International Surgery Journal
Bharath SV et al. Int Surg J. 2021 Apr;8(4):1155-1159
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20211289

Original Research Article

A prospective observational study on thyroid malignancy

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Received: 07 March 2021
Revised: 20 March 2021
Accepted: 23 March 2021

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ABSTRACT

Background: Thyroid cancers are a complex group of tumours with wide variety of histological presentation and biological behaviour, and prognosis range. In their early stages, they behave like other benign conditions of the thyroid. The success of treatment lies upon early diagnosis and proper management. The aim of the present study is to evaluate the modes of presentation, the incidence of various pathological types, and assess their clinical, behaviour and surgical management.
Methods: The present study is observational, time-bound, consists of patients prospectively and consecutively diagnosed and histologically confirmed thyroid malignancy.
Results: This study showed females 80.66% are commonly affected than males 19.44%. The most frequent malignancy is papillary 86.11%, followed by follicular carcinoma 11.11%, medullary carcinoma 2.78%. Cervical lymph nodes are involved in four 13.88% of patients. In patients undergone iodine ablation, 5.56% of them had a recurrence. Mortality at two years was 2.7%. In this study, Thyroid cancer is commonly seen between twenty-one to thirty years.
Conclusions: The incidence of thyroid malignancies is more common among women (80.66%) than men**.** Papillary carcinoma (86.11%) is the common differentiated thyroid cancer. The prevalence of distant metastasis is 2.78% to the vertebral body. In our study, 41.66% of patients belongs to less than 30 years of age; this may be due to the trend of overdiagnosis due to the introduction of ultrasonography guided Fine needle aspiration study.

Keywords: Differentiated thyroid cancer**,** Thyroid malignancy, Thyroidectomy, Cervical lymphnodes

INTRODUCTION

Worldwide, thyroid cancer (TC) is a relatively rare neoplasm; however, it is the commonest endocrine gland malignancy.[1] In 2018, an estimated 567,000 incident TC cases were registered, ranking ninth among all cancer incidence with 130,889 males and 436,344 females. About 41,000 TC deaths were estimated to occur worldwide, out of which 15,557 males and 25,514 females.[2] In India, the thyroid cancer incidence rate in women is increased from 2.4 to 3.9.[3] The thyroid cancer rates show considerable variation among different regions of India. The thyroid cancer incidence in women less than thirty years, thirty to forty-four years, forty-five to fifty-nine years, sixty to seventy-five years, and more than seventy-five years was 121%, 107%, 50%, 15%, 27%.[3] In recent decades incidence of TC have gone up in developing countries, albeit to varying degrees.[4-7] Increased incidence of thyroid malignancy is attributed to environmental risk factors, including a deficit or excess of iodine intake, medical radiation, and nutrition-related factors.[8] The advent and availability of advanced diagnostic techniques, imaging modalities, imaging-guided aspiration cytology, tissue biopsies, and newer biochemical markers have led to the early identification of malignant thyroid nodules. To the present-day, surgery remains as standard care with or without iodine 131 isotope ablation. Hence this study is done to evaluate the modes of presentation, clinical behavior, and surgical management of the disease.

METHODS

This prospective, observational, and clinical study on thyroid cancer was conducted in southern India's tertiary care center from 1St September 2014 to 31st August 2017. This study includes patients selected on a non-probable convenience sampling method with histopathologically confirmed TC cases. The institutional ethical committee and review board gave their approval to this study, and consent was obtained from the participant before being enrolled. The IBM SPSS program for Windows was used to analyse the results. Sampling technique used is nonprobability sampling.

Statistical tests used are univariant analysis, proportions and percentages

Inclusion criteria

Pathologically confirmed thyroid cancer patients (this also include FNAC is benign, but final histopathology is malignant) and patients who are willing to take part in studies were included in the study.

Exclusion criteria

Exclusion criteria excluded the patients less than 14 years of age, patients are referred to this hospital after the primary treatment, benign disease on histopathology, patients treated before and after this study period was not considered and patients were not willing to consent to the study.

