

CHAPTER I. INTRODUCTION

1.1. Overview.

The reason for this study is to establish the incidence of missed malignancy on patients operated for benign multinodular goiter (MNG) diagnosed on fine needle aspiration (FNA) at Chris Hani Baragwanath Academic Hospital. To achieve this goal, we will compare the final histology (post-operative) with the FNA (pre-operative). The concern is that not all goitres require surgery and that decision is based on FNA and on clinical ground; therefore there is a risk of missing malignancy. FNA is the current gold standard that guides the management of goitre and it has a vital role to prevent unnecessary surgery.

1.2. Clinical presentations

A goitre usually presents as an anterior neck mass with or without retrosternal extension that moves up with swallowing; but other nodules may be detected incidentally during radiological evaluation of the neck. It can cause pressure symptoms related to the GIT and airways. It is commonly euthyroid but it can present with features of hyperthyroidism or hypothyroidism.

1.3. Diagnosis: role of FNA on the diagnosis of thyroid pathology.

The current gold standard for the diagnosis of thyroid diseases is FNA and this can be done with or without ultrasound guidance ^{1,2}. However there is a 1-13% incidence rate of false negative result^{3,4} and this emphasizes the need for repeat FNA and adequate follow up. Furthermore, the FNA cytology may be diagnostic or non-diagnostic. It is considered diagnostic if it is unequivocally benign, malignant or

suspicious of malignancy, whereas a non-diagnostic fine needle aspiration refers to either inadequate or indeterminate specimens.

Non-diagnostic FNA is either repeated or a biopsy is obtained in the form of lobectomy to get a tissue diagnosis (histology) that will dictate further management. FNA is important in the decision making of MNG and has significantly decreased the number of unnecessary thyroidectomies for benign disease^{1,5-9}. With reference to Bethesda classification, thyroidectomy is indicated in all categories except in THY 2 (benign goitre)(table 1).

Table 1. Currently recommended format of reporting thyroid FNA result (Bethesda classification) ⁶

Category	Cytological findings
THY 1	Insufficient specimen
THY 2	Benign (nodular goitre)
THY 3	Atypia of unknown significance
THY 4	Suspicious of neoplasm (follicular)
THY 5	Suspicious of malignancy (papillary, medullary, lymphoma)
THY 6	Definite malignancy

Patients in the category of benign cytology will only require surgery for:

- Cosmetic reasons.
- Pressure symptoms to the airway or gastrointestinal tract.
- Hyperthyroidism where there is contraindication to radioactive iodine.

The rest of the patients are followed up.

Current literature reports that FNA misses malignancy in around 7.2% of cases (ranging from 1-13%) when final histology is obtained post thyroidectomy ^{3,4}. This is partly explained by the fact that the dominant nodule is not necessarily the one

associated with malignancy as even smaller non-palpable nodules could harbor malignancy. Reported incidence of a missed malignancy is between 0.7 and 2.2% if ultrasound-guided FNA is used ^{10,11}

Ultrasound-guided FNA is particularly beneficial because it enables pursuit of “suspicious” nodule based on the following specific criteria: mixed echogenicity (cancer being hypoechoic), microcalcifications, microlobulated, irregular border having an anteroposterior diameter greater than the transverse, increased intranodular blood flow and the presence of a nodule “halo” in Doppler flow ^{1,7,12,13}

There are two techniques of FNA:

- Slide technique.
- Thin layer technique: this technique seems to be more advantageous.

A specimen is labeled adequate if it comprises of 6-8 groups of cells with number of 10 or more/group. If cancer is represented in all groups, malignancy is confirmed but if the malignant cells are present in few of them, it is termed suspicious.

Ultrasound guided FNA is not routinely done.

Prerequisite:

Nodule > 1cm difficult to aspirate.

Nodule < 1cm suspicious.

It is used in deep nodule, small nodule, non-palpable nodule, complex nodule and non-palpable adenopathy.

