A Clinical Study on Malignant Neoplastic Thyroid Swellings

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ABSTRACT

BACKGROUND
More thyroid malignancy cases occur in women. FNAC (Fine Needle Aspiration Cytology) and histopathology play a key role in resolving this diagnostic challenge. A study was conducted to correlate the age, gender parameters with the clinical findings in thyroid malignancies by considering the histopathological examination (HPE) as the gold standard.

METHODS
It was a prospective study conducted in the department of Surgical Oncology, GSL Medical College, Rajahmundry, Malignant thyroid neoplasm individuals of any age, either gender who were fit thyroidectomy were included in the study. FNAC of the thyroid gland and lymph nodes was done. Data was analyzed using SPSS 21.0. Chi square test was used to find the statistical significance. $P > 0.05$ was considered to be statistically significant.

RESULTS
In this study, 52 HPE proven cases were studied, female male ratio was 5.5. Majority (28.8 %) of the study subjects were belong to 21 – 30 years. Majority (36.5 %) of the study volunteers had swelling for < 3 months and right side swelling was common. Papillary thyroid carcinoma (PCT) was common.

CONCLUSIONS
Thyroid carcinoma was common among females and PCT was common. FNAC contributed significantly to the preoperative investigation in thyroid swelling patients but despite its well-recognized value there are limitations to the technique.

KEYWORDS
Thyroid, Swelling, Carcinoma, Age

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BACKGROUND

The thyroid gland is one of the largest endocrine glands. Various systems in our body, namely nervous, endocrine and the immune system are connected physiologically to this. Thyroid cancer is the commonest of all endocrine malignancies, worldwide and its incidence has been increasing many-fold over the decades. But thyroid cancer is relatively uncommon, accounting 1 % of all malignancies. Mutated protooncogenes and loss of function in growth suppression genes are the two genetic processes that lead to thyroid neoplasia. Most of these genetic abnormalities are acquired, but 5 % to 10 % of papillary thyroid carcinomas are thought to be familial[1]. Ionizing radiation can cause genetic mutations leading to malignant transformation. This association is much stronger for thyroid cancer than for other malignancies, and radiation is the only clearly established environmental risk factor for thyroid malignancy.

Gender wise, the > 75 % thyroid malignancy cases occur in women but high mortality was reported among men.[2] Most of the thyroid malignancies clinically present as solitary thyroid nodules clinically indistinguishable from benign neoplasms and nonneoplastic nodules and posing a significant diagnostic challenge.

FNAC and histopathology play a key role in resolving this diagnostic challenge and help the clinicians in taking choice on management of these patients. Though FNAC is commonly used as a diagnostic tool for thyroid malignancies, it is associated with many shortcomings. Hence the histopathology is considered a gold standard.[3]

With these study was conducted to correlate the age, gender parameters with the clinical findings in thyroid malignancies by considering the histopathological examination (HPE) as the gold standard.

METHODS

It was a prospective study carried on clinically confirmed thyroid cancer individuals. Study was conducted in the Department of Surgical Oncology, GSL Medical College, Rajahmundry, and Andhra Pradesh. Study was conducted from August 2015 to 2017. The study protocol was approved by the Institutional Ethical Committee.

Malignant thyroid neoplasm individuals of any age, either gender who were fit for thyroidectomy were included in the study. Individuals who did not submit the informed consent, those were diagnosed to be benign, follicular neoplasms were excluded from the study.

The clinical history with duration and progression of symptoms along with age and gender were collected. The routine blood investigations, thyroid profile, radiography of the chest, neck, viral markers and FNAC of the thyroid gland and lymph nodes. Ultrasound of the neck was done in all cases to determine whether thyroid swellings are multinodular or solitary nodules and to determine the cervical nodal involvement. Indirect laryngoscopy was done in all patients to determine the status of the vocal cords specifically their movements. HPE of the excised specimen was done in all cases and the findings compared to those of ultrasonography and FNAC. All the patients underwent surgery after proper consent. Most of the patients were discharged with a clean and healthy wound except a few with post-operative complications.

Data was analysed using SPSS 21.0. Chi square test was used to find the statistical significance. P > 0.05 was considered to be statistically significant.