Preoperative

Patients are subjected to clinical assessments and investigations. Investigations include thyroid hormone level, thyroglobulin, antithyroglobulin antibodies, serum calcium level, ultrasound of neck (morphology of thyroid gland, cervical lymphnodes), and USG guided fine needle aspiration cytology of the thyroid gland. Contrast-enhanced computer tomography was conducted in Patients with infiltration features to a surrounding structure, enlarged lymphnodes, or suspected tracheomalacia. Patients with hyperthyroidism received antithyroid drugs until the surgery day to prevent a perioperative thyroid crisis. The otolaryngologist assessed vocal cord motility preoperatively in all the patients.

Surgical procedure

The American thyroid association 2009 guidelines and the American joint commission on cancer 7th edition were used for staging the disease. The FNAC, frozen section, and histopathologic diagnosis were used to decide the Surgery's extent, total thyroidectomy, or hemithyroidectomy. The neck dissection and central compartment clearance decision were taken based on the findings of clinical, radiology, intraoperative assessment, frozen section diagnosis, and poor prognostic features of thyroid cancer. Patients symptomatic for hypocalcemia in the postoperative period received oral or intravenous supplements, depending on severity. All patients are assessed postoperatively for vocal cord palsy. In intermediate and high-risk patients, radioiodine scanning was done.

Follow-up

We conducted follow-up visits for all patients at 1-, 3-, 6, and 12-month intervals in coordination with endocrinologists. Patients underwent thyroid profile test, thyroglobulin, antithyroglobulin antibodies and ultrasonography of the neck. All individual patient's data are entered at each visit to the hospital.

RESULTS

Incidences

During this study period, 2800 patients are admitted to the hospital with various newly diagnosed oncological diseases, including eighty-three thyroid cancer patients. Eleven patients are excluded from studies. Eight of them had benign lesions in the postsurgical histopathological examination. Three patients lost during the follow-up period. A total of seventy-two patients were considered for final analysis; thus, thyroid cancers accounted for 2.39% of oncological disease. Females are commonly affected than men with a ratio of 5:1. The population standard deviation is σ 12.55 Table 1.

Table 1: Characteristic of a patient with thyroid cancer (n=72).

Variables	Value
Age range (year)	16-66
Mean±SD	37.44±12.56
Median age	33
Gender percentage (%)	
Female	58
Male	14
Clinical symptoms (%)	
Swelling in front of the neck	68 (94.44)
Hoarseness of voice	8 (11.11)
Dyspnoea	2 (2.78)
Lymph node enlargement	6 (8.11)
Bony Pain (Metastasis)	2 (2.78)
Dysphagia	0
Duration of symptoms when presented (%)	
<3 months	0 (0)
Three months to 1 year	10 (13.88)
One year to 3 year	26 (36.11)
3 to 5 years	10 (13.88)
5 to 10 years	18 (25)
Ten years	8 (11.11)

Duration of symptoms

A malignant thyroid nodule was found within five years of onset swelling with considerable variation among the patients. In four patients, it is high.

Characteristic of the swelling

The goitre was classified on USG finding as a multinodular, solitary nodule, lobe involvement, diffuse enlargement of the gland (Table 2).

Table 2: Clinical characteristics of the thyroid.

Type of goiter		No. of patients	Percentage (n=72) (%)
Multinodular		64	88.89
Solitary Nodule		7	8.33
Diffuse		1	2.78
Lobe involvement			
Unilateral	Right lobe	12	16.67
	Left Lobe	6	8.33
	Only isthmus	0	0
Both the lobe involved		44	61.11
Both the lobes with the isthmus		10	13.89

X-ray neck

All the patients underwent an x-ray neck anterior-posterior view and lateral view. The deviated trachea was found in fourteen patients. Sixteen patients had calcification of glands; Tracheal rings are regular.

FNAC of the thyroid gland

The majority of FNAC are papillary carcinoma, follicular neoplasia, adenomatous goitre, Colloid goitre, medullary carcinoma. FNAC was repeated in two patients out of three, which are inconclusive initially. One patient did not agree to repeat FNAC patient underwent a frozen section (Table 3).

