PAPILLARY THYROID CANCER: A HISTOPATHOLOGICAL REVIEW IN ACCRA, GHANA

Running title: Papillary thyroid cancer in Ghana

Abstract. There is paucity of information on papillary thyroid cancer in Ghana. The aim of this study was to determine the relative proportions of thyroid malignancies diagnosed in our institution that were PTC, the trend and the clinico-pathological characteristics. **Materials and methods:** A review of all thyroid malignancies diagnosed in our department from January 1994 to December 2013 was conducted. Data were entered and analysed using SPSS software (Version 23 Chicago). **Results:** Papillary thyroid cancer was the commonest thyroid malignancy (52.7%). There was a gradual decline in the numbers of cases during the period under review. Approximately 60.3% of the patients were younger than 40 years. The great majority (77.6%) were females with a female to male ratio of 4:1. Four patients (4) presented with symptoms of metastatic disease (headache in 2; pathological fracture of the femur in 1; and dysphagia - 1). Many of the patients (62.9%) presented after 2 years with large anterior neck swelling. PTC was commonly diagnosed in total thyroidectomy specimens (43.1%). Follicular variant of PTC was the commonest histological subtype (75.6%). Lymphovascular invasion was found in approximately 16.4% of the cases. Nine of the cases (7.8%) showed extra-glandular involvement. **Conclusion**: The study found papillary thyroid cancer to be the commonest thyroid malignancy. There was a gradual declined in the number of cases over the period of study. Many of the patients were younger than 40 years of age and presented late with large palpable neck swellings. Approximately, 4.3% of patients presented with metastatic disease.

KEY WORDS: Papillary thyroid cancer, trend, Ghana.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is a low grade differentiated epithelial carcinoma of the thyroid gland.[1] The incidence of PTC varies globally in relation to the method of study,[2] prevailing environmental conditions, such as the iodine content of the diet and water,[3-13] radiation exposure[14-17] and background thyroid disease such as Hashimotos thyroiditis[18] and

more recently, also in connection to iodine prophylaxis. [22,23] In Ghana, there is no published data from the atomic nuclear resctor on a group of persons or individuals who have been exposed to radiation fall-out and subsequent development of thyroid malignancies. Furthermore, there are two radio-oncology centres in Ghana, the Korle-Bu Teaching Hospital (KBTH) and Komffo Anokye Teaching Hospital (KATH) in Accra and Kumasi respectively. These centres were recently established and there are also no published data on treatment-related thyroid cancers from them. Ghana started the national iodization programme in 1996, based on the endemicity of iodine deficiency in the country.[24] Similarly, there are no data available on the iodine prophylaxis and the development of thyroid cancers in Ghana since the introduction of iodized salt into the country. The aim of this study was to determine the relative proportions of thyroid malignancies diagnosed in our institution that were PTC, the trend and the clinico-pathological characteristics.

MATERIALS AND METHODS

STUDY DESIGN

This was a retrospective review of all reported thyroid cases in the Department of Pathology, Korle-Bu Teaching Hospital (KBTH) from January 1994 to December 2013.

STUDY SITE

The study was conducted in the Department of Pathology of KBTH, the largest referral hospital in Ghana. Specimens are received from Korle-Bu Teaching Hospital itself, Accra Metropolis and the surrounding towns and districts. The Department also receives surgical specimens from other regions of the country.

INCLUSION CRITERIA

The eligibility criterion was thyroid malignancy.

EXCLUSION CRITERIA

All cases with incomplete records and all other diagnosed thyroid conditions that are not

malignancies.

All poorly fixed thyroid specimens

DATA COLLECTION

Histopathology request forms and the histology reports of thyroid malignancies from the period January 1994 to December 2013 were reviewed. Data was collected on the age at diagnosis, sex, nature and duration of the presenting complaint, and type of surgical specimen. The histological types of thyroid malignancies, as well as other histological findings, including nodal involvement and lympho-vascular invasion were included.