RESULTS

In this study, 52 histopathologically proven cases of thyroid cancers were studied. Gender wise, 84.6 % (44) were female and 15.4 % (8) were male and the female male ratio was 5.5 (Table 1). Majority (28.8 %) of the study subjects were belonging to 21 – 30 years followed by 41 – 50 years (19.2 %), 31 – 40 years (17.3 %), 61 – 70 years (13.5 %), 11 – 20 years (11.5 %) and 51 – 60 years (9.6 %) (Table 2). Gender wise, among female, PCT was the predominant (79.5 %), followed by FCT (13.6 %), ACT (4.5 %) and MCT (2.3 %). Whereas, among the male, 100 % were PCT cases (Table 3).

Gender	Frequency	Percent
Females	44	84.6
Males	8	15.4
Total	52	100.0

Table 1. Gender Wise Distribution of the Study Participants

Age	Number	%
11 – 20	6	11.5
21 – 30	15	28.8
31 – 40	9	17.3
41 – 50	10	19.2
51 – 60	5	9.6
61 – 70	7	13.5
Total	52	100.0

Table 2. Age Wise Distribution of the Study Participants

Malignancy	Female	Male	Total
PCT	35 (79.5)	8 (100)	43 (82.7)
FCT	6 (13.6)	0	6 (11.5)
MCT	1 (2.3)	0	1 (1.9)
ACT	2 (4.5)	0	2 (3.8)
Total	44 (100)	8 (100)	52 (100)

Table 3. Gender Wise Distribution of Different Types of Thyroid Malignancies among the Study Participants, n (%)

The above table shows the duration of swelling among the study subjects. Majority (36.5 %) of the study volunteers had swelling for < 3 months, 34.6 % had between 6 months to one year, 19.2 % had between 3 to 6 months, 7.7 % had between 1 to 2 years and 1.9 % had swelling from 2 to 5 years. Solitary nodule was present in 61.53 % of the study subjects, multinodular in 26.92 % followed by 7.7 % had uniformly enlarged and uneven irregular nodules in 3.8 % members. In this research, 44.2 % had swelling in right side, left side in 30.8 %. Diffuse in 19.2 % and 5.8 % had isthmus.

Pain was reported by 5.8 %, dyspnoea by 5.8 %, dysphagia by 3.8 %, change in voice by 5.8 % and enlarged lymph nodes in 17.3 % study members. Laryngoscopy findings showed that one subject (1.9 %) had left vocal cord paralysis. Euthyroid was detected in 86.5 % (45), hyperthyroid in 1 (1.9 %) and hypothyroid in 11.5 % (6).

Majority of the study subjects (53.8 %) belong to Papillary Thyroid Carcinoma (PCT), follicular neoplasm (25 %). Benign was detected in 9.6 %, suspicious PCT in 5.8 %, Anaplastic Thyroid Carcinoma (ACT) in 3.8 % and Medullary Thyroid Carcinoma (MCT) in 1.9 %. HPE showed that majority of the study subjects were diagnosed to be PCT (82.7 %) followed by Follicular Thyroid Carcinoma (FCT) (11.5 %), ACT (3.8 %) and MCT (1.9 %). In this study, when the diagnostic findings of FNAC and HPE were correlated, it was found to be statistically significant (Table 4).

FNAC	HPE				Total
	PCT	FCT	MCT	ACT	
Benign	5 (11.6)	0	0	0	5 (9.6)
PCT	28 (65.1)	0	0	0	28 (53.8)
Suspicions PCT	3 (7)	0	0	0	3 (5.8)
Follicular neoplasm	7 (16.3)	6 (100)	0	0	13 (25)
MCT	0	0	1 (100)	0	1 (19)
ACT	0	0	0	2 (100)	2
Total	43 (100)	6 (100)	1 (100)	2 (100)	52 (100)
Statistical analysis	Chi-square = 124.093, P = 0.0001, Statistically significant				

Table 4. Comparison of FNAC and Histopathology Findings among the Study Participants, n (%)

