

# Incidental Cancer in Benign Thyroid Disease: An Experience at the University Hospital of the West Indies

R Forde, M Brown, A Mitchell

## ABSTRACT

**Introduction:** There has been a marked increase in the incidence of thyroid cancer worldwide over recent decades. Some studies have suggested that the probability of finding malignancy is similar in both multinodular goitres and solitary nodules. There is a paucity of data regarding incidental thyroid cancer (ITC) in the West Indies literature. The aim of this study is to report our experience with ITC in order to examine the frequency of cancer in resected specimens for benign thyroid disease and to better characterize this entity.

**Methods:** A retrospective chart review was performed on 753 patients who had a final histological diagnosis of benign thyroid disease after surgery between 2000 and 2009 at the University Hospital of the West Indies (UHWI). Twenty-one patients who had ITC had their charts analysed regarding the preoperative findings and histopathological diagnosis and this was compared to the preoperative and histological findings for 65 patients who had frank malignancy with no benign thyroid disease. The data were analysed using SPSS 22 software.

**Results:** There were 753 patients with postoperative histopathological reports of multinodular goitre (MNG). Twenty-one of the 753 patients (3%) with MNG were found to have a malignancy. The mean (SD) age of presentation of ITC was 48 (11.7) and the female-to-male ratio was nine to one. There were similar demographics for the 65 patients with frank thyroid carcinoma. There were no statistically significant preoperative clinical or diagnostic findings associated with ITC. Eighteen (86%) ITCs were of the papillary type. Follicular carcinoma was seen in 9% and hurthle cell carcinoma accounted for only 5%. There were no cases of medullary or anaplastic carcinoma. While in the frank carcinomas, papillary accounted for 70%, follicular 9% and 7% each for medullary and anaplastic carcinoma.

**Conclusion:** The frequency of cancer in multinodular goitre in Jamaica of three per cent is lower than other frequencies seen worldwide of both ITC and cancer arising from a solitary nodule. It is seen more commonly in the middle-aged females. Patients with MNG need a careful evaluation for the risk factors and require investigations such as an ultrasound and fine needle aspiration cytology (FNAC). Incidental thyroid cancers are most common of the papillary type which has a good prognosis.

**Keywords:** Incidental thyroid cancer, incidentalomas, multinodular goitre

# Cáncer Incidental en Enfermedades Tiroideas Benignas: una Experiencia en el Hospital Universitario de West Indies

R Forde, M Brown, A Mitchell

## RESUMEN

From: Department of Surgery, Radiology, Anaesthesia and Intensive Care and ENT Division, The University of the West Indies, Kingston 7, Kingston, Jamaica, West Indies.

Correspondence: Dr R Forde, Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Kingston 7, Jamaica, West Indies. Email:royantonioforde@hotmail.com, draforde@gmail.com

**Introducción:** *Ha habido un marcado aumento en la incidencia del cáncer de tiroides en todo el mundo durante las últimas décadas. Algunos estudios han sugerido que la probabilidad de encontrar malignidad es similar tanto en el bocio multinodular como en los nódulos solitarios. Hay escasez de datos sobre el cáncer incidental de tiroides (CIT) en la literatura de West Indies. El objetivo de este estudio es reportar nuestra experiencia con el CIT con el fin de examinar la frecuencia de cáncer en especímenes resecados para tratar enfermedades tiroideas benignas y para caracterizar mejor esta entidad.*

**Métodos:** *Se realizó una revisión retrospectiva de las historias clínicas de 753 pacientes que tuvieron un diagnóstico histológico definitivo de enfermedades tiroideas benignas después de la cirugía entre 2000 y 2009 en el Hospital Universitario de West Indies (HUWI). A veintiún pacientes que tuvieron CIT se les analizó sus historias clínicas en relación con los hallazgos preoperatorios y el diagnóstico histopatológico, comparándose estos luego con los hallazgos preoperatorios e histológicos de 65 pacientes que tenían evidente malignidad sin enfermedad tiroidea benigna. Los datos fueron analizados utilizando el software SPSS 22.*