STATISTICAL ANALYSIS

Data were entered into a statistical database (SPSS software version 23 Chicago).

a. Descriptive statistics were computed for the ages (mean, range, standard deviation) of all patients included in the study.

c. The proportions of thyroid specimens that contained malignancy were calculated for each year.

d. The proportions of papillary thyroid cancer were calculated for each year.

e. Annual trend in the proportion of papillary thyroid cancer over the period 1994 – 2013 was determined.

f. The histological subtypes of papillary thyroid cancer were described.

g. Results were presented as histograms for all continuous variables, while pie charts were used for categorical variables.

RESULTS

Annual distribution of papillary thyroid cancer (PTC) from January 1994 to December 2013

From January 1994 to December 2013, 116 (52.7%) out of a total of 220 thyroid malignancies diagnosed in our institution were PTCs. There was a gradual decline in the numbers of PTC diagnosed over the period**. (Table 1, Figure 1).**

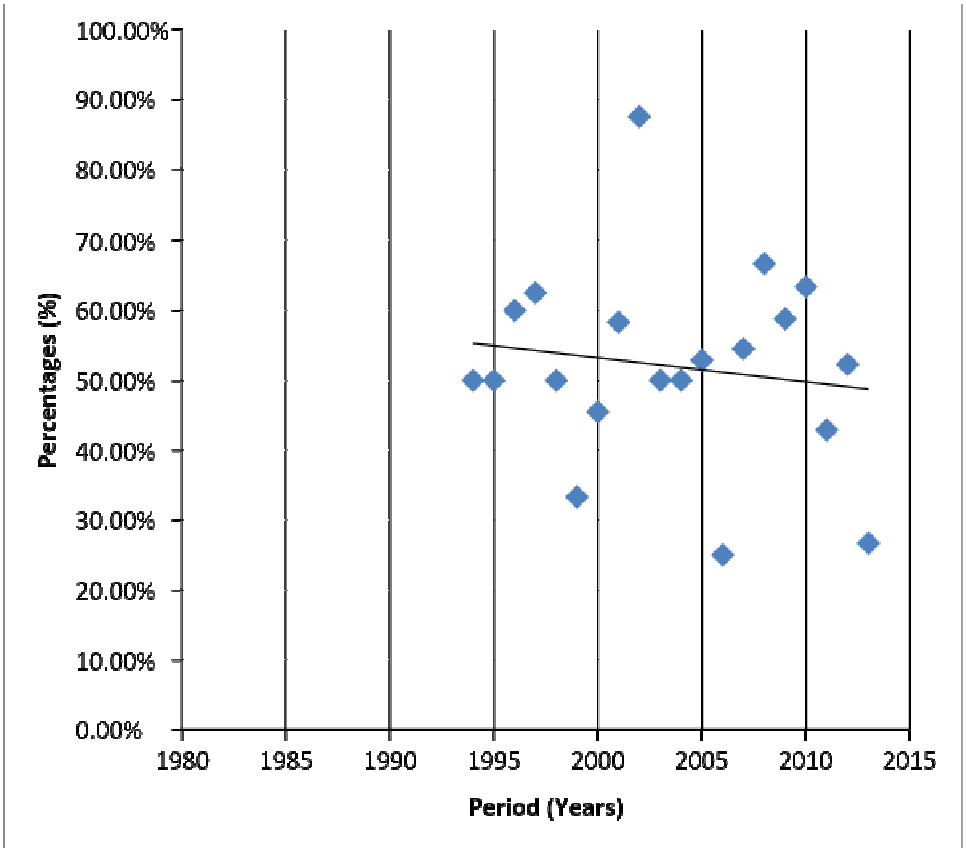

Figure 1: Trend in papillary thyroid cancer in the Department of Pathology from 1994 to 2013

Table 1. Annual distribution of papillary thyroid cancer (PTC) from January 1994 to December 2013

