Original Article

A Clinicopathological Study of Thyroid Cancers at King Edward Medical University / Mayo Hospital, Lahore

Shahida Niazi,[1] **Madiha Arshad,**[2] **Mulazim Hussain Bukhari**[3]

Abstract

Objective: The study was conducted to determine the frequency and clinicopathological aspects of various types of thyroid cancers in patients presenting with goitres and thyroid nodules.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: It was an 11 year retrospective study commencing from January 2000 to December 2010 conducted at the Department of Pathology, King Edward Medical University, Lahore, Pakistan.

Materials and Methods: Clinical data and Histopathology Reports of 2785 thyroid surgical specimens referred from the Surgical Units of Mayo Hospital, Lahore were reviewed and malignant cases were retrieved for inclusion in this study. Patients from both sexes and all age groups were included.

Results: Reports of a total of 2785 thyroid specimens were reviewed, out of which 170 cases (6.10%) were found to be thyroid cancers. These comprised of 130 cancers (76.47%) in females and 40 cases (23.52%) in males giving a female to male ratio of 3.25:1. Patients ranged in age from 8 years to 90 years. Papillary Carcinoma was the commonest thyroid cancer comprising of 116 cases (68.23%), followed by Follicular Carcinoma which constituted of 24 cases (14.11%). Medullary Thyroid Carcinoma, Anaplastic Thyroid Carcinoma, Non-Hodgkin Lymphoma and Poorly Differentiated (Insular) Carcinoma each constituted of 11 cases (6.47%), 10 cases (5.88%), 4 cases (2.35%) and 2 cases (1.17%) respectively. 2 cases (1.17%) of Carcinoma Larynx showed local extension into the thyroid and there was a single case of Mixed Medullary / Papillary Carcinoma.

15 cases (8.82%) of these thyroid cancers were seen in children and adolescents. Papillary Carcinoma was also the commonest thyroid cancer in children comprising of 13 cases. One case of Papillary Carcinoma was detected incidentally in an excised Thyroglossal duct cyst. Medullary Carcinoma (associated with MEN II syndrome) and Follicular Carcinoma constituted one case each of these childhood cancers.

Conclusions: Papillary Carcinoma was the commonest morphological type of thyroid cancer in both sexes and all age groups. All major histological types of thyroid cancers were more common in females.

Key Words: Papillary Carcinoma (PC), Follicular Carcinoma (FC), Medullary Thyroid Carcinoma (MTC), Anaplastic Thyroid Carcinoma (ATC), Thyroglossal Duct Cyst Carcinoma (TDCC).

Niazi S.[1]
Department of Pathology, King Edward Medical University, Lahore – Pakistan

Arshad M.[2]
Department of Pathology, King Edward Medical University, Lahore – Pakistan

Bukhari M.H.[3]
Department of Pathology, King Edward Medical University, Lahore – Pakistan

Introduction

Although thyroid nodules and diffuse enlargements called goitres are a common clinical presentation of thyroid disease, thyroid cancer is a relatively rare neoplasm, its incidence varies geographically and ethnically around the world. It represents only 1.5% of all malignancies but is the most common endocrine cancer.[1,2] Thyroid malignancy may present either as a solitary cold nodule, as a multinodular goitre (MNG), or as an enlarged cervical lymph node.[3] The frequency of finding malignancy in surgically excised cold solitary nodules varies from 4 – 38% in different studies depending upon the age, sex, racial, genetic, geographical and environmental factors.[4-6] Cold nodules occurring at the extremes of age, particularly in men are more likely to be malignant.[7] The incidence of finding thyroid cancer in solitary nodules in children is much higher ranging from 14 – 50%.[8,9] The chances of MNG's harbouring malignancy varies from 3 – 17% in different series depending on how carefully the surgically specimens are examined.[10-13]