1.4. Multinodular goiter.

Benign goitre represents the majority of all thyroid pathologies whereas only a small minority are malignant ¹⁴. MNG is the most common disease of the thyroid and it affects 5 to 7% of the world’s population ¹⁴. It usually presents as an anterior neck mass that moves up with swallowing. The enlargement may be grossly multinodular

with or without a dominant nodule or can present as a solitary nodule. Although the majority of goitres are found in the neck associated with or without retrosternal extension, in a small minority it is diagnosed as a superior mediastinal mass when the thyroid gland is completely intrathoracic.

1.5. Causes of goitre.

MNG results from defective thyroid hormonogenesis for various reasons that include iodine deficiency (by far the most common)¹⁴, binding of iodine by goitrogens in foods (thiocyanate in cassava, vegetables of the brassica family) and dyshormonogenesis due to the deficiency or genetic defect of enzymes involved in hormone synthesis^{14,15}.

1.6. Risk of malignancy.

The risk of malignancy in the background of multinodular goiter is around 7.2%. Clinically, it is proportional to the size of the nodule. A palpable nodule carries the possibility of malignancy of roughly 10 to 14%; whereas recurrent laryngeal nerve involvement or enlarged neck lymph node are in keeping with malignancy.

Moreover, a family history of thyroid malignancy, previous external beam irradiation and exposure to high dose radioactive iodine are among the high risk factors in developing malignancy in MNG.

1.7. Thyroid cancer.

The most common malignancy of the thyroid is papillary carcinoma (80%), followed by follicular carcinoma (10-20%)^{16,17,25,26}. There are literatures suggesting the rise of

follicular carcinoma in iodine deficient countries¹⁶ and it remains the most frequently diagnosed thyroid malignancy in blacks in South Africa and on the rest of the African continent^{17,24,28} despite iodination of table salt since the 1980s. There is also a possibility that the follicular variant of papillary carcinoma can be mistaken as a follicular carcinoma or a benign histology to be labeled as a malignancy for the following reasons^{17,18} :

- A partially encapsulated hyperplastic nodule of a benign goiter can mimic malignancy.
- If the papillary component is overlooked, the specimen can be falsely diagnosed as a follicular carcinoma.

1.8. Incidental cancer.

Incidental cancer refers to the cancer that is discovered in the final histology post-operatively but was missed on pre-operative investigation (FNA).

In a recent study by Pisanu et al ¹⁹ (2009), 14.2% of histology of non-malignant fine needle aspiration results turns out to be malignant.

The risk of under-diagnosing malignancy in patients with multinodular goitre presenting to the department of Surgery at Chris Hani Baragwanath academic hospital is unknown.

1.9. Aim of the study

Therefore the aim of our study is to establish the prevalence of incidental malignancy and its histological type on patients who underwent thyroidectomy for MNG at Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg South Africa.

CHAPTER 2. METHODS

2.1. Study design

We audited the records of patients who underwent thyroidectomy at CHBAH between January 2005 and December 2010. Records included operating theatre entries, patient files and histopathology reports at the South African National Health Laboratory Service. Patients were referred to surgery from medical endocrinology, from our cluster hospitals or directly to our surgical outpatient department, resulting in non-uniform work-up. In general, it is our policy to do thyroid function tests and ultrasound scans on all patients; those with hyperthyroidism are referred for a thyroid scan, and the rest (euthyroid and hypothyroid) will have FNA.

2.2. Inclusion criteria

All cases with preoperative FNA of benign goitre and post-operative histology constitute our study group. The patients without post-operative histology are excluded.

2.3. Thyroid function test

The patient functional status were recorded and subdivided in three categories:

- Hyperthyroidism.

- Euthyroidism.
- Hypothyroidism.

We looked at malignancies in relation to the functional status of the patient

2.4. Type of thyroidectomy

Different types of thyroidectomy are performed depending on the underlying pathology. Total thyroidectomy with or without lymph node dissection depending whether we are dealing with benign or malignant disease. Papillary and medullary carcinoma will require lymph node dissection whereas total thyroidectomy alone is sufficient for follicular carcinoma. A lobectomy + isthmusectomy is indicated for benign unilateral goitre. In bilateral benign goitre total or near total thyroidectomy is the treatment of choice while subtotal thyroidectomy is viewed as substandard and is no longer recommended^{14,15}. There is no surgical indication for anaplastic carcinoma except for airway compromise where it is sometime indicated to split or to debulk the tumour to gain access to the trachea for a palliative tracheostomy.