Surgery

The American joint committee on cancer 7th edition used to stage the disease (Table 3). Patients underwent standard surgical procedures. All patients underwent vocal cord examination preoperatively as shown in the Table 4.

Complication

Fifteen (20.83%) had postoperative complications; three had permanent hypoparathyroidism, five had unilateral vocal cord palsy, three patients had seroma formation, one patient had surgical site infection. Three had a reoccurrence in the cervical lymph node.

Table 3: FNAC and histopathology characteristics of the thyroid gland.

Variables	Percentage (%)
Papillary carcinoma	44 (52.77)
Follicular neoplasia	10 (13.88)
Adenomatous goiter	10 (13.88)
Colloid goiter	04 (11.11)
Medullary carcinoma	02 (2.77)
Inconclusive	01 (2.77)
Anaplastic carcinoma	00 (0)
Finale histopathology	
Papillary carcinoma	56 (77.78)
Follicular carcinoma	14 (19.44)
Medullary carcinoma	02 (2.78)
Anaplastic carcinoma	0
Lymphomas	0
No. of patients in each stage according to AJCC 7th edition	
Stage I	47 (65.27)
Stage II	09 (12.5)
Stage III	06 (8.33)
Stage IV A	08 (11.11)
Stage IV B	0 (0)
Stage IV C	2 (2.75)

Table 4: Details of surgical treatment.

Variables	Percentage (%)
The extent of surgery (n=72)	
Total thyroidectomy	60 (83.33)
Hemithyroidectomy	12 (16.67)
Completion thyroidectomy	8 (11.11)
Neck dissection	
No neck dissection	27 (37.5)
Central	29 (40.27)
Unilateral neck dissection	5 (6.94)
Bilateral neck dissection	11 (15.28)
Vocal cord status	
Before Surgery, palsy noted	3 (4.17)
After Surgery	8 (11.11)
Recurrent laryngeal nerve sacrificed due to disease	5 (6.94)
Parathyroid glands	
Number of auto transplantation done	6 (8.33)

DISCUSSION

Demographic profile

Most of the patients, 37.5%, are 21-30 years, 23.61% of people are 31-40 years, 19.44% of patients are 41-50 years, and 16.67% are more than 50 years (Table 1). Study by Karkuzhali et al. showed that most of the patients were less than 45 years (73.7%), and the remaining 26.3% of the patients were more than 45 years.[9] Among the study participants, females (80.66%) were more commonly affected than males (19.44%). This

gender preference has proven in studies worldwide that women are affected three times more than men, with an estimated 77% of women of the total cases.[10] A similar study undertaken in a tertiary care center in South India for papillary carcinoma showed that out of 377 patients, 307 patients are females, 81.4%.[11] The higher incidence of thyroid malignancy found in females was probably because of endogenous estrogen hormone on thyroid tumor cells. In experimental studies, the estrogen effect on thyroid cells is mediated through estrogen receptor alpha and beta. The alpha receptors upregulation stimulates tumorigenesis, and beta receptors downregulation act as a tumor suppressor.[12]

Presentation

The typical clinical presentation was the neck swelling in sixty-eight (94.44%) patients. Eight patients (11.11%) presented with hoarseness of voice. In addition to thyroid swelling, twelve patients (16.66%) had enlarged cervical lymph nodes; two patients (2.7%) had severe back pain due to metastatic lesions. Similarly, a study undertaken in Italy showed that 98.7% are presented with swelling in the neck, and cervical nodes were also involved in thirty-one (13%) patients.[13] Another study conducted by Mehrotra et al had different lymphadenopathy incidence findings; 59% are cervical lymphadenopathy, 7.2% are mediastinal lymphadenopathy. The extracapsular thyroid invasion is seen in 10%, and 4.2% had distant metastasis.[14]

The final diagnosis and associated features in the present study, the histopathology results show papillary carcinoma in fifty-six (77.78%), follicular carcinoma in fourteen patients (19.44%), medullary carcinoma in two patients (2.78%). Eight patients (11.11%) had metastatic disease, five had in the cervical lymph node, and two patients had a lumbar vertebra. This is like another south Indian study.[11]