Thyroid cancers display a spectrum of morphological variants, each type manifesting a different epidemiologic pattern and representing a discrete biological entity. The vast majority are the follicular cell derived "Differentiated Thyroid Carcinomas" and include Papillary Carcinoma (PC) and Follicular Carcinoma (FC).[14] PC is the most common malignant tumour of the thyroid in countries having iodine sufficient or iodine – excessive diets comprising about 80% cases of thyroid cancer.[6,14] It is also the commonest thyroid malignancy in children and populations exposed to ionizing radiation during nuclear fall – out accidents and radiotherapeutic treatment for various head and neck lesions.[15] Papillary Carcinoma may be discovered incidentally during routine histological examination of thyroid glands excised for other diseases and small foci of occult PC's may be found in about 12% of autopsy cases.[16] These tumours tend to be biologically indolent with an excellent prognosis – more than 90% survival at 20 years.[14] In contrast dietary iodine deficiency is associated with a high risk of developing FC which constitutes 10 – 20% of thyroid cancers. Clinically it is more aggressive, occurs in an older age group and carries a higher mortality compared with PC.[17]

Medullary Thyroid Carcinoma (MTC) arises from the parafollicular C cells and represents 3 – 5% of thyroid cancers. Genetic susceptibility appears to be important in the genesis of this cancer when seen in children associated with MEN II syndromes.[18,19] Anaplastic Thyroid Carcinoma (ATC) or Undifferentiated Thyroid Carcinoma is one of the most aggressive human cancers accounting for less than 5% of thyroid cancers. In contrast to the "Differentiated forms" of thyroid cancer, the prognosis of patients with ATC is so poor that it is measured in terms of months rather than years.[20] Primary Non-Hodgkin Lymphoma (NHL) of the thyroid is a rare clinical entity constituting less than 2% of thyroid cancers. Most of these are the diffuse B cell type (MALT) lymphomas.[21,22]

Materials and Methods

This was a retrospective study comprising of a review of 2785 thyroid surgical samples submitted to the Histopathology Section of the Department of Pathology, King Edward Medical University, Lahore, Pakistan, during an 11 year period commencing from 1st January 2000 to 31st December 2010. These cases had been referred from the Surgical Units of Mayo Hospital, Lahore and included thyroid surgical specimens from both sexes and all age groups.

The study reviewed previously diagnosed and reported cases of thyroid cancer detected in excised solitary thyroid nodules and multinodular goitres. Detailed clinical records and computer data files of these cases were retrieved and all relevant information was recorded in a proforma. These details included patients' name, age, gender, address, occupation, brief medical and surgical history including history of previous thyroid surgery, reports of relevant laboratory investigations like thyroid scan, ultrasound, fine needle aspiration cytology (FNAC) and previous biopsy reports in cases of recurrent thyroid nodules. The proforma also recorded details about the exact type of surgical procedure performed (e.g. lobectomy, partial thyroidectomy, total thyroidectomy, radical neck dissection etc.) and the per-operative findings like gross description of the surgical specimen, size of the tumour nodule, encapsulation, adherence to the surrounding neck structures and status of the cervical lymph nodes was noted.

Additional information regarding detailed description of the gross specimen and the tumour and its microscopic features alongwith the final diagnosis / opinion was noted from the computerized histopathology reports. In some controversial cases blocks and slides were retrieved and reviewed again taking second opinions from other specialized centres with the help of immunohistochemical stains. Results and data was

compiled in the form of tables and charts and calculated as percentages and ratios. The findings and results so obtained were compared with other similar local and international studies.

Results

Clinical data and computerized histopathology reports of 2785 thyroid surgical specimens received between January 2000 to December 2010 were retrieved and reviewed at the Department of Pathology, King Edward Medical University, Lahore. Out of 2785 cases analysed retrospectively, 170 cases (6.10%) were diagnosed as thyroid cancers. The remaining 2615 cases (93.89%) comprised of goitres, follicular adenomas, hyperplastic nodules, colloid cysts, inflammatory conditions like Hashimoto thyroiditis and granulomatous thyroiditis etc.

Breakup of the various morphological types of thyroid cancers as seen in our study is depicted in Table 1. Out of 170 malignant cases, Papillary Carcinoma (PC) was the commonest type accounting for 116 cases (68.23%), followed by Follicular Carcinoma (FC) which comprised of 24 cases (14.11%). Medullary Thyroid Carcinoma (MTC), Anaplastic Thyroid Carcinoma (ATC) and Non-Hodgkin Lymphoma (NHL) each constituted of 11 cases (6.47%), 10 cases (5.88%) and 4 cases (2.35%) respectively. Poorly Differentiated (Insular) Carcinoma comprised of 2 cases (1.17%) and there was a single case of Mixed Medullary / Papillary Ca in a 40 year old man.