It is our policy to perform total thyroidectomy for bilateral disease and differentiated malignancy associated with lymph node dissection where applicable (medullary and papillary carcinoma) or lobectomy + isthmusectomy for unilateral benign disease. Subtotal thyroidectomy is viewed as an inadequate procedure for both benign and malignant disease¹⁵.

2.5. Data collection

Data collected comprised demographic characteristics, thyroid function test results, FNA results, type of thyroidectomy and post-thyroidectomy histological findings. A sub-group consistent with MNG on final histology was identified and the percentage of missed malignancy with benign pre-operative FNA was determined. Excluded from this subgroup analysis were all patients with unavailable FNA results or FNA findings other than benign goitre.

2.6. Ethic approval

Ethical approval for the study was obtained from the Human Ethics Committee of the University of the Witwatersrand, Johannesburg, and the Research Review Board of CHBAH.

2.7. Statistical analysis

This observational cross sectional descriptive study uses mean, range and proportion by ratio or percentage. All data were collected on Microsoft excel spread sheet.

2.8. Demography

All patients that meet the inclusion criteria are represented irrespective of the gender, race or age. We expected an overwhelming majority of black Africans in keeping with the demography of the population studied.

2.9. Pre-operative FNA, post-operative Histology and incidental malignancy

Of all the FNA results, we selected those with benign report (THY 2) and the percentage of malignancy evaluated. The benign FNA represented the most common FNA report. The post-operative histopathological report of all cases were looked at and correlation with the pre-operative FNA was made. Specifically the malignant histology reports were compared with the pre-operative benign FNA (THY 2) to evaluate the incidence and the histopathological subtype of missed malignancy. In case of missed cancer, we will endeavor to understand how the malignancy were missed looking at the size of the nodule, the degree of lobe involvement or the bilobar disease.

CHAPTER 3. RESULTS

3.1. Demography

From the 166 thyroidectomies performed on 162 patients; there was 139 females and 23 males with a Female to Male Ratio of 6 to 1. The average age was 46 ranging from 15 to 79 years old (table1). The overwhelming majority of patients were of Black African origin.

Table 2. Patient demographics (N=162)

Male, n (%)	23 (14.2)
Female, n (%)	139 (85.8)
Female: male ratio	6:1
Age (years), mean (range)	46 (15-79)
Black, n (%)	146 (90.1)

3.2. Findings

There were 166 operations performed on 162 patients. Most of the patients were euthyroid 84.6% (137/162). The hyperthyroid and hypothyroid group represented 9.3% (15/162) and 6.2% (10/162) respectively. Total thyroidectomy and lobectomy represented the majority of the procedures 91.0% (151/166), depending on whether the disease involves one or two lobes. There were 74 total thyroidectomies (44.6%) and 77 lobectomies (46.4%). Other procedures include subtotal, near total, completion thyroidectomy, debulking and biopsy of supraclavicular mass with respective incidence of 3.0% (5/166), 1.2% (2/166), 2.4% (4/166), 1.8% (3/166) and 0.6% (1/166). There were 15 additional procedures (three tracheostomies and 12 lymph node dissections). A total of 120 pre-operative FNA results were available for evaluation, the remaining 42 FNAs were missing (20/42), not done (10/42) either because of hyperthyroidism or there was a biopsy obtained from other source (Fig.1)



Figure 1. Thoracic spine surgery for spinal pathological compression fracture that reveals follicular cancer.

or was unsuccessful (12/42). On cytological analysis, 78/120 FNAs suggested benign nodular goitre and the rest were labeled either atypical cell, malignancies (medullary, anaplastic, papillary), follicular tumour or Hashimoto thyroiditis (Table 3).

Table 3. Correlation between FNA and final Histopathology.