Surgery

Sixty patients (83.33%) underwent total thyroidectomy; twelve (16.67%) had hemithyroidectomy, eight had completion thyroidectomy. Eleven patients had bilateral modified radical neck dissection. Five had unilateral modified radical neck dissection; one underwent a palliative total thyroidectomy in a patient with metastasis. In two patients, total thyroidectomy was done with a frozen section; Fine-needle aspiration cytology was benign in these two patients but clinically suspicious of malignant disease. The two patients with medullary carcinoma underwent total thyroidectomy with central compartment lymph node dissection. At the one-point radical neck, dissection was the treatment of choice. Later less aggressive "berry picking" approach was practiced for removing macroscopically involved neck nodes. This led to high recurrence rates.[15] With the improvement in neck surgery techniques, the en bloc dissection of anatomic neck compartments is uniformly recommended by the guidelines as the procedure of choice in patients with evidence of neck disease.[16]

Postoperative period

Five of seventy-two patients had recurrent nerve (RLN) palsy confirmed by ENT specialist; these five-patient had unilateral RLN palsy. One patient had bilateral among the three who had vocal-cord palsy due to involvement by the tumor. This patient underwent a tracheostomy. Twenty of seventy-two had hypocalcemia in the immediate postoperative period. Three of the six patients of the auto-transplanted parathyroid gland had permanent hypoparathyroidism.

Postoperatively, patients with differentiated thyroid malignancy are divided into high and low risk group for recurrence. High-risk group patients are started with thyroxine to achieve the TSH level<0.1 mU/L. Low-risk patients with total thyroidectomy started with a supplement dose of thyroxine endocrinologist follows up all these patients for individualization of thyroxine dose and long-term complication. I^{131} ablations was done in sixteen patients of differentiated thyroid malignancy patients.

All seventy-two patients were followed up with ultrasonography of neck, TSH, thyroglobulin, and antithyroglobulin antibody levels, initially at an interval of 3 months for two visits. After the initial two visits once in six months, follow-up visits were done to the surgery department in addition to their routine follow-up with endocrinologists. Three patients (4.16%) were lost during follow-up. One patient (1.38%) died after two years of the primary cause was ARDS, who had follicular carcinoma with vertebral metastasis. After three years of iodine ablation, two patients (2.77%) found had developed cervical lymphadenopathy. On evaluation, these patients found to be having recurrent papillary carcinoma accounting for 2.78%. Samaa et al found with the best practices, recurrence rates have been recorded to range from 8% to 23% by.[17,18] In our study, only 2.78% had a recurrence, but this cannot be compared with other studies as they are long-term for more than ten years.

Limitations

The sample may not be actual representations of incidence of characteristics, like age and sex, as it contains only volunteers. We are unable to report the long-term result for survival and complications.

CONCLUSION

The increased occurrence of thyroid cancer is due to over-diagnosis by higher diagnostic intensity and more intensive medical monitoring, which may be one reason for this growing trend. However, environmental risk factors such as ionizing radiation, excessive iodine use, and obesity may have played a role in the TC rise. The

preferred treatment is a combination of Surgery and adjuvant iodine 131 therapy. Age, sex, tumor size, stage of the disease, the prevalence of the extrathyroidal spread, and completeness of resection all significantly affect the prognosis of a patient. Despite the best practice, recurrence rates are reported in the vicinity of 8% to 23%. Clinical examination, imaging modalities, and markers help in the detection of residual and recurrent disease early. Uncontrolled locoregional or distant illness, on the other hand, can lead to mortality.

ACKNOWLEDGEMENTS

Author would like to thank to Dr. Suresh A. Mayya, professor of surgery, and Dr. Moosabba M. S, professor of surgery, deserve my deepest gratitude. They are very supportive in preparing this study methodology and delivering the findings in the most concise way possible. It was a great privilege and honour to study and work under their guidance.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bharath SV, Lakshminarayana B, Mehta R. A prospective observational study on thyroid malignancy. Int Surg J 2021;8:1155-9.