Regarding sex distribution of thyroid cancers females constituted 76.47% (130 cases) and males 23.52% (40 cases) giving an overall female to male ratio of 3.25:1. The major morphological categories of thyroid cancer were more common in females (Table 2).

Age range of patients in our study was from 8 years to 90 years. Maximum number of malignant cases (106 cases or 62.35%) were seen in the 21-50 years age group (Table 3). 15 cases (or 8.82%) of thyroid malignancy were seen in children and adolescents aged less than 20 years. These comprised of 13 PC's, 1 FC and 1 MTC. 2 of these childhood cases were observed in children both aged 8 years. One was an incidental PC in an excised thyroglossal duct cyst in a boy and the other was a Minimally Invasive FC in a girl. All other childhood cancers were seen in the 2nd decade. 2 cases of thyroid cancer were diagnosed in elderly females (both aged 90 years); one was a PC and the other was an ATC (Table 3).

Considering the various types of PC's, 83 cases (71.55%) constituted of the Usual or Classic type (Fig. 1), 17 cases comprised of the Follicular Variant of Papillary Carcinoma (FVPC), (Fig. 2), 8 cases of the Encapsulated Variant, 3 cases of the Cystic Variant, 4 cases of the Micropapillary type & 1 case was of PC in a Thyroglossal cyst. Overall the Variants constituted 33 cases or 28.44% of the total 116 Papillary Carcinomas. 32 cases (27.58%) of PC's showed Metastatic deposits in the cervical lymph nodes. Age range of patients with PC was from 8 years to 90 years with a female to male ratio of 3.83:1.

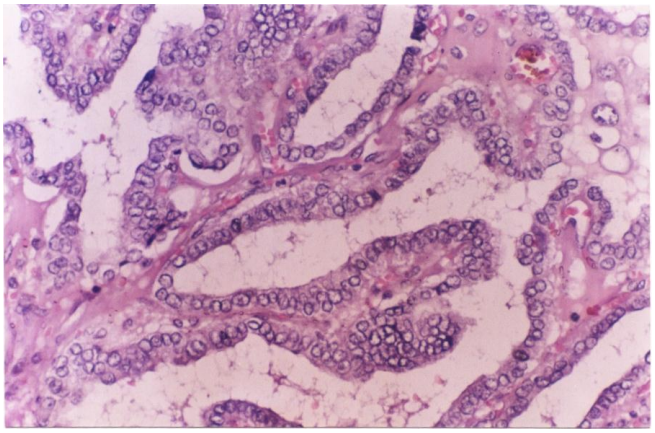

Fig. 1: Papillary carcinoma showing prominent fibrovascular cores and nuclei with ground glass appearance, overlapping and grooves (H & E, 300x).

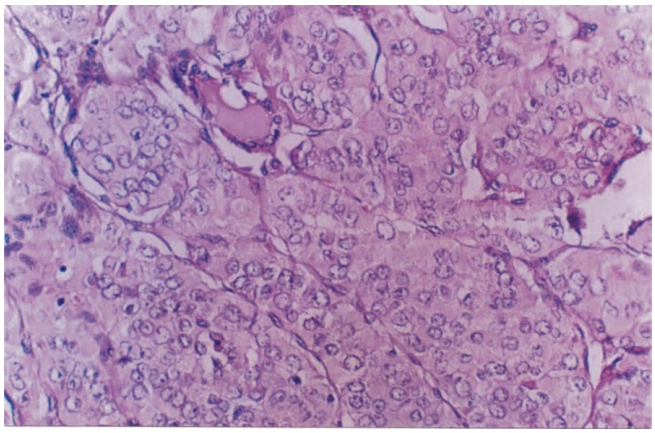

Fig. 2: Follicular variant of papillary carcinoma showing ground glass nuclei and follicular pattern (H & E, 300x).

Out of 130 thyroid cancers reported in females, PC's comprised of 92 cases (70.76%) and out of 40 thyroid cancers in males, PC's comprised of 24 cases (60%). PC was thus the most common thyroid cancer in both sexes and all age groups.

