had cytology findings which were suspicious for cancer. Two additional patients were suspected to have cancer based on history of previous cancer resection and recurrent nodules in one case and hard lymphadenopathy on clinical examination in another case.

Utilization of these tests varied based on costs borne by the patient (Table 2). Ultrasound, which is fully subsidized by the hospital, was performed in 85% of the patients. Thyroid function tests, which are partly subsidized, were used in 67% of patients. FNA, despite being subsidized, biopsy, was performed in only 30% of patients reviewed at the time of this study.

### Diagnoses

The most common preoperative diagnosis was goiter (n = 55). Figure 1 shows the distribution of thyroid disease seen in this population. Goiters are further classified as nontoxic multinodular, toxic multinodular, recurrent multinodular and simple/solitary thyroid nodule. Most were multinodular (83.6%) compared with simple (16.4%) and 15% of all patients with goiter had signs and symptoms of hyperthyroidism. Figure 2 describes the overall characteristics of goiters at Mulago Hospital.

Cancer was suspected in 10% of patients (n = 9). Four had papillary thyroid cancer on FNA, two had follicular neoplasm and one had medullary thyroid cancer. One cancer was noted on physical examination to be suspicious for locally advanced thyroid cancer based on fixed bilateral glands. The patient was awaiting thyroid FNA biopsy at the time of this analysis. Another patient had a history of thyroidectomy for thyroid cancer of unclear type and was

**Table 1:** Most common presenting symptoms

	% (n)
Compressive symptoms	39% (35)
Signs of hyperthyroidism, e.g. tremors, palpitations, weight loss	30% (27)
Multiple signs and symptoms	20% (18)
Cosmetic concerns	16% (14)

**Table 2:** Utilization of preoperative testing

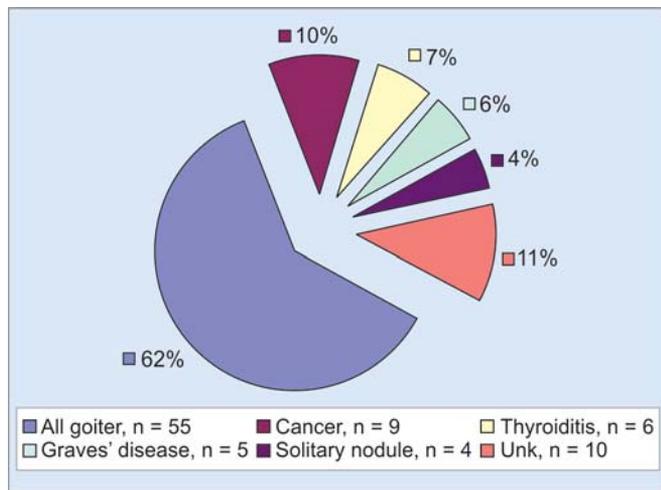
Type of test	Rate of utilization, % (n)
Ultrasound	85% (76)
Thyroid function tests	67% (60)
FNA biopsy	30% (27)

being reassessed for a new palpable lesion in the thyroid bed. Overall, 10 patients were awaiting accurate diagnoses at the time of this study.

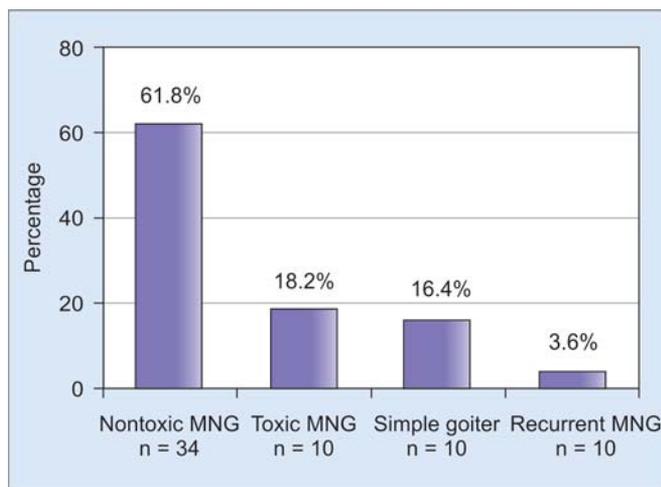
**Treatment**

Of 89 patients, 21 had or were awaiting surgery (Table 3). The standard practice for thyroid resections at Mulago Hospital is to remove all macroscopically affected thyroid tissue and leave the grossly normal tissue behind. With