Year	Total number of TM	Total number of PTC	PTC as a % of total TM
1994	8	4	50.0
1995	6	3	50.0
1996	5	3	60.0
1997	8	5	62.5
1998	4	2	50.0
1999	6	2	33.3
2000	11	5	45.5
2001	12	7	58.3
2002	8	7	87.5
2003	18	9	50.0
2004	10	5	50.0
2005	17	9	52.9
2006	4	1	25.0
2007	11	6	54.5
2008	15	10	66.7
2009	17	10	58.8
2010	11	7	63.4
2011	14	6	42.9
2012	19	10	52.3

2013	**15**	**4**	**26.7**

Age characteristics of patients diagnosed with PTC

The ages of patients diagnosed with PTC ranged from 16 to 88 years with a mean age of 38.2 years (SD ± 15.7) and a modal age group of 30 – 39 years (27.8%). Many of the patients (60.3%) were younger than 40 years of age, **Table 2.** There were 90 females (77.6%) and 26 (22.4%) males, giving a female to male ratio of approximately 4:1

Table 2. Age groups of patients diagnosed with PTC from 1994 - 2013

Age group (years)	Frequency (n)	Percentage (%)
≤ 19	9	7.0
20 -29	30	26.0
30 - 39	32	27.8
40 - 49	18	17.7
50 – 59	14	12.2
≥ 60	13	11.3
Total	116	100.0

Clinical presentation and laterality of symptoms

A total of 111 cases (95.7%) out of the 116 patients diagnosed with PTC presented with a neck swelling, while 4 (4.3%) presented with symptoms relating to tumour invasion and metastases (advanced disease). Of the 111 neck swellings, 2 (1.8%) presented with cervical

lymphadenopathy, while 109 (98.2%) had thyroid gland enlargement **(Figure 2).** Of the 4 patients who had symptoms of advanced disease 2 presented with headaches (1 brain tumour, 1 dura mass), 1 - pathological fracture of the femur and 1 - dysphagia due to infiltration of the glottis by tumour.

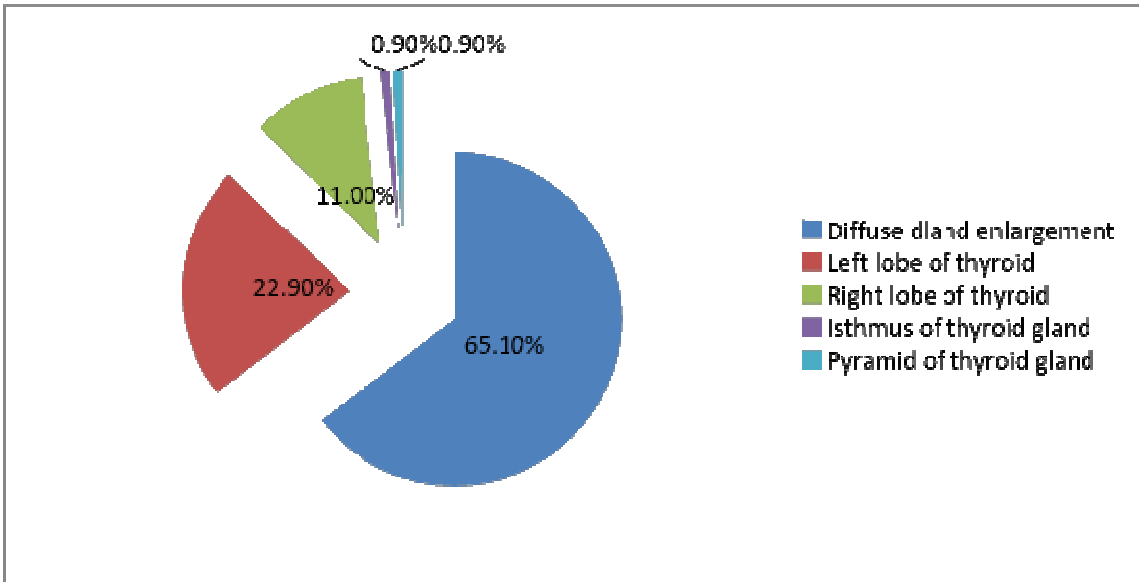

Figure 2. Site of involvement of the thyroid gland by PTC

Duration of symptoms of PTC at presentation

A total of 67 cases (57.8%) out of the 116 patients diagnosed with PTC had stated the duration of their symptoms at presentation. Sixteen patients (16; 23.9%) presented late in 3 years of noticing the swelling **(Figure 3).**

