A Retrospective Study of Clinicopathological Profile and Treatment Outcomes of Thyroid Malignancies Presented to a Tertiary Care Teaching Hospital

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ABSTRACT

Introduction: Thyroid cancer is on the developing world over – almost doubling in the past ten years. This is mainly due to improved awareness, screening and diagnosis of the nodular disease. Thyroid cancer has an apparent gender predisposition with women being affected three times more than men and 8th most mostly occurring cancer among women. To analyze the clinicopathological profile of thyroid cancer patients and to assess the pattern of treatment and long-term treatment outcomes.

Material and methods: The current study was retrospective case record review of all the thyroid cancer cases including all the histopathological confirmed cases of thyroid cancer. The statistical analysis was carried out by using IBM SPSS version 21.

Results: A total of 67 subjects were included with a mean age of 44.72 ± 14.99 years. Females were 68.66% and males 31.34% of the study population, 61 (91.05%) people had usual presentation of neck swelling of various sizes and other associated findings. Thyroid function test showed that 91.04% (61) showed euthyroid status, 40.3% (27) had a total thyroidectomy, 95.52% (64) of the patients were alive and well.

Conclusion: The study bears evidence to the fact that papillary carcinoma is the most commonly occurring form of differentiated thyroid cancer (70.6%). The prevalence of distant metastasis is 4.48% and most commonly found in the lung. The disease is more prevalent among women than men.

Keywords: Thyroid Cancer, Retrospective, Thyroid Function Test, Tertiary Care, Iodine Uptake, Node Status, I 131 Ablation, Papillary, Clinicopathological, Malignancy

INTRODUCTION

The morbidity and mortality relating to cancer are both omnipresent and severe, with an incidence of 14 million new cases and 8 million cancer-related deaths in 2012. There is no country, age or socio-economic denomination that is free of this disease. The worldwide incidence as of 2012 is 182 per 100,000 and mortality 102 per 100,000. The burden of cancer worldwide is estimated to increase to 20 million new cases by 2025.[1]

Thyroid cancer is on the developing world over – almost doubling in the past ten years. This is mainly due to improved awareness, screening and diagnosis of the nodular disease. Its incidence is estimated to be at 202 per 100,000 population in countries belonging to high or very high HDI as compared to 96 per 100,000 population in countries of low or medium HDI like India. Thyroid Cancer has an incidence of 89 per 100,000 among women in the Republic of Korea, which is the highest worldwide.[1] The estimated total deaths of thyroid cancer globally was 40,000 in 2012. The mortality due to thyroid cancer is 18 per 100,000 in countries with higher HDI as compared to 23 per 100,000 in countries with low/ medium HDI. This shows a clear implication of the effect of HDI on mortality.

It contributes to 0.1-0.2% of the malignancies in India. Its age-adjusted incidence is 1 per 100,000 in males and 1.8 per 100,000 in females. The incidence of thyroid cancer is noted to be specifically high in the Papumpare district of Andhra Pradesh, Thiruvananthapuram and Kollam in Kerala with the highest incidence being 27 per 100,000 population.[2]

Thyroid cancer has an apparent gender predisposition with women being affected three times more than men, with an estimated 77% of the total cases occurring in women. It is the 8th most mostly occurring cancer among women.[1] The etiology of thyroid cancer remains mostly misunderstood. The risk of developing cancer in those persons with benign nodules is 3-6 times more than those unaffected. Exposure during childhood to ionizing radiation is an important etiological factor for papillary carcinoma (5% of the patients). The other associated factors are body mass index,dietary iodine deficiency (specifically in follicular cancer thyroid), conditions like acromegaly, familial adenomatous polyposis syndrome, Cowden syndrome, genetic component (non-medullary thyroid cancer).[1]

Clinical presentation of thyroid tumors ranges from insolent to rapidly aggressive. Almost 95% of the present thyroid malignancies are of the differentiated subgroup (papillary or follicular). They are treated effectively by surgery followed by radioactive iodine update. It is reported that 10% of these will develop distant metastasis, which requires further intervention.[3]