this approach, it becomes academic to discuss of partial, subtotal and near-total thyroidectomy as the residual tissue will be determined by the intraoperative findings. The approach is as conservative as possible since, patients may never comeback for follow-up or be able to afford replacement therapy. The pseudocapsule, which is a normal compressed thyroid tissue, gives a nice plane of dissection and makes it easy to determine the amount of thyroid tissue that could be left behind in a partial or subtotal thyroidectomy. When a lobectomy is decided upon, the plane of dissection is the true thyroid capsule. Typically, unilateral lobectomies or partial thyroidectomies are preferred, particularly due to concern for advanced presentation and higher risk of complications in the patient population with advanced disease. Problems with the availability, cost and compliance of thyroxine treatment limit the extent of operation especially for patients who have traveled across the country to the referral hospital to have surgery. Based on this, the clinical preference is to consider the risks of leaving disease behind as lower than the risks of total thyroidectomy except in cases in which thyroid cancer is suspected preoperatively or intraoperatively. In those situations, total thyroidectomy with therapeutic lymph node dissection is the treatment of choice. Graves’ disease, in this setting, is diagnosed clinically as antibody testing is not available and is treated operatively when the glands are large or cannot be treated medically because of the cost of radioactive iodine (\$800-1200 per patient). Postoperative pathology data was not collected for this study as final results may require weeks to months.



**Fig. 1:** Epidemiology of thyroid disease at Mulago Hospital, Kampala, Uganda



**Fig. 2:** Distribution of goiter cases

	Number of patients
Partial thyroidectomy	6
Subtotal thyroidectomy	1
Total thyroidectomy	2
Unilateral lobectomy	3
Partial lobectomy	1
Planned	7
Operation but no information	1
<b>Total surgical treated</b>	<b>21</b>

**Complications**

Postoperatively, patients are monitored for 24 hours and then discharged if stable. The cross-sectional nature of this study did not allow for follow-up on postoperative complications. Nevertheless, standard monitoring after total thyroidectomy at Mulago Hospital includes checking postoperative calcium levels as well as clinical signs, such as Chvostek’s sign and Trousseau’s sign. Recurrent laryngeal nerve palsy is minimized intraoperatively with careful dissection on the thyroid gland. In all patients, preoperative indirect laryngoscopy or direct laryngoscopy is performed to assess baseline function. Postoperatively, vocal cord function is assessed at bedside. The patients are asked to talk and produce a high pitch sound to test the nerve. Indirect laryngoscopy is done 3 to 6 months later to assess for palsy in those patients who persistently have a hoarse voice. Risk of neck hematoma, a particularly challenging complication, is evaluated clinically by observing the effluent in the drainage bag if a drain is

inserted. However, sometimes the tube drain is deceptive. Thus, patients are also closely monitored for tension in the neck, dyspnea, restlessness, sweating and pallor in the early postoperative setting. Future studies, based on this prospectively established database, will be needed to determine the rates and impact of postoperative complications after thyroid operations.

## DISCUSSION

Goiter continues to be an endemic problem in many parts of the world.<sup>5,9</sup> Advanced disease is fairly common, and this puts these patients at higher risk for perioperative complications.<sup>10-12</sup> Costs and waiting times appear to affect utilization and access to routine diagnostic studies for the management of thyroid disease. The use of fully subsidized studies, such as ultrasound was greater than partially subsidized tests, such as thyroid function tests. FNA was only done on 30% of patients. The reasons for this are unclear but the data may not have been captured by this pilot study. Nevertheless, many barriers to availability, accessibility, affordability and acceptability may affect Ugandan surgeons' ability to diagnose and treat patients appropriately and close evaluation of barriers to obtaining surgical care for advanced thyroid disease is urgently needed.

This study also raises many interesting clinical questions. Hyperthyroidism was diagnosed in 27% of patients in this database which is high for a setting with endemic iodine deficiency. The etiologies for this finding were Graves' disease and multinodular goiter. These results may reflect the conversion of nonfunctioning nodules to hyperfunctioning state after iodine supplementation (Jod-Basedow effect) and could represent the transition from iodine deficient to iodine sufficient states. Other possibilities could include autonomous hyperfunctioning nodules to compensate for hypothyroidism or inaccurate laboratory reference ranges for this patient population.<sup>13</sup> Additionally, thyroid cancer was a concern in 26% of patients who underwent FNA biopsy which reflects a higher rate than has been reported in other studies of routine thyroid disease in the African setting.<sup>5,14,15</sup> Unfortunately, this study did not collect detailed data on the interpretation of these FNA biopsies but it would be useful to know the frequency of malignant, suspicious and indeterminate lesions to determine, if this high prevalence of cancer could be due to convenience sampling, technique or training in FNA biopsy, or training and experience in interpreting cytologic features of thyroid neoplasm.