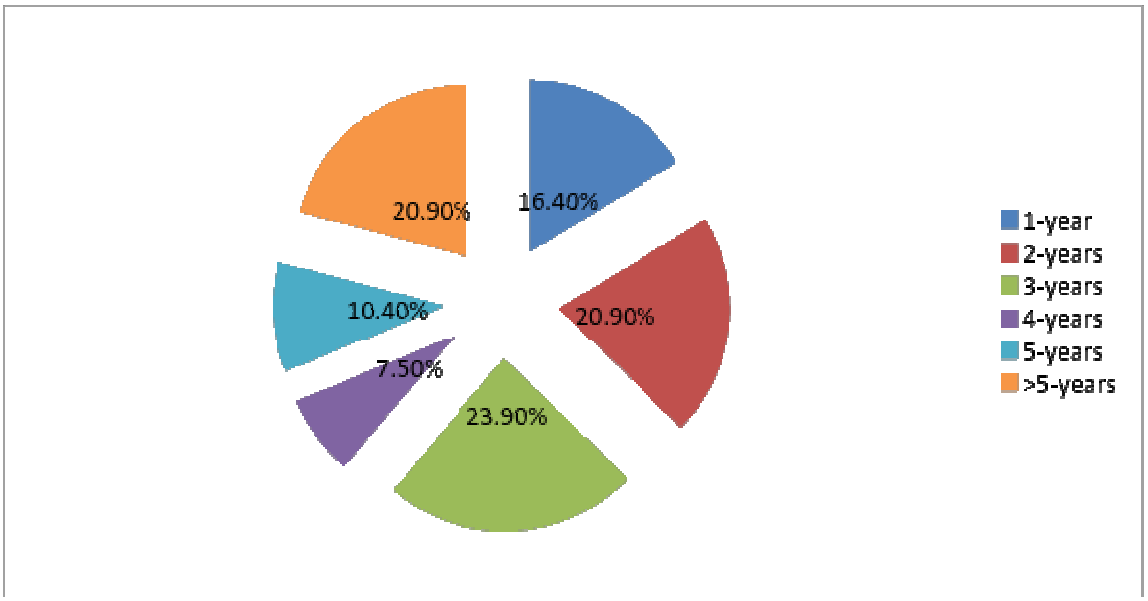

Figure 3. Duration of symptoms of PTC at presentation

Types of surgical specimens

A total of 50 PTC (43.1%) out of the 116 were diagnosed using specimens from total thyroidectomies. This was followed by 31 PTCs (29.8%) disgnosed using specimens from lobectomies **(Figure 4).**