DISCUSSION

Studies from western world mentioned that, 0.6 % thyroid malignancies in male 0.6 % and 1.6 % in female. Whereas, the Indian studies mentioned 1.2 % and 1.9 % of malignancies in men and women, respectively. In this study, maximum patients were females (84.60 %) and female male ratio was 5.5 (Table 1). Female dominance was mentioned in various other studies also. However, some disparity with this study and literature. The female male ratio was 3.1 as per Wani et al.[4], and 1.9 by Nagarkar et al.[5] But this was declared to be 5.1 by T Pramod et al.[6]

When the data was categorized by histology, the incidence of PTC or FTC was three-times higher in women than in men. Whereas ATC was 2 times common in women than men. There was no significant difference in the incidence of MTC between men and women. In PCT the female male ratio was 4.37 and in the other carcinomas there were no male members. Definitely the female preponderance was detected. Small samle size may be the reason especially in this study. But this study can be compared with study by Pramod et al.[6] PCT constitutes 82.69 % of all sub types, while there was no case of thyroid lymphoma registered in the sample. When the present study was compared to other studies a slight rise in the incidence of PCT can be seen. The rise PCT incidence rate may represent either a true increase in the occurrence of disease or an increasing number of diagnoses due to escalating levels of diagnostic scrutiny. With more widespread use of ultrasonography and FNAC biopsy and with many radiographic incidentalomas discovered on nonthyroid imaging, a larger number of clinically occult, small thyroid nodules are being detected and investigated.

In this study majority members were belong to 21 – 30 years age group. Maximum incidence of thyroid malignancies were seen between 21 – 50 years. The mean age of presentation was 37.92 yrs. The youngest subject to present with thyroid malignancy was 11 year female child. ACT present in old age groups, both cases of ACT were above 60 yrs. FCT and PCT were distributed on either side of the mean age. The mean age was mentioned to be 48.14 years by Fabio et al.[7], 48 years by Mathew et al. and 36 years by Pramod et al.[6] The peak incidence of thyroid malignancy according to this study was 4th decade of life.

The duration of each swelling are grouped into regular time intervals and studied. Most of the subjects (36.5 %) had the swelling within a short duration of 3 months. And almost all swellings were below 1 year duration. This indicates the shorter duration and rapid progression of malignant thyroid tumours.

Most (73.3 %) of the patients in this study presented with symptoms during the past 3 months to 2 years. Only 6.6 % had swelling for > 5 years. Similar findings by Pramod et al.[6] also. The 2 ACT were of 3 and 4 months duration indicating fast growth of this subtype of thyroid malignancy. The occurrence of malignancy is more in solitary thyroid nodules (STN) compared to multinodular goiter. Clinically detected STN was the most common entity, accounting for 32 (61.53 %) of these patients. The next common entity was multi nodular goiter (MNG), in 14 (26.92 %) patients. According to literature, STN had higher risk of malignancy than multiple nodules. Clinically, STNs are common, being present in up to 50 % of the elderly population. The majority of STNs were malignant. The present study also shows a dominance of STN presentation in thyroid malignancies. A single dominant or solitary nodule is more likely to represent carcinoma than a single nodule within a multinodular gland, with an incidence of malignancy from 2.7 to 30 % and 1.4 to 10 % respectively as mentioned by Barroeta et al[8] and Abu-eshy et al.[9] From the above studies it's clear that the thyroid malignancies with clinically solitary nodule is more dominant than multinodularity in general population. While irregular and uneven hard swellings are usually anaplastic carcinoma thyroid in almost all studies, a few of the thyroid malignancies present as a generalized uniform swelling without any nodularity. Most of the thyroid malignancies in males were multinodular in this study. But STNs were frequently seen in women.

Commonest presenting symptom of thyroid malignancy in this study was swelling in front of the neck. Robbinsons et al.[10] mentioned the same in 100 % of the study members and it was mentioned to be 96.9 % by Wani et al. [4] Other symptoms like hoarseness of voice, dysphagia, dyspnoea and cervical lymphadenopathy were present in minority of patients and are comparative to other studies. Pain is nonspecifically present in any type of thyroid malignancy, while dyspnoea, dysphagia and hoarseness of voice are compressive symptoms which indicate either a large muitinodular goitre, a long standing swelling, or in case of anaplastic papillary carcinoma due to infiltration of underlying structures. Lymph node swellings are present in 9 (17.3 %) of the subjects of which 5 are papillary carcinoma thyroid, 2 were ACT, one each MCT and FCT.