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The available treatment modalities for differentiated cancer are surgery, radioactive iodine uptake adjuvant, TSH suppressive therapy, external beam radiation therapy (EBRT), and systemic treatment. For A-DTC (advanced differentiated thyroid cancer) surgery is the primary treatment of choice. All gross diseases must be resected with minimal morbidity. For those with minimal invasion, a conservative approach like shave procedure can be tried. Even in those patients with distant metastasis, surgery is recommended for reducing symptoms of airway compromise and hemorrhage.[3]

RAI adjuvant is given to eliminate the microscopic disease following shave procedures and to destroy residual disease following conventional surgeries. EBRT is advised for those with invasion into trachea, esophagus or where is there gross disease as an adjuvant. The data supporting the effectiveness of EBRT is still unsatisfactory and controversial. For TSH suppression, the levels recommended are at less than 0.1 μU/L and the dose is adjusted based on the response. Systemic treatment is recommended when the tumor is not responding to RAI when the tumor is near critical, which cannot be subjected to local therapy. In this regard, Doxorubicin is the most effective agent. Others, like Sorafenib and Levantines, have been studied to show promise in Phase III trials.[4,5]

In metastatic cancers, the recommended treatment is TSH suppression and RAI therapy primarily. Other options are surgery, cryoablation, radiofrequency ablation (RFA), and ethanol ablation, chemo-embolization, EBRT.[3]

The recent guidelines as on 2015 according to the ATA recommends more conservative approaches to managing DTC with measures such as lobectomy in place of total thyroidectomy, monitoring TSH suppression depending on the recurrence of disease.[6] Studies have shown that papillary microcarcinoma can be subjected to active surveillance post-surgery, favoring a more wait and watch approach.[7]

Extensive genomic analysis has led to the introduction of selective BRAF inhibitors, i.e. dabrafenib[8], and vemurafenib,[9] Axitinib, pazopanib, motesanib, and sunitinib is targeting VEGFR show promise.[10] Use of immunotherapy with Pembrolizumab, against the programmed death protein-1, in combination with Levantines or envatinib is being researched into.[3]

Though less aggressive approaches are proven, the same for advanced DTC remain unexplored. It is pertinent to explore the use of predicting variables and potential biomarkers, which will help to determine which cases do progress to advanced DTC and to make sure they are treated with the appropriate regimen. Other areas which require intense research are learning the right time to start systemic treatment, the molecular profile of thyroid cancers and exploring the possibility of immunotherapy.[3]

Despite advancement in diagnosis, treatment of thyroid cancer, there is still a massive deficit in the literature with regard to the clinical outcomes of treatment. Very few studies have been done to assess the pattern of treatment of the rarer medullary forms of carcinoma thyroid and outcomes.[11] The epidemiology, as well as the clinicopathology of thyroid carcinomas, differ according to geography, and it is important to predict its clinical outcomes to find innovative and more pliable treatment modalities.[12] In this context, the present study was planned to analyze the clinicopathological profile of thyroid cancer patients and to assess the pattern of treatment and long term treatment outcomes. To analyze the clinicopathological profile of thyroid cancer patients presenting to a tertiary care teaching hospital in south India. To assess the pattern of treatment and long-term treatment outcomes among the study population

MATERIAL AND METHODS

The current study was retrospective case record review of all the thyroid cancer cases diagnosed in the department of oncology, a tertiary care teaching hospital in South India.

The study population included all the histopathological confirmed cases of thyroid cancer treated in the study setting between January 2000 to December 2006. The data collection for the study was done in January 2018.

Since the study was a retrospective case record review, no ethical approval was sought. It was also not possible to obtain informed written consent from participants. The confidentiality of the study participants was maintained throughout the reporting of the results.

The socio-demographic, clinical, radiological and histopathological findings were retrieved onto a structured proforma. The other details included the type of treatment provided, the occurrence of various pot operative complications and the management of the same.

The statistical analysis was carried out by using IBM SPSS version 21. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like a bar diagram, pie diagram and box plots. Considering the sample size available, only descriptive analysis was possible, and no inferential statistics or P values were presented.