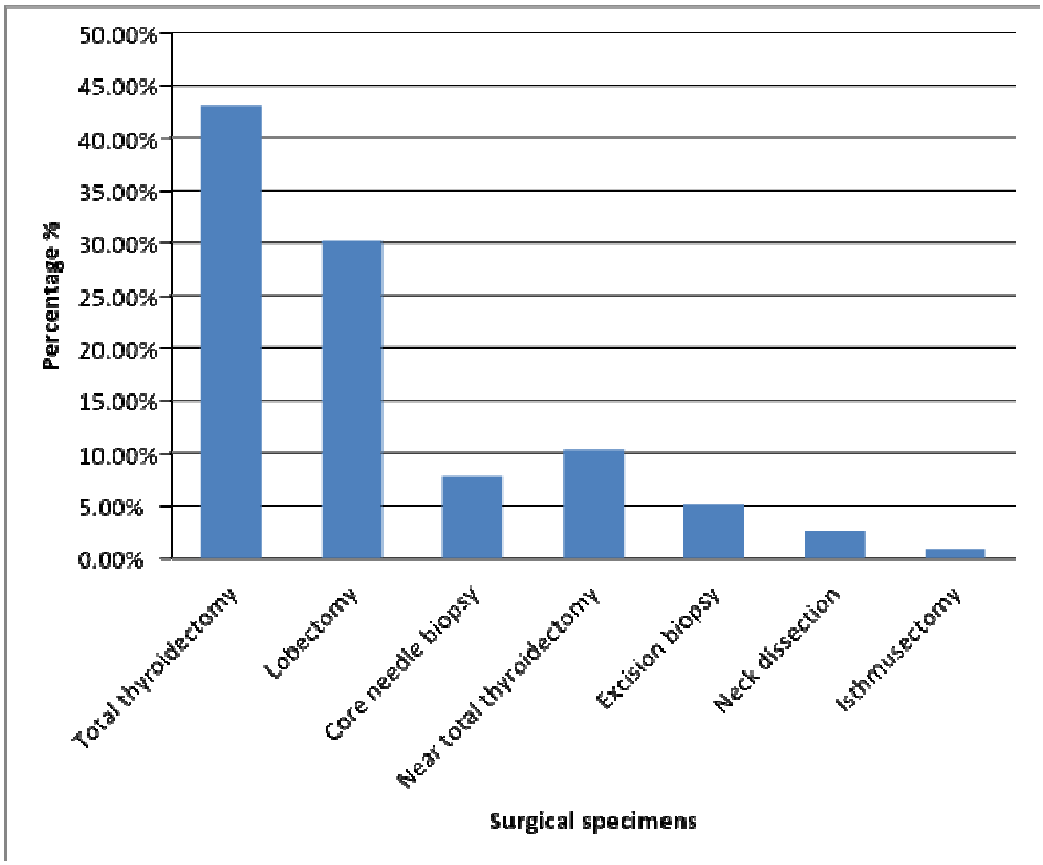

Figure 4. Types of surgical specimens

Histological variants of PTC

There were 75 (64.7%) conventional and 41 (35.3%) variants of PTC in this study. Follicular variant of PTC (diagnosed in 31, 75.6%) was the commonest variant **(Figure 5).**

Background thyroid disease

A total of 49 (42.2%) out of the 116 cases of PTC had background thyroid disease. There were 37 (75.5%) multinodular goitres and 12 (24.5%) with lymphocytic thyroiditis.