FNA	NUMBER= 162	HISTOLOGY
Atypical cell	13	5 Ca (4P,1F)
		2 Adenoma
		4 MNG
		2 Hashimoto
Benign Goitre	78	4 P (3FV,1PV)
		2 Adenoma
		1 Not found
		71 MNG (including 7 solitary nodule)
Not found	20	3 Ca (1F, 2P)
		2 Adenoma
		15 MNG (including 3 toxic MNG)
Follicular tumor	7	3 Adenoma
		1 A
		1 P (FV)
		2 MNG
Papillary ca	11	(7FV,4 PV).
Unsuccessful	12	2 P (1 FV, 1 Micropapillary)
		4 Adenoma
		6 MNG
Not done(due to previous biopsy, or not needed)	10	2 Biopsy (1F,1P)
		8 Toxic MNG
Anaplastic CA	1	1 A
Poorly differentiated tumor	1	1 A
Fluid aspirate(?tb, hiv +ve)	1	1 Thyroid cyst
Hurthle cell neoplasm	5	1 MNG
		2 Ca (P and F)
		2 Adenoma
Medullary ca	1	1 M
Hashimoto	1	1 Hashimoto

3.3. Incidental carcinoma

From our study population of 78 available benign FNAs; one case was excluded due to missing histology and 7 cases had single nodule. Of the 70 cases of MNG, Incidental malignancy was reported in 5.7% (4/70).

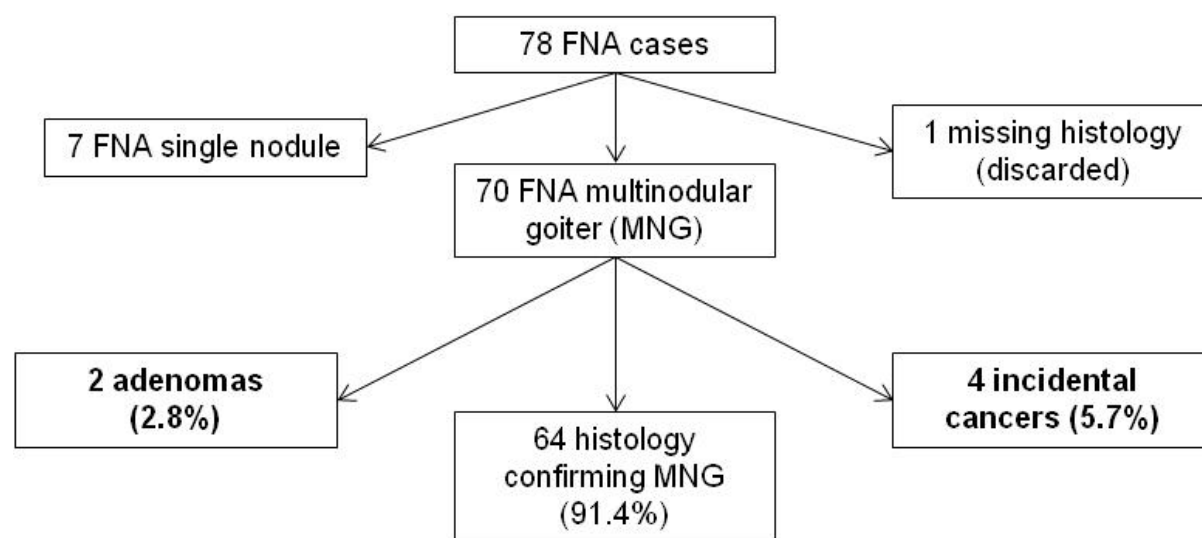


Figure 2. Breakdown of 78 FNA results of benign goitre

All the incidental malignancies were papillary carcinoma with follicular variant representing the commonest histological subtype (75%). (Table 4)

Table 4. Histopathological types and size of nodules of incidental cancers in MNG

Case	Age (years) /Gender	Histology	Size (cm)	Pathologist comment	Thyroid function	Procedure
1	43/F	FV	15x10x30	Diffuse tumour confined to left lobe	Euthyroid	Left lobectomy
2	29/F	FV	2.7x3x6	Tumour confined to the right lobe	Euthyroid	Right lobectomy
3	33/F	FV	5x4.1x3	Tumour confined to the right lobe	Euthyroid	Right lobectomy
4	16/F	PV	4.5x5x3	Multicentric tumour	Euthyroid	Total thyroidectomy

F: Female, FV: Follicular variant of papillary carcinoma, PV: Pure (classical) variant of papillary ca