In this study of 52 subjects of the thyroid malignancy, pre-operative indirect laryngoscopy findings identified left vocal cord palsy in a single subject. Rest of the cases were with normal movement of the vocal cords. Vocal cord paralysis can occur in both benign and malignant thyroid disease. The

etiology of the paralysis (VCP) is not always evident, but can often be explained by direct invasion or compression of the recurrent laryngeal nerve by malignant thyroid disease. In the case of benign thyroid disease, the paralysis could be idiopathic or could be caused by compression or stretching of the nerve. Knowledge of preoperative vocal cord paralysis is imperative for appropriate surgical planning and management. In this study, 1.9 % of patients undergoing thyroid surgery were found to have preoperative VCP. A study by Shafkat et al.[11], 110 of these patients were diagnosed with VCP. There was no significant difference between men and women in terms of the presence or absence of preoperative VCP. On the other hand, the study found age to be a significant factor; it was considerably higher in patients with preoperative VCP. Chiang et al.[12] also noted this finding in a study looking at thyroid tumours with preoperative recurrent laryngeal nerve palsies.

In this study, 87 % members were euthyroid, 12 % showed hypothyroid status with elevated serum TSH levels above baseline. Only one subject was hyperthyroid. A number of studies have shown that serum TSH concentration is an independent risk predictor for the development of thyroid cancer, the progression of thyroid cancer, or both. The association between serum TSH and risk of thyroid cancer has been proposed by Franklyn et al.[13] in the first study, a nonsignificant trend towards decreased cancer risk was found in patients with serum TSH below the normal range. In a second study published Polyzos et al.[14] the authors found that the risk of malignancy increases with serum TSH concentrations, Haymartef et al.[15], reported a frequency of differentiated thyroid cancer was 16 % when TSH was < 0.06 mIU / liter and 52 % when TSH was higher than 5.00 mIU / liter.

In this present study of the 52 cases of thyroid malignancy, FNAC was able to diagnose accurately in 59.61 % (31) cases as definite malignancy, 13 cases as follicular neoplasms (25 %), 3 cases as suspicious malignancy (5.76 %) and 5 cases as benign (9.61 %).

Five cases were wrongly interpreted as benign, which later turned out to be malignant on HPE. All five cases were PCT. In this study the false negative (FN) results were 9.61 %. The FN FNAC results may occur because of sampling error, coexistence of benign and malignant lesions, or cytomorphologic overlap between benign and low grade malignant tumors. In this study specificity cannot be calculated because the study contains only true positives, false negatives and not false positives & true negatives (benign thyroid lesions). Finally FNAC sensitivity was 90.38 in this study. It was reported to be 95.2 by Fatemeh et al.[16], 92.7 by Jogai et al.[17] and 95 by Gharib et al.[18]

Cytohistological correlation was present in 90.38 % of cases in this study. The sensitivity of the FNAC being 90.38 % and there was significant association between two groups is statistically significant. Monisha et al.[19] reported cytological correlation in 80 % of cases and it was 80.28 % by Pinky Pandey et al.[20] FNAC contributes significantly to the preoperative investigation in patients with thyroid swelling but despite its well-recognized value there are limitations to the technique.

The reported pitfalls are those related to specimen adequacy sampling techniques, the skill of the aspirator performing the aspirations, the experience of the cytopathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasms and inadequate, indeterminate FNAC. One major limitation of thyroid cytology is its inability to distinguish between follicular adenoma from follicular carcinoma. WC Faquin et al.[21] reported that 15 – 30 % of FNAC diagnosed follicular neoplasm were actually carcinomas. In this study, the subjects are cases of thyroid malignancies, hence all pre-operative follicular neoplasms are either follicular carcinomas or follicular variants of papillary carcinomas.

CONCLUSIONS

Thyroid carcinoma is common among females and PCT is the commonest. Swelling was the commonest clinical symptom. The diagnostic accuracy for FNAC was 59.61 % and sensitivity was 90.38 %. FNAC contributed significantly to the preoperative investigation in patients with thyroid swelling but despite its well-recognized value there are limitations to the technique.

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