There are many limitations to this study. The cross-sectional study design means that there is no follow-up

data on these patients. The small sample size and selection bias limit the conclusions that can be drawn. The single time point design also does not allow causality to be inferred. For example, while costs and waiting times appeared to affect the rate of utilization of diagnostic studies, this study design is inadequate to establish this finding as a causal relationship. The sample size of this study is small and limits the analysis of subgroups, such as patients with thyroid cancer to make meaningful conclusions. More steady research support on the ground will be needed to allow for continuous data collection and analysis and shift the focus from snapshots to longer term studies. Additionally, the study focused on patients presenting for surgical evaluation at a tertiary care center and, therefore, may be biased toward patients who are willing to transcend sociocultural barriers to access care, such as fear or distrust of surgery, concerns of infectious risks from hospitalization and cost of treatment. Furthermore, this study may have selected out those patients who are symptomatic due to advanced disease and are thus willing to obtain surgical consultation as a last resort. Therefore, the population studied in this case may not be representative of the general population of patients with thyroid disease in Uganda.

Nevertheless, many areas exist for future investigation based on our findings. Comparative studies of the epidemiology of thyroid disease between low- and high-income countries may be a rich area for research. Many have noted the differences in the pathology of thyroid cancer in areas with and without iodine deficiency. Follicular thyroid cancer, which is a more aggressive malignancy, has been noted as the most predominant subtype in iodine-deficient areas compared with papillary thyroid cancer which is most common in iodine sufficient settings. The rates of follicular cancer may be decreasing in some parts of sub-Saharan Africa due to aggressive policy measures to increase iodine intake.<sup>16</sup>

Additionally, there is very little data available regarding complication rates in the perioperative period in the African setting. The incidence of perioperative mortality, recurrent laryngeal nerve injury, recurrence of thyroid disease, permanent hypocalcemia, neck hematoma, need for re-exploration and infection could not be assessed in this study but these risks largely remain unknown in this setting. Rumstadt et al showed that thyroid surgery can be performed with low complication rates under basic surgical conditions in Burkina Faso by visiting surgeons.<sup>5</sup> However, other local African surgeons have reported higher rates of complications suggesting that resource-constraints have a significant influence on incidence.<sup>17</sup>

Postoperative mortality rates after thyroid operations in sub-Saharan Africa range from 3 to 10% in the reported literature compared with almost zero in developed countries and these rates are surely underestimates because of anesthetic and airway challenges in treating patients with advanced thyroid disease.<sup>11,12</sup> Reported rates of perioperative mortality may also be inaccurate due to suboptimal data collection systems and case series reporting which have inherent biases.<sup>3</sup>

Finally, there is a recent increased interest in the global health community in quantifying and understanding the global burden of surgical disease. Weiser et al have reported that only a fraction of surgical procedures are performed in the poorest countries in the world suggesting that there a vast burden of unmet surgical need which includes thyroid disease.<sup>18</sup> Research into the barriers of accessing surgical care in resource-constrained settings offers critical insight into areas for immediate action. Cultural, financial and structural barriers to access need to be explored further so that effective interventions may be enacted.<sup>19</sup> Academic institutions, in particular, may be uniquely poised to improve this inequity in access to surgical care through collaborations in research and clinical practice that raise the profile of unmet global burden of surgical disease.

Indeed, there are many challenges to research in resource-constrained settings, such as Uganda, not the least being the enormous lack of human resources, an organized medical record system and infrastructural limitations. The massive shortage of health care workers in Africa is well known as are the various factors that contribute to external and internal brain drain that draw clinicians away from the bedside or the operating room and may diminish the resources available to study endemic diseases, such as goiter.<sup>20-22</sup> The lack of an organized medical records system hampers efforts to understand the basic epidemiology of disease. Research conducted during patient care has the risk of delaying care for subsequent patients and is not a revenue neutral activity as it is in the United States and other settings that use medical records for billing purposes. Last, physical resource limitations, such as inconsistent access to equipment (e.g. thermometers and bloodpressure cuffs were rarely available), lack of support staff to collect data or keep records and limitations of patients' ability to pay deleteriously impact both surgical care and research.

## CONCLUSION

This study outlines the current epidemiology of thyroid disease at a tertiary referral center in sub-Saharan Africa. Numerous challenges, including barriers to accessing

testing and treatment for thyroid disease, exist in such resource-constrained settings. Uganda and other sub-Saharan countries bear a disproportionate burden of advanced surgical thyroid disease with almost zero resources put toward research or treatment. At the minimum, partnerships across countries offer prime opportunities to conduct research and help address the global burden of these endemic diseases which still affect large numbers of patients around the world.

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