3.4. MNG on final histopathology

Overall on final histopathology 66.0% (107/162) of the cases were due to MNG including 11 toxic MNG. The remaining cases were due to malignancy 21.6% (35/162) and others 12.3% (adenoma, Hashimoto thyroiditis and Graves' disease)

Table 5. Findings on final Histopathology

Histology	Number = 162
Malignancy	35
Goitre	107
Adenoma	15
Grave's disease	1
Hashimoto	3
Not found	1

3.5. Thyroid malignancy

The total percentage of malignancy was 21.6% (35/162); of note in one case there was coexistence of two malignancies (papillary and follicular carcinoma). The most common histopathological type was papillary carcinoma 75% (27/35). 45.8% (11/24) of the papillary carcinoma were diagnosed on preoperative FNA. In the remaining case the FNA suggested either atypical cell, benign goitre or were not available. The overall mean age was 47.4 years (15-79), predominantly female 80% (28/35).

Table 6. Distribution of 36 malignancies in 35 patients.

Malignancy	Variant	Number=	Percentage
		36	
Papillary	FV	16	75
	PV	10	
	micropapillary	1	
Follicular		5	13.8
Anaplastic		3	08
Medullary		1	02

CHAPTER 4. DISCUSSION.

4.1. Multinodular goitre

MNG is the most common pathology of the thyroid gland. It is also the most frequent indication for thyroidectomy in our hospital despite the implementation of iodination of salt in South Africa since the 1980s²⁰. Although other factors could have caused MNG in our patients, persistent iodine deficiency could still be considered since the iodine content in different brand of salt marketed in South Africa varies^{21,22}. MNG can present as a dominant or as a solitary nodule. Surgery is considered when there is pressure symptoms or cosmetic concern with its psychological implication.

Infrequently, the patient can present with toxic MNG that also add to the indication

for surgery. In our study, there were 11 cases of toxic MNG out of the 107 diagnosis of MNG when final histology was obtained.

4.2. Fine needle aspiration

This is currently the gold standard diagnostic tool for goitre since the biopsy is best avoided for the thyroid gland is well vascularized and there is risk of hemorrhage. When needed, biopsy is often obtained after diagnostic lobectomy in case of failed or equivocal FNA. In our study 91.4% (64/70) of MNG diagnosed on FNA were confirmed in final histopathology. Only 4 cases of benign goitre on FNA turn out to be malignant (incidental carcinoma). This has therapeutic implication since majority of the cases are benign; expectant management with follow up can significantly decrease the rate of unnecessary operation and therefore diminish the risk of complication post thyroidectomy. The reason why FNA missed obvious malignancy in our study can be explained by the fact that not all nodules harbor malignancy. In general, the bigger the size, the higher the risk of malignancy. Nodule of small size (<4 cm) has 1.3% of cancer vs. the nodule of more than 4 cm (4.3%)⁷. To predict which nodule is suspicious for malignancy, sonographic findings are needed that can suspect malignancy even in non-dominant nodule. The use of ultrasound contributed to the low incidence (0.7 and 2.2 %) of incidental cancer in Lowhagen T and Grant CS study respectively^{10,11}. However, it is not routine practice to perform FNA under sonar guidance since it can heavily impact on the workload of the sonographer. It is usually recommended for smaller nodule <1 cm (deep seated or non-palpable) or nodule >1 cm (suspicious, complex, difficult to aspirate). The FNA preceded thyroidectomy in the majority of our cases. It was not sensitive enough to diagnose all the 35 cancers pre-operatively, but all FNA reports of malignancy were confirmed on final histopathological examination. The sensitivity of FNA to diagnose papillary

carcinoma was only 45.8% (11/24). Nevertheless, even in the case of histologically confirmed cancer not diagnosed by FNA, the patient will still qualify for diagnostic lobectomy because according to the Bethesda classification (table 1), all categories will require surgery except for the THY2 (clearly benign disease).