**Resultados:** *Hubo 753 pacientes con reportes postoperatorios histopatológicos de bocio multinodular (BMN). Se halló que veintiuno de los 753 pacientes (3%) con BMN tenían un tumor maligno. La edad promedio (SD) de la manifestación del CIT fue 48 (11.7) y la relación hembra-varón fue de nueve a uno. Hubo una demografía similar para los 65 pacientes con carcinoma de tiroides clínicamente evidente. No hubo hallazgos diagnósticos o clínicos preoperatorios estadísticamente significativos asociados con el CIT. Dieciocho (86%) de las malignidades de CIT fueron de tipo papilar. Se observó carcinoma folicular en 9%, en tanto que el carcinoma de células de Hürthle representó sólo el 5%. No hubo casos de carcinoma medular o anaplásico. Si bien dentro de los carcinomas clínicamente evidentes, los papilares representaron un 70%, los foliculares representaron un 9%, y 7% los carcinomas medulares y anaplásicos respectivamente.*

**Conclusión:** *La frecuencia de cáncer en el bocio multinodular en Jamaica, estimada en un tres por ciento, es menor que otras frecuencias observadas en todo el mundo tanto con respecto a CIT como en relación con el cáncer proveniente de nódulos solitarios. Se observa más comúnmente en las mujeres de mediana edad. Los pacientes con BMN necesitan una evaluación cuidadosa de los factores de riesgo y requieren investigaciones tales como ultrasonidos y citologías de aspiración con aguja fina (CAAF). Los cánceres tiroideos incidentales son comúnmente de tipo papilar, los cuales tienen un buen pronóstico.*

**Palabras claves:** Cáncer incidental de tiroides, incidentalomas, bocio multinodular

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## INTRODUCTION

Thyroid cancer represents the most common cancer in the endocrine glands and may occur as a solitary nodule or a dominant nodule in a multinodular gland (1). There has been a marked increase in the incidence of thyroid cancer worldwide over recent decades (2). The incidence of thyroid cancer ranges from 0.9% to 13% (3). The majority of thyroid cancers are well differentiated and are of a follicular origin and includes: papillary, follicular and hurtle cell carcinoma. Medullary carcinoma accounts for 6% of thyroid cancers and anaplastic carcinoma which is an aggressive malignancy, accounts for 1% (3). A thyroid incidentaloma may be discovered during a histopathologic examination of surgical specimens

of thyroidectomy for benign thyroid disease. The diagnosis of incidental thyroid carcinoma (ITC) in patients operated on for a benign disease is frequent (4). The prevalence has been found to vary between 4% to 17% (5). The incidence of malignancy in solitary nodules is not significantly higher (5). These studies suggest that the risk of malignancy in both multinodular goitres (MNGs) and solitary nodules are similar. This would suggest that both MNG and the solitary nodule should be evaluated to detect any underlying malignant disease. But, there is a paucity of data regarding incidental thyroid cancer (ITC) in the West Indies literature and there are no data published on the prevalence of thyroid cancer in benign thyroid disease in Jamaica. We report our experi-

ence with ITC in order to examine the prevalence of cancer in resected specimens for benign thyroid disease and to better characterize this entity in terms of its clinical characteristics and histopathological types.