FC's constituted 24 cases (14.11%) with a female to male ratio of 5:1 and an age range between 8 years to 70 years. 12 cases were diagnosed as Minimally Invasive Follicular Carcinomas showing full thickness capsular penetration (Fig. 3), 8 cases showed both capsular and vascular invasion with tumour cell emboli in the blood vessel lumina. 4 cases were labelled as Widely Invasive Follicular Carcinoma with extensive gross and microscopic infiltration into the surrounding extrathyroidal tissues of the neck.

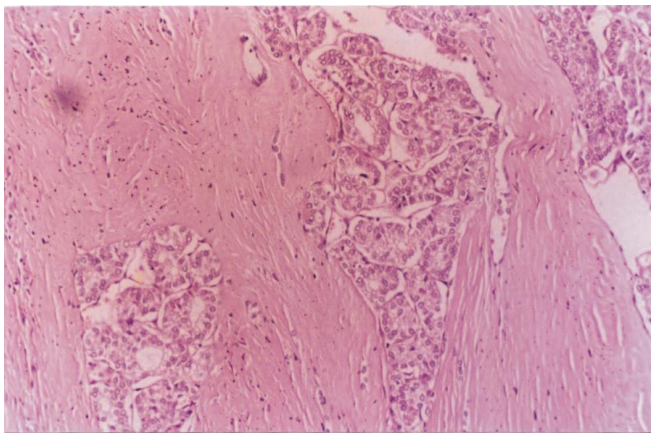

Fig. 3: A well differentiated follicular carcinoma invading the capsule (H & E, 200 x).

MTC comprised of 11 cases (6.47%) with a female to male ratio of 2.66:1 and an age range from 12 years to 40 years. Youngest patient in this category was a 12 year old boy with MEN 2A syndrome. All patients were advised Congo Red immuno-staining for confirmation of amyloid deposits.

All 10 cases (5.88%) of ATC (Fig. 4) were seen in patients above the age of 55 years. Our oldest patient (a 90 year old female) belonged to this category. Female to male ratio was 2.33:1.

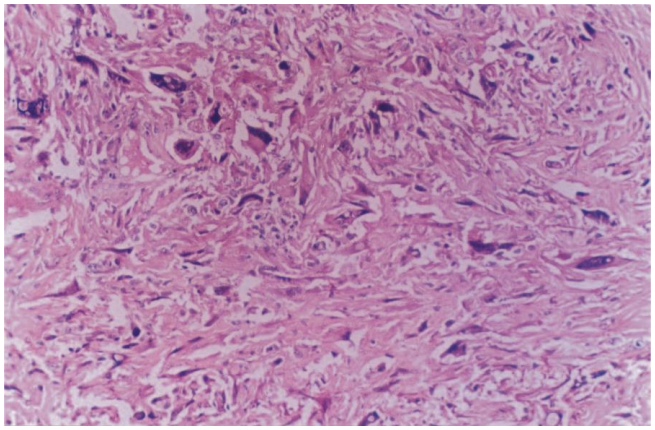

Fig. 4: Anaplastic thyroid carcinoma showing spindling, tumour giant cells, hyperchromatic and pleomorphic nuclei (H & E, 250x).

Cases of NHL and PD (Insular) Carcinoma were uncommon morphological types of thyroid cancer

Table 1: Morphological break-up and Frequency of Thyroid Cancers (n = 170).

Category	Number of Cases	Percentage
Papillary Carcinoma	116	68.23
Follicular Carcinoma	24	14.11
Medullary Carcinoma	11	6.47
Anaplastic Thyroid Carcinoma	10	5.88
Non Hodgkin Lymphoma	4	2.35
Poorly Differentiated (Insular) Carcinoma	2	1.17
Local Extension (Carcinoma Larynx)	2	1.17
Mixed Medullary / Papillary Carcinoma	1	0.58
Total	170	100

Table 2: Sex Distribution and Frequency of the Various Morphological Types of Thyroid Cancers (n = 170).

Morphological Category	No. of Cases	Sex		Ratio
		Females	Males	F : M
Papillary Carcinoma	116	92	24	3.83 : 1
Follicular Carcinoma	24	20	4	5: 1
Medullary Carcinoma	11	8	3	2.66 : 1
Anaplastic Carcinoma	10	7	3	2.33 : 1
Non Hodgkin Lymphoma	4	2	2	1 : 1
Poorly Differentiated (Insular) Carcinoma	2	1	1	1 : 1
Local Extension (SCC Larynx)	2	0	2	0 : 2
Mixed Medullary / Papillary Carcinoma	1	0	1	0 : 1
Total	170	130 (76.47%)	40 (23.52%)	3.25 : 1

Table 3: Age Distribution of Thyroid Cancers (n = 170).