RESULTS

A total of 67 subjects were included in the final analysis. The minimum age of the subject was 15 years, and the maximum age was 85 years, with a mean age of 44.72 ± 14.99 years. The age distribution of the study participants showed a majority of the subjects (46.27%) in and in 41 to 50 years age group. There was a female preponderance as females constituted 68.66% of the study population and males constituted 31.34% of the study population. (table 1)

Parameter	Number	Per cent
Age group		
Below 20	2	2.99%
21 to 40	25	37.31%
41 to 50	31	46.27%
61 and above	9	13.43%
Gender		
Male	21	31.34%
Female	46	68.66%

Table-1: Demographic profile of study population (N=67)

Type of presentation	Number	Percent
Usual presentation	61	91.05%
Cardiac tamponade	1	1.49%
Compression fracture	1	1.49%
Cystic mass neck	1	1.49%
Rib swelling	1	1.49%
Right tonsillar enlargement	1	1.49%
Thyroglossal cyst	1	1.49%
Previous history		
No previous history	56	83.58%
Left hemithyroidectomy	3	4.47%
Right hemithyroidectomy	3	4.47%
Total thyroidectomy	1	1.49%
Total thyroidectomy with right-sided radical neck dissection	1	1.49%
Total thyroidectomy with left RND done	1	1.49%
D5 vertebra biopsy and fixation done	1	1.49%
Papillary Carcinoma Thyroid	1	1.49%

Table-2: Descriptive analysis of the type of presentation and history (N=67)

Parameter	Number	Percentage
Final diagnosis (HPE)		
Papillary	48	70.6%
Follicular	12	17.9%
Medullary	3	4.5%
Papillary and follicular	3	4.5%
Papillary and medullary	1	1.5%
Nature of disease		
Primary disease	55	82.09%
Recurrent disease	9	13.43%
Metastatic disease	3	4.48%
Risk Stratification		
High risk	26	38.81%
Intermediate risk	27	40.30%
Low risk	14	20.90%
Thyroid Function Test		
EU thyroid status	61	91.04%
Hypothyroid	6	8.96%
Iodine Uptake		
No uptake	60	89.55%
Increased uptake in the dorsal spine	1	1.49%
Not performed	6	8.96%
Node Status		
Node positive	18	26.86%
Negative	49	73.14%

Table-3: Descriptive analysis of Final diagnosis and associate features in the study population (N=67)

Among the 67 subjects, 61 (91.05%) people have presented with the usual presentation of neck swelling of various sizes and other associated findings. The remaining 6 (8.95%) had an atypical presentation. The atypical presentations were cardiac tamponade. Compression fracture of rib, cystic neck swelling, rib swelling, tonsillar enlargement and thyroglossal cyst in 1 subject each. There was no previous history of thyroid disease or procedure in 56 patients. Right, and left hemithyroidectomy was done in the past in 3 (4.47%) subjects each. Total thyroidectomy with various degrees of neck dissection was done in 3 subjects, one subject each underwent D5 vertebral biopsy with fixation and surgical procedure for papillary carcinoma of the thyroid. (Table 2)

Procedure	Frequency	Percent
Surgical procedure		
Total thyroidectomy	27	40.3%
Total thyroidectomy with unilateral fnd	14	20.9%
Left hemithyroidectomy	4	6.0%
Completion thyroidectomy	4	6.0%
Total thyroidectomy with bilateral fnd	3	4.5%
Right hemithyroidectomy	3	4.5%
Total thyroidectomy (frozen section study was done)	2	3.0%
Total thyroidectomy with tracheal resection	1	1.5%
Total thyroidectomy with left paratracheal dissection	1	1.5%
Total thyroidectomy with excision of thyroglossal cyst	1	1.5%
Total thyroidectomy with bilateral paratracheal dissection	1	1.5%
Rib resection	1	1.5%
Recurrent nodule excision with left fnd	1	1.5%
Left radical neck dissection	1	1.5%
Left hemithyroidectomy with left fnd	1	1.5%
Excision recurrent nodal with right supra omohyoid neck dissection	1	1.5%
Completion thyroidectomy with left-sided fnd	1	1.5%
I131ablation		
30mci	35	52.24%
35mci	1	1.49%
50mci	5	7.46%
100 mci	1	1.49%
Not Given	25	37.31%