## SUBJECTS AND METHODS

The research proposal for this study was approved by the University Hospital of the West Indies/The University of the West Indies/Faculty of Medical Science/Ethics Committee. The archives of the Department of Pathology at the UHWI were reviewed over a ten-year period from 2000 to 2009 and all the reports on the final histological diagnosis of benign thyroid disease were extracted. From those reports, all the cases with ITC in benign thyroid disease were further analysed and the total number was used to determine the frequency of ITC in benign thyroid disease. Benign thyroid disease included: nodular hyperplasia, diffuse hyperplasia and thyroiditis. Incidental thyroid cancer in this study was defined as cancers discovered in benign thyroid disease during a histopathological examination of surgical specimens of thyroidectomy. The patients who met these criteria had their charts reviewed for the data regarding clinical features, preoperative diagnostic investigations and histopathological diagnosis. These results were compared with patients with frank carcinoma who had no benign thyroid disease during the same time period to determine if there were any similar characteristics between the two groups using Pearson Chi-square analysis. All the data were analysed using the Statistical Package for the Social Sciences (SPSS) 22 software to look at variables such as the mean, median, range and proportions.

## RESULTS

There were 753 patients with postoperative histopathological reports on MNG. Twenty-one of the 753 patients (3%) with MNG were found to indicate a malignancy. The mean age of the patients with ITC was 48 years [standard deviation SD, 11.7]. The patients with frank

cancer had a similar mean age of 48 years (SD, 18.6). Ninety per cent of patients with ITC were females compared to 73% of the patients with frank cancer who were females ( $p = 0.088$ ).

Pain was a presenting feature in 4.5% of the patients with ITC compared to 1.5% with frank carcinoma. Hoarseness was seen in 4.8% of the patients with ITC compared to 12.3% of those with frank cancer. A prior history of radiotherapy was seen in 1.5% of the patients with frank cancer compared to none for the ITC group. There were similar proportions in each group complaining of dysphagia and recent rapid growth (Table 1).

Table 1: Presence of historical features in patients with incidental thyroid cancer *versus* those with frank thyroid cancers

Historical features	Incidental thyroid cancer (%)	Frank thyroid cancer (%)	<i>p</i> -values
Pain	4.8	1.5	0.7
Hoarseness	4.8	12.3	0.8
Dysphagia	9.5	9.2	0.9
Recent rapid growth	4.8	4.6	0.8
Prior history of radiotherapy	0	1.5	0.8

In terms of sonographic findings, 19% of the patients with ITC had sinister ultrasound findings compared to 23.1% of the patients with frank thyroid cancer ( $p = 0.9$ ). No patient with ITC had suspicious lymphadenopathy on ultrasound compared to 9.2% of the patients with frank thyroid cancer ( $p = 0.2$ ) while 4.8% of the patients with ITC had a dominant nodule on ultrasound. There was no statistical significance of the ultrasound findings overall (Table 2).

The fine-needle aspiration cytology (FNAC) results were obtained in five patients with incidental and 32 patients with frank cancer. Both ITC and frank cancer had similar proportions of benign FNAC results approximately 9% ( $p = 0.2$ ). The FNAC was indeterminate in 14.3% of the patients with ITC and

Table 2: Ultrasound findings in patients with incidental thyroid cancer *versus* those with frank thyroid cancers

Ultrasound findings	Incidental thyroid cancer (%)	Frank thyroid cancer (%)	<i>p</i> -values
Suspicious cervical lymphadenopathy	0	9.2	0.2
Sinister ultrasound findings	19	23.1	0.9
Multiple nodules (> 1 nodule)	28.6	20.3	0.7
Solitary nodule	4.8	12.3	0.7
Dominant nodule	4.8	9.2	0.8
Nodules < 1 centimetres (cms)	0	1.5	0.8
Nodules > 4 (cms)	4.5	9.4	0.9

Table 3: Fine needle aspiration cytology results in patients with incidental thyroid cancer versus frank thyroid cancer

FNAC results	Number of patients with ITC (%)	Number of patients with frank thyroid carcinoma (%)
Benign	2 (9.5)	6 (9.2)
Malignant	0 (0)	13 (20)
Indeterminate/suspicious	3 (14.3)	12 (18.5)
Non-diagnostic	0 (0)	1 (1.5)

FNAC: Fine-needle aspiration cytology; ITC: incidental thyroid cancer

18.5% of the patients with frank cancer. The FNAC result was malignant in no patients with ITC and in 13 patients with frank cancer (Table 3).