Age in Years	Number of Cases	Percentage
1 – 10	2	1.17
11 – 20	13	7.64
21 – 30	42	24.70
31 – 40	43	25.29
41 – 50	21	12.35
51 – 60	26	15.29
61 – 70	15	8.82
71 – 80	6	3.52
81 Plus	2	1.17
Total	170 cases	100

comprising 4 cases (2.35%) and 2 cases (1.17%) respectively. 2 cases (1.17%) of primary Squamous Cell Carcinoma of the Larynx showed local extension into the overlying thyroid gland. Both cases were seen in elderly males. A single case of Mixed Medullary / Papillary Carcinoma was diagnosed in a 40 year old male.

Discussion

Thyroid cancer is an unusual and fascinating malignancy that has intrigued the medical profession for years because of tremendous variation in its biological behaviour, geographical distribution, tumour aggressiveness and prognosis depending upon the particular histopathologic subtype.

A review of different studies show variable figures regarding the incidence of malignancy in isolated thyroid swellings and MNG's. According to Mazzaferri,[7] of all thyroid nodules removed surgically an estimated 8 – 17% are carcinomas. A study by Ahmed and associates[4] showed 23.7% of thyroid nodules to be malignant. Another study in Kharian[5] reported a figure of 4.6%. Belfiore[6] quoted a similar figure of 4.6% in his study. A study by Hung[8] showed 25.5% of cold nodules in children and adolescents to be malignant, and recommended the surgical removal of all STN's in children. Likewise all MNG's should also be viewed with a high index of suspicion of harbouring cancer. In our present study 170 cases (6.10%) out of 2785 thyroid surgical specimens were reported as cancers. Our previous study in 2007[3] reported a figure of 5.74% thyroid cancers. A study in Karachi[23] quoted a figure of 14.35%, and another study by Najam-ul-Haq at Rawalpindi[11] reported only 3% cases of cancer in goitres. In Qureshi's study[13] conducted at Jamshore the incidence of malignancy was 9.39%. A study in Yemen by Al Jaradi[24] in 2005 gave an alarming high figure of 21% cancers in goitres. This wide variability in the reported figures in different studies suggests that age, sex, genetic and dietary factors like iodine intake and environmental factors like radiation exposure play a role in determining the variable risk of cancer in patients with thyroid nodules and MNG's.[6]

Regarding sex distribution the female to male ratio

was 3.25:1 in this study. According to Li Volsi[25] all thyroid disorders occur more frequently in females and thyroid cancer is no exception. However, whereas the female: male ratio for certain thyroid disorders is substantially higher (about 9:1) the ratio for thyroid cancer is 3:1. Hence thyroid enlargement in a male should be regarded with suspicion. In a study conducted at Auckland, New Zealand[26] females outnumbered males by 4:1 and a study in Saudi Arabia reveals thyroid cancer to be the 2nd commonest malignancy in females after breast cancer and thyroid cancer ranked 14th position in males.[27] Figures from different studies in Pakistan also show a female: male ratio of 4.7:1,[10] 4.5:1,[12] 3.2:1,[28] 4:1[4] and 3.75:1.[3] In a study conducted at Bombay, India,[29] thyroid cancer was 3 times more frequent in females than males but this relative excess varies with the histologic type and age of the patient. The relative predominance of thyroid cancer in females raises the possibility of hormonal factors in its etiology and pathogenesis.[29]

Age range of our patients with thyroid cancer was between 8 years – 90 years. Maximum number of cancer cases were seen in the 3rd, 4th and 5th decades. Studies by Ahmed,[4] Bukhari,[10] and Sarfraz[28] also report thyroid cancer to be common in the 3rd, 4th and 5th decade of life. In this study, 15 thyroid malignancies (9%) were seen in children and adolescents less than 20 years of age. Thyroid cancer is a relatively uncommon malignancy in children accounting for only 0.5 – 3% of all paediatric malignancies and 10 – 15% of childhood head and neck cancers.[9] According to Skinner,[30] 10 – 15% of all thyroid cancers occur in patients less than 20 years old, and comprise mainly of Papillary Carcinomas.