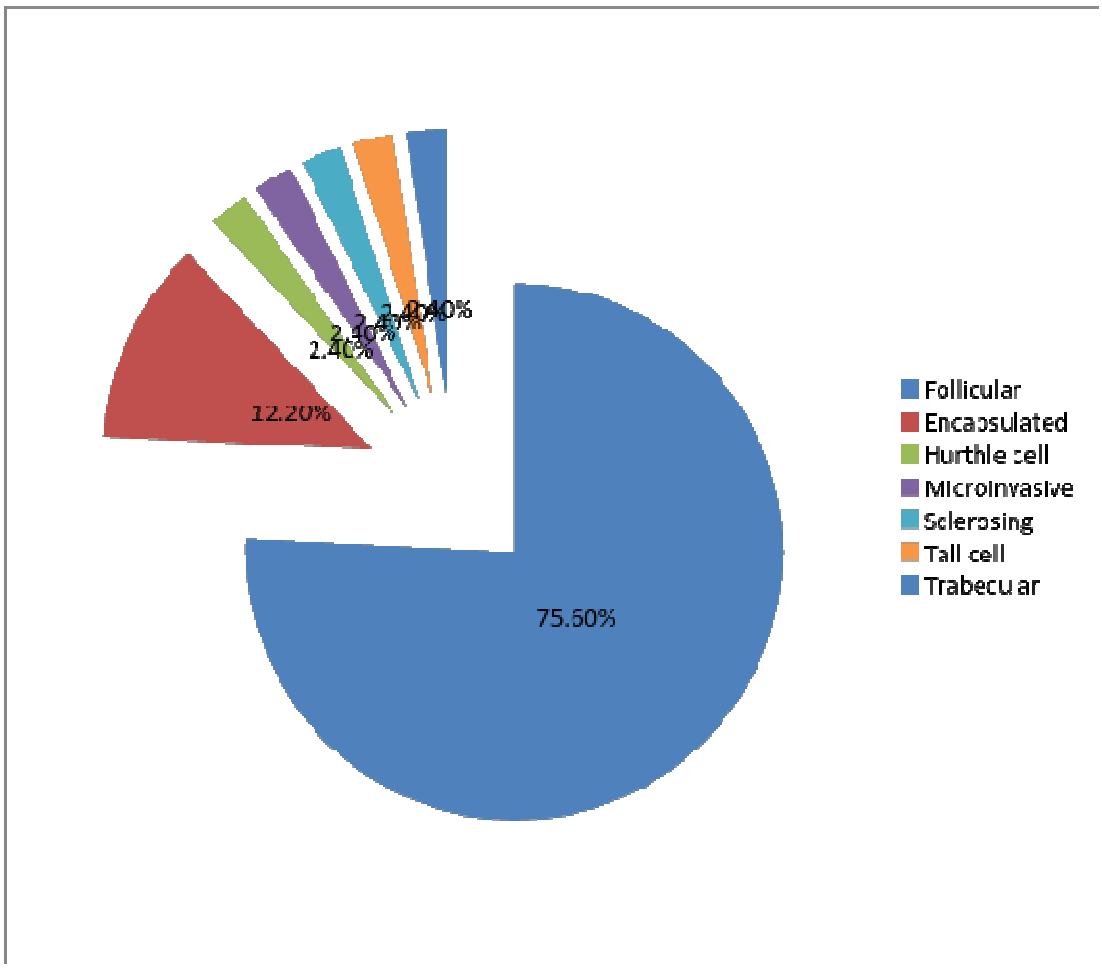

Figure 5. Histological variants of PTC

Lymphovascular invasion

Eleven (11, 9.6%) and 8 (6.9%) out of the 116 PTC showed nodal and vascular invasion respectively.

Invasion of surrounding structures and distant metastasis

Nine (9) out of the 116 PTCs had spread to other organs and structures such as the neck muscles (4), glottis (2), the brain (1) dura (1) and bone (1).

DISCUSSION

During the period under review, papillary thyroid cancer (PTC) was found to be the commonest thyroid malignancy diagnosed in our institution, accounting for 52.7% of all the thyroid malignancies. The predominant of any subtype of thyroid cancer depends largely on the geographical location and the prevailing environmental conditions.[2] Predominance of PTC in this current study supports previous studies in Ghana [3,4], some parts of Africa [5,6] and other parts of the world [7,8] that found PTC as the commonest differentiated carcinoma of the thyroid gland. This, however, differs from publications from some geographic locations with very low iodine levels [9,10] that found FTC as the commonest with PTC being the second common type to be of differentiated thyroid cancer.[11,12,13] Historically there is a link between PTC and ionizing radiation [14,15] For instance, children exposed to radioactive fallout from Chernobyl have been found to have an increase incidence of PTC [16,17.] In Ghana there are no published data on any major radiation exposure from the country's atomic nuclear reactor in Accra. There are two radiotherapy centres in Ghana, one in KBTH in Accra and the other in KATH in Kumasi; these two centres are recent establishments and there are, so far, no published data on patients who have had head and neck radiation indicating how many of them went on to develop thyroid malignancy as a complication of the treatment. Therefore, the issue of ionizing radiation as a risk factor for thyroid cancer in Ghana currently cannot be ascertained.