Eighteen (86%) of the ITCs were of the papillary type. Follicular carcinoma was seen in 9% and hurthle cell carcinoma accounted for only 5%. There were no cases of medullary or anaplastic carcinoma in the incidental group. In the frank carcinomas group, papillary type accounted for 70%, follicular 9% and 7% each for medullary and anaplastic types (Figure).

carcinoma in terms of age and the females outnumbered the males. There were no statistically significant preoperative clinical or diagnostic findings associated with ITC. Eighteen (86%) of the ITCs, were of the papillary type. Follicular carcinoma was seen in 9% of the patients and hurthle cell carcinoma accounted for only 5%. There were no cases of medullary or anaplastic carcinoma. While in the frank carcinomas, papillary type accounted for 70%, follicular 9% and medullary and anaplastic each accounted for 7% .

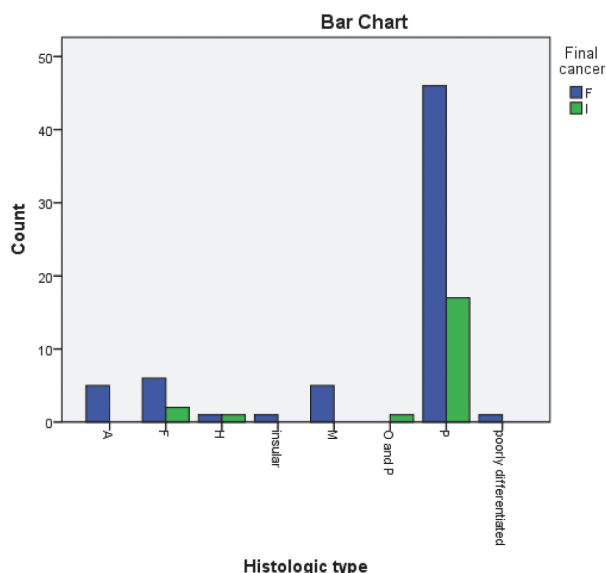


Figure: Distribution of histological types between incidental (I) and frank (F) thyroid cancer.

Abbreviations for the histologic type: P: papillary; F: follicular; M: medullary; A: anaplastic; O: oncocytic

**DISCUSSION**

There were 753 patients with postoperative histopathological reports of MNG . Twenty-one of the 753 patients (3%) with MNG were found to contain a malignancy. The mean age of presentation of ITC was 48 years and the female to male ratio was nine to one. There were similar demographics for the patients with frank thyroid

Thyroid cancer is the leading cause of death among endocrine cancers after carcinoma of the ovary (3). The incidence has increased by up to five-fold over the past 60 years (1). The possible reasons given are: ionizing radiation, gender hormones and iodine deficiency (1). It may present with a thyroid swelling which may be a solitary nodule or multiple nodules. Thyroid nodules are seen in four to seven per cent of the population by palpation of the neck and 30 to 50% by ultrasonography (5). It has been stated that less than 5% of these nodules are malignant (5). Other studies have quoted as high as 10% (3). All solitary nodules should be viewed with a suspicion of malignancy, but what about multiple nodules. The dominant nodule in a MNG has the same risk of malignancy as that of a solitary nodule (3). One meta-analysis has reported a lower prevalence of cancer in the MNG as compared to the solitary nodules (6). The overall incidence of thyroid cancer in males is 0.85% and 2.5% in females (3). We found a similar ratio in our group of patients with frank cancer.

Thyroid incidentalomas for the purpose of this study was defined as a malignancy found in a background of benign thyroid disease on histopathological evaluation of a surgical specimen which was not pre-operatively diagnosed as malignancy. The prevalence of malignancy in MNG has been reported as 6.9% (7). Other studies have reported as high as 11.1% (8). As high as 29% has been seen in some studies (1). How-

ever, only 3% of our patients with benign thyroid disease were found to have had a thyroid malignancy. This may be explained by our slower development compared to our overseas counterparts who may have greater exposures to the risk factors such as ionizing radiation.