PC was the commonest histological type of thyroid cancer comprising of 68.23% cases and a female to male ratio of 3.83:1. Patients ranged in age from 8 years to 90 years. Maximum number of cases were seen in the 3rd, 4th and 5th decade. In my previous study in 2007,[3] PC constituted 71.05% with a F:M ratio of 5.75:1. A study by Shah[31] showed a somewhat similar value of 69%. Comparatively higher figures of 90.2%[10] and 77.89%[23] regarding PC were seen in two recent studies reported in Karachi. This significant increase in the incidence of PC could probably be attributed to the prophylactic introduction of high quantities of iodine in food supplies.

The Usual or Classic PC is characterized by certain well defined histopathological features like papillae with fibrovascular cores, empty looking ground glass, clear nuclei (Orphan Annie) of large size with overlapping quality, deep grooves and pseudoinclusions.[32] 25 – 50% cases also demonstrate psammoma bodies.[32] Morphologic Variants include follicular, solid, cystic, cribriform, micropapillary, encapsulated, tall cell, columnar, diffuse sclerosing, and oxyphilic types.[14,32] According to Li Volsi,[32] these Variants comprise 15 – 20% of PC's; some having important prognostic implications whereas others appear to be histologic curiosities. In our study, the Variants comprised of 33 cases (28.4%).

The commonest Variant called Follicular Variant of Papillary Carcinoma (FVPC) shows the typical nuclear morphology of PC but no papillae. Instead it shows a follicular architecture occupying about 80% of the neoplasm.[33,34] Fortunately it possesses the same good prognosis associated with classic PC.[34] In our present study, this variant comprised of 17 cases (14.65%) out of 116 PC's. Tielens[34] reported a figure of 12% for this variant in his study. Second in frequency in our study was the Encapsulated Variant constituting of 8 cases (6.89%) showing the gross features of an adenoma with total encapsulation and microscopically demonstrating the typical cytologic features of classic PC. 4 cases (3.44%) comprised of Micropapillary Carcinomas which are defined as PC's measuring less than 1 cm in diameter.[32] There were 3 cases (2.58%) of the Cystic variant of PC in which typical PC was seen within the lumen of a Colloid Cyst. 1 rare case (0.86%) comprised of PC arising in a Thyroglossal Duct Cyst in an 8 year old boy. Carcinoma arising within a Thyroglossal Duct Cyst is a rare event constituting only 1% of thyroid cancers.[35] Only about 215 cases have been reported in world literature mainly in adults.[36] 90% cases of these cancers are PC's followed in decreasing frequency by Squamous Cell Carcinoma, FC or Hurthle Cell Carcinoma.[35,37] Diagnosis is made incidentally during surgery for the removal of a persistent thyroglossal duct cyst.[37]

PC tends to invade the lymphatics leading to regional lymph node metastasis.[14,32] In our study, 32 cases (27.58%) showed metastatic deposits in the cervical lymph nodes. Other studies however document that 50% or more patients have nodal metastases at the initial diagnosis.[14,32] Some patients have only cervical lymph node enlargement with no obvious clinical manifestation of a tumour in the thyroid, therefore this possibility should always be considered in the differential diagnosis of cervical lymphadenopathy.[32]

Out of 170 thyroid cancers, 15 cases (9%) were seen in children and adolescents. These constituted of 13 PC's (86.66%), 1 MTC and 1 FC. This corresponds

to our past study[38] in which PC constituted 90% cases of childhood thyroid cancer. Our youngest patient of PC was an 8 year old boy with PC detected as an incidental finding in a Thyroglossal Duct Cyst.

FC is characterized by follicle formation and lacking the nuclear features of PC.[14,33] 2 types have been described: the Encapsulated Variant (Minimally Invasive) and the Widely Invasive Variant. The diagnosis of Encapsulated FC is one of the most controversial subjects in thyroid pathology. Grossly it resembles an adenoma and is diagnosed as cancer upon histologic demonstration of capsular and / or vascular invasion.[33] According to Yamashina,[39] thorough circumferential sampling of all encapsulated follicular lesions is the key to accurate diagnosis of FC. The Widely Invasive Variant lacks encapsulation and shows widespread infiltration of the blood vessels and adjacent extrathyroidal tissue.[17] FC disseminates hematogenously producing metastasis to the lungs, bones and brain.[14,17] In our study FC's constituted 24 cases (14.11%) of thyroid cancers. Studies in Pakistan have quoted variable figures of 10.52%,[3] 21.05%,[4] 11.60%,[31] 23.8%[28] and 33.33%.[11] The high incidence in the latter 2 studies is probably due to iodine deficiency in the Northern Areas of Pakistan which constitutes the goitre belt. In our study an 8 year old girl had Minimally Invasive FC showing capsular invasion, which is a rare tumour in children.