4.3. Histopathological findings of malignancy

There was 26.1% (35/162) of reported malignancy of which 4 cases were incidental finding. The papillary carcinoma was by far the most common malignancy in both the incidental and non-incidental cancer with 100% and 75% occurrence respectively. Likewise, the follicular variant represented the most frequent histological subtype (3/4 of the cases) in both group. This is in contrast with Rumstadt et al's²³ report of true follicular carcinoma in their incidental cancer on patient with MNG. The incidental cancer in our patients were larger than 4 cm in diameter and therefore prognostically significant. Our results echoed the findings of Pisanu et al¹⁹ who reported similarly large incidental cancers in patient undergoing thyroidectomy for benign goitre.

Our incidence of 75% for papillary carcinoma and 13.8% of follicular carcinoma are opposite to the findings by Mulaudzi et al²⁴ from another tertiary hospital within South Africa who reported an incidence of 16% and 68% respectively in black patients with thyroid cancer at King Edward VIII Hospital in Durban. Possible explanation is that South Africa is no longer considered iodine deficient area or follicular variant of papillary cancer could have been be misinterpreted as true follicular carcinoma. It is also possible that pseudo-encapsulated adenoma or hyperplastic nodule of benign goitre could be misinterpreted as follicular carcinoma.

The pattern of occurrence of thyroid cancers in our study was consistent with the profile of thyroid cancers in iodine rich areas^{3,18,25}. Our incidental cancer predominantly papillary carcinoma is also in keeping with recent findings in many regions around the world^{13,16}. Only one of our four patients with incidental thyroid cancer had features of classical papillary carcinoma, the remaining three had the characteristics of the follicular variant of papillary carcinoma. It is probable that some of these tumours could have been diagnosed as follicular carcinomas if no special emphasis had been placed on nuclear features and immunochemistry^{17,18,26}. The 5.7% prevalence of missed malignancy in this study is within the range reported previously. Figures in the literature range from 0.7% to 13% with an average of 7.2%. The availability of ultrasound-guided FNA, the limitations of cytology, the cytologist's expertise and the iodine status of the environment are factors that probably explain the worldwide difference in incidence.

Our 5.7% false negative rate for FNA in detecting cancer is similar to the findings of Rumstadt et al²⁷ (false negative rate 6%) in their retrospective audit of MNG post thyroidectomy. The incidental cancer rate in our study was far lower than the rate in benign thyroid disease reported by Bradly et al⁴. The following shortcomings should be noted. Only patients who had thyroidectomy were included in the study, so our findings may not reflect the true incidence of thyroid cancer in our region. Many patients with small nodule are managed non-surgically by endocrinologists. However, it is likely that their inclusion would have reduced the incidence of thyroid cancer, because patients who are not referred for surgery generally have small nodules that are unsightly and do not cause pressure symptoms. Although these small nodules (<4 cm) can still be malignant, the prevalence of malignancy is lower than in larger nodule. We had no access to the information on how the FNAs of

patients with clinical features of MNG were done. It is highly unlikely that ultrasound guidance was used, which could explain why the pre-operative FNA missed malignancy in all four cases of incidental cancer with large tumours almost replacing the entire lobe. It is also possible that the FNA may have sampled the area of intra-tumoural necrosis. Ultrasound-guided FNA is likely to avoid these problems. Three of the four patients with incidental cancer had inadequate procedure. Had the presence of cancer been known pre-operatively, they would have had total thyroidectomies.

Age is important in the prognosis of differentiated thyroid malignancy of follicular origin. In patients of favorable age (<40 years for male and <45 years for female, there are only two stages, stage I and II (stage III and IV behaving the same as stage II). Interestingly, all our patients with incidental cancers were female, aged < 45 years, and fell into the low-risk group. However, the sample is small and statistical power is low. The mean age of the four patients with incidental cancers was 30.25 years, versus 50 years in the 31 patients with non-incidental cancers. Incidental cancers accounted for 11.4% (4/35) of all cancers in our study.

Cosmetic concerns play an important role in the decision-making. Our impression is that many patients feel uncomfortable about keeping their goitre, even if it is small and benign, and request surgery. The fact that so many patients with benign FNA undergo surgery will reduce the incidence of missed malignancy. Furthermore, patients with pressure symptoms qualify for surgery irrespective of the FNA findings.