Females have a higher incidence of ITC than males. In our study, 90% of patients with ITC were females. It is suggested that some hormonal factors might be involved in the pathogenesis (3). The risk factors suggested are recent pregnancy within about five years and exogenous oestrogens. Although positive associations have been found between hormonal factors and the incidence of thyroid cancer, they are generally weak and inconsistent across various studies (3). These cancers are rare in children. The average age in our study was 47 years. This is similar to the average age seen in other studies (9). We postulate that older patients have a longer time for exposure to the risk factors and, hence, these cancers are seen more commonly in the older age groups. The most sensitive clinical indicator of a malignancy in a goitre is a painless hard lump (5). In our studies, other preoperative suspicious factors such as: rapid increase in size, hoarseness and exposure to irradiation were not found to be significantly associated with ITC. A more useful study to do in the future would be a case control study comparing one group with ITC to another group of patients with benign thyroid disease and looking at the preoperative factors to determine whether there is a statistically significant difference. The risk factors found for malignancy in MNG are: the family's history of thyroid pathology, personal history of cervical radiation treatment, prior surgery and the presence of cervical adenopathies (10).

Microcalcifications and blurred margins are the strongest correlates for malignancy (11). Fine needle aspiration cytology detected no cases of malignancy in the ITC group. Fourteen per cent of the patients in the incidental group had an indeterminate FNAC. Sinister findings on ultrasound were seen in 18.2% of the patients with ITC. In the literature, ultrasound and FNAC have revealed sensitivities of 30.3% and 64.1% (12). Other studies have reported sensitivities as high as 80.6% for FNAC (5). Ultrasound does not have a high sensitivity in detecting ITC, so evidence-based indications for surgery are needed.

Eighty-six per cent of our ITC were of the papillary type. One study reported as low as 33% papillary and 33% follicular (3). Another study reported as high as 100% (7). Radiation is one of the major aetiologic factors for papillary cancer and iodine deficiency is a factor

for follicular carcinoma. In our setting, there is not a high incidence of iodine deficiency goitre. This also explains the lower incidence of follicular cancer seen in those patients with frank cancer as well. Incidental papillary cancer is associated with a good prognosis even if no completion thyroidectomy or further neck dissection is performed (13). None of our ITCs were of the anaplastic or medullary type, which were seen in the frank cancer group. Other studies have quoted as high as 23.8% of their ITC being anaplastic (3) and the finding of the medullary type in their ITC group (5). Anaplastic carcinoma has been associated with iodine deficient areas (3) and, hence, might explain the absence of this pathology in our ITC cases.

This study was a retrospective chart review looking at the characteristics of ITC. A more useful study to obtain more statistically significant data would be to conduct a case study comparing patients with ITC to those patients with benign disease to determine whether there is any difference in the preoperative findings between the two groups. This would allow us to identify any preoperative factors that may be used to raise the suspicion of the possibility of cancer in benign thyroid disease and, hence, offer these patients surgical treatment instead of observation. The strengths of this study was a large sample size of over 700 patients with benign thyroid disease and, so, this allowed us to calculate an accurate frequency of cancer in benign thyroid disease. The limitations were the incomplete data obtained in terms of clinical features and diagnostic findings for some of the cases.

## CONCLUSION

The frequency of cancer in MNG in Jamaica of three per cent is lower than other frequencies seen worldwide of both ITC and cancer arising from a solitary nodule. It is seen more commonly in middle-aged females. Patients with MNG need a careful evaluation for risk factors and require investigations such as an ultrasound and FNAC. Incidental thyroid cancers are most commonly of the papillary type which has a good prognosis. A case study will be required to compare the ITC group of patients with patients with a final histological type of benign disease to determine if there are any differences in the clinical characteristics or diagnostic tests that would aid in increasing the suspicion of cancer in a MNG in our setting.

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