The proportion of PTC in this study (52.7%) is relatively lower than the 57 – 85% range found in some studies of thyroid carcinomas,[18,19,20,21] In our study, there was a gradual decline in the numbers of PTC diagnosed over the period, and this may suggest a possible decline in the number of this this condition in the future. The trend of PTC in this current study differs from studies that showed an increased incidence of papillary carcinoma especially in regions that practice iodine prophylaxis/supplementation. [22,23] The national iodization programme was started in Ghana in 1996 following research that found that Ghana was part of the world endemic iodine deficient regions. [24] However, there is no data on the incidence of PTC before and after the initiation of the iodization programme. Also, we do not have data to conclude if our patients with PTC had iodine prophylaxis or not. There is the need for a prospective study across the country that will look at the association of dietary iodine in-take and PTC in Ghana.

PTCs were diagnosed in a relatively younger age group with a mean age of 38.2 years with female preponderance. These findings are comparable to studies that found PTC to be a cancer of younger ages with mean age of around 40 years with females predominating.[25,26]

In this study, the great majority of PTC patients presented with a palpable anterior neck swelling, which is in keeping with studies across the globe.[19,27] Approximately, 4.3% of our patients visited health facilities with symptoms such as headache, pathological fracture and dysphagia. This are not primary symptoms of thyroid cancer. These symptoms were however found by examination and further investigations to be as a result of metastatic PTC. This finding supports studies that found that the primary presentation of PTC may be a metastatic disease.[28,29] Our study also found that patients with PTC commonly presented late to health facilities; this is similar to previous studies.[30,31] PTC was commonly diagnosed in total thyroidectomy specimens, which is in keeping with findings in other studies. [31,32,33]

The current study found the commonest variant of PTC to be the follicular subtype (75.6%), which is similar to the study by Ricardo et al.[34] Papillary thyroid cancer (PTC) has a propensity to metastasize through the lymphatics, and the rate may be as high as 30 - 50%.[35] The current study found nodal involvement by PTC to be 9.5%, a much lower value than what is found in the literature. For instance, a study by Zuberi et al in Pakistan found nodal involvement by PTC at the time of diagnosis to be 40%.[36]

Younger age at diagnosis, the female gender and the histological variant (conventional type) of PTC have been found to be good prognostic factors.[37,38] In this current study, many of the patients were younger than 40 years of age at the time of diagnosis; the great majority were females with the conventional type PTC. Furthermore, it was found that 9.5% of the patients had lymph node involvement, with 7.8% having extra-glandular spread at the time of histological diagnosis. Studies have shown that patients with node metastases at diagnosis have higher recurrence rate but not a higher mortality rate. [39,40] The authors, therefore, potentially suggest that the 52.7% patients with confirmed PTC in our study may have favourable outcome if the surgery is combined with chemotherapy.

In conclusion, this study found papillary thyroid cancer to be the commonest thyroid malignancy

in our institution with a gradual decline in the number of patients with PTCs over the study period. It is a disease of young patients who usually presented late, with a neck swelling, to health facilities; the prognosis is favourable.

Ethical clearance

Permission to conduct and publish this work was obtained from The Head of Department of Pathology School of Biomedical Sciences, College of Health Sciences, University of Ghana Legon.

Availability of data

The data used to prepare this manuscript will be made available on demand.

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LEGENDS

Table 1. Annual distribution of papillary thyroid cancer (PTC) from January 1994 to December 2013

Figure 1: Trend in papillary thyroid cancer in the Department of Pathology from 1994 to 2013

Table 2. Age groups of patients diagnosed with PTC from 1994 - 2013

Figure 2. Site of involvement of the thyroid gland by PTC

Figure 3. Duration of symptoms of PTC at presentation

Figure 4. Types of surgical specimens

Figure 5. Histological variants of PTC