4.4. Hyperthyroidism

We had few cases of hyperthyroidism. Of note, there was only one case of Graves' disease; this particular patient had a large goitre (Fig.3) with pressure symptoms (dysphagia and dyspnea) that required total thyroidectomy. Our figure is likely to be biased because in our institution most of these cases are treated medically with anti-thyroid medication followed by radioactive iodine. The majority of cases of hyperthyroidism were toxic MNGs (11 cases) with two cases of toxic adenoma and one malignancy (follicular carcinoma). It is our policy not to perform FNA on hyperthyroid patients as the FNA finding in that context can mimic malignancy.

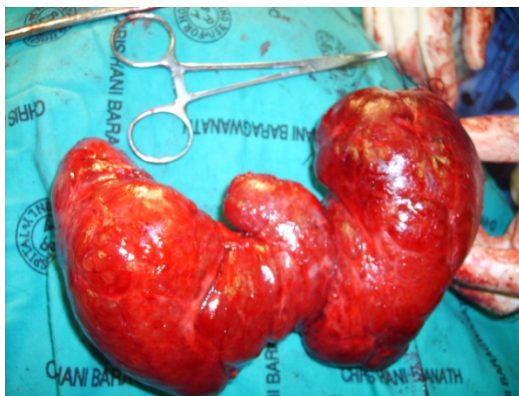


Figure 3. Large goitre from a patient with Grave's disease

4.5. Limitation of the study

4.5.1. Missing or incomplete data

Being a retrospective study, some data were either missing or incomplete. It was not possible to find out whether the FNA done on our patients were sonar guided although we presume that it is highly unlikely that sonar guided FNA were commonly used.

4.5.2. Selection bias

Our study includes only the patients who had surgery for MNG. The non-operated group is likely to have small nodule therefore not posing cosmetic concern or causing pressure symptoms.

Hyperthyroidism can be under estimated since not all cases are treated surgically. Graves' disease is mostly treated non-operatively (anti-thyroid drugs and radioactive iodine).

4.5.3. Sample size

The relatively small sample size can affect statistical analysis and this fact should be taken into consideration in the interpretation of the results.

CONCLUSION

Thyroidectomy is a procedure that can result in significant morbidity that can be disabling to the patient; it should be performed when there is a clear indication and the benefit should justify the risk. The FNA and clinical presentation (pressure symptoms, cosmetic consideration, hyperthyroidism) guide the management. The risk of malignancy is a concern in a benign goitre especially in a high risk individual. Such individual should be counseled about the potential benefit of surgery, the need for follow up and the complications of surgery.

In our study, the risk of incidental cancer in patients with MNG undergoing thyroidectomy was 5.7%, and the commonest histological subtype was papillary

carcinoma, mainly the follicular variant. Patients, especially those at relatively high risk, should be made aware that there is a slight risk of missing malignancy. The use of ultrasound-guided FNA is likely to lower this risk.

Recommendations.

1. A lot of unnecessary surgery can be avoided on patient with benign FNA since the risk of incidental malignancy is not significant. It is unnecessary risk to operate on benign FNA without appropriate indication.
2. In South Africa, since the implementation of the iodination of the salt three decade ago, it will be interesting to evaluate our current iodine status because our result suggests that we are iodine sufficient nation.

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APPENDIX A

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

R14/49 Dr Ifongo Bombil

CLEARANCE CERTIFICATE

M110325

PROJECT

Incidental Cancer in Multinodular Goitre Post
Thyroidectomy (revised title)

INVESTIGATORS

Dr Ifongo Bombil

DEPARTMENT

Department of Surgery

DATE CONSIDERED

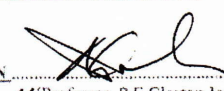
25/03/2011

DECISION OF THE COMMITTEE*

Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 21/08/2013

CHAIRPERSON 
// (Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr TE Luvhengo

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix B. List of corrections

1. Page xii. SAJS (South African Journal of Surgeons) change to: (South African Journal of Surgery)
2. Page 4. Line 23: malignants changed to “ malignant”
3. Page 8 line 6: Pathology changed to “pathology”
4. Page 11 line 4: “respectively” added after “...9.3% (15/162) and 6.2% (10/162)”
5. Page 20 line 15 “cancer s” changed to “cancers”
6. Page 23 line 8. Paragraph 2 has been revised