Table-4: Descriptive analysis of surgical procedure and I 131 ablation done in the study population (N=67)

The histopathology results, the most common type of papillary in 70.6% (48), followed by follicular type in 17.9% (12), medullary in 4.5% (3), papillary and follicular 4.5% (3), and papillary and medullary 1.5% (1). 82.09% (55) had primary disease, 13.43% (9) had recurrent disease, 4.48% (3) had metastatic disease. According to the risk stratification, 38.81% (26) fell at high risk, 40.30% (27) intermediate-risk 20.90% (14) belonged to low risk. Thyroid function test showed that 91.04% (61) showed euthyroid status, 8.96% (6) had hypothyroid. With regard to radioactive iodine uptake, no uptake was seen in 89.55% (60) persons, was increased in the dorsal spine in 1 person, and not performed in 6 persons. Nodal status was mainly negative in 73.41% (49) and positive in 26.86% (18) persons.

40.3% (27) of the total participants had a total thyroidectomy, 5 had total thyroidectomy with FND, four each had complete thyroidectomy and left hemithyroidectomy, three each had right hemithyroidectomy, and total thyroidectomy with bilateral FND. 2 each had undergone total thyroidectomy

Postoperative I131scan	Number	Percent
10 percent uptake	9	13.43%
6 percent uptake	7	10.45%
7 percent uptake	2	2.99%
8 percent uptake	8	11.94%
9 percent uptake	1	1.49%
insignificant tracer in neck	1	1.49%
no uptake	33	49.25%
Not done	6	8.96%
TSH Suppression		
ELTROXIN 100mgm	1	1.49%
ELTROXIN 150mgm	2	2.99%
ELTROXIN 200mgm	2	2.99%
ELTROXIN 250mgm	2	2.99%
ELTROXIN 300mgm	53	79.10%
NOT GIVEN	7	10.45%
Follow-up I 131 Scan		
Minimal neck uptake (WBS normal)	1	1.49%
Normal study	45	67.16%
Not done	21	31.35%
Status of the patient		
Alive and well	64	95.52%
Died due to myocardial infarction in Feb 2016	1	1.49%
Died of ageing dec2015	1	1.49%
Died of endobronchial metastasis	1	1.49%

Table-5: Descriptive analysis of postoperative I131 scan, TSH suppression, follow up 131scan, status of the patient, in study population (N=67)

with right FND and total thyroidectomy with left FND. In 2 persons, total thyroidectomy was done with a frozen section.1 each had undergone complete thyroidectomy with left-sided FND, excision recurrent nodal with right supra omohyoid neck dissection, left hemithyroidectomy with left FND, left radical neck dissection, recurrent nodule excision with left FND, rib resection, total thyroidectomy with bilateral paratracheal dissection, total thyroidectomy with removal of thyroglossal cyst, total thyroidectomy with left paratracheal dissection, total thyroidectomy with left RND, total thyroidectomy with left-sided FND, total thyroidectomy with left-sided radical neck dissection, total thyroidectomy with right FND, total thyroidectomy with right RND and total thyroidectomy with tracheal resection. I131 ablation was not given in 37.31% (25). Among those who were given, 30 mci was the most commonly administered dose in 52.24% (35). 7.46% (5) were administered a dose of 50 mci and one each was administered doses of 100mci and 35 mci respectively.

Follow up evaluation

Postoperative follow up showed most 49.25% (33) showed no 1131 uptake. 8.96% (6) the uptake study was not done. Among the others 13,43% (9), 11.94% (8), 10.45% (7), 2.99% (2) showed 10, 8, 6 and 7 percent uptake respectively. One each showed 9 per cent uptake and insignificant tracer.79