There were 11 cases (6.47%) of MTC in our study. Other studies in Pakistan have quoted figures of 4.5%,[10] 5.26,[12] 9.09%,[13] 3.16%,[23] 4.8%[28] and 9.7%.[31] Our youngest patient of MTC was a 12 year old boy diagnosed as MEN2A with elevated serum calcitonin and CEA levels. His two elder brothers had died of MTC, pheochromocytoma and hyperparathyroidism. This case has been reported in our previous study in 2006[38] on thyroid tumours in children & adolescents. MTC exists in 2 clinical forms: Familial MTC and Sporadic MTC. Lesions of Familial MTC are multiple, appear early in life, affect more than one family member and are associated with MEN 2 syndromes.[18] Once recognized as Familial MTC, all first degree relatives should be regularly screened by serum calcitonin levels and genetic testing to detect germ line mutations in the RET protooncogene and treated by prompt prophylactic thyroidectomy.[18,19] Sporadic MTC presents as a solitary palpable mass in the neck during the 5th or 6th decade and is less aggressive than MTC associated with the MEN 2 syndromes.[18] Microscopy of MTC's shows polygonal tumour cells forming nests, trabeculae, follicles, pseudopapillary or carcinoid like patterns. Acellular amyloid deposits and calcifications are detected in the stroma.[18,19] We reported an additional single case of Mixed Medullary / Papillary Carcinoma in a 40 year old man. Bukhari et al[10] also reported a similar case in their study.

The histogenesis of ATC has been a subject of controversy in medical literature. In more than 15% cases these tumours may be associated with a well differentiated form of thyroid cancer (PC or FC) suggesting that ATC originates from transformation of a well differentiated thyroid cancer.[40] Most cases are seen in elderly females.[20] ATC's demonstrate a variable histological pattern some showing spindle cells, others showing giant cells, squamoid cells, large cells or small cells, so that ATC's may be confused with sarcomas, some carcinomas, melanomas or large cell anaplastic lymphomas.[20,40] In our study, ATC's comprised of 10 cases (5.86%) which is in accordance to Shah's study.[31] Other studies quote values of 7.89%,[3] 2%,[10] 3.16%[23] and 4.8%.[28] Our oldest patient (a 90 year female) belonged to this category. In our study all patients with ATC were over 55 years of age.

NHL's constituted a small but significant number of patients comprising 4 cases (2.35%) in this study which is consistent with the study of Shah and Muzzafar[31] who gave figures of 2.9%. In our previous study[3] only 2 cases (5.26%) were diagnosed as NHL. Lymphomas may involve the thyroid as part of systemic lymphoma or may arise primarily in the thyroid.[21] Invasion into the surrounding strap muscles and soft tissues is seen in 50 – 60% cases. Systemic lymphoma with secondary thyroid involvement indicates a poor prognosis.[22]

Conclusions

This study concludes that all patients with thyroid enlargement either as a solitary nodule, multiple nodules or diffuse involvement should have a thorough clinical evaluation and fine needle aspiration biopsy followed by surgical excision to rule out the possibility of malignancy. Sudden changes in the size of the gland, the appearance of new and hard, irregular nodules, hoarseness of voice or dysphagia and cervical lymph node enlargement may signify a malignant change and are indications for surgical excision and histopathological evaluation. The incidence of thyroid cancer in Pakistan is on the increase. This could be attributed to the increased awareness of the disease and other contributing factors including genetic susceptibility, dietary and

environmental factors like iodine deficiency or excess, radiation exposure and particular geographic locations. The prophylactic introduction of iodine in the diet could be a possible cause for the increase in the relative frequency of Papillary Carcinoma over Follicular Carcinoma. Estimation of the iodine content in food & water is suggested for the future control and prevention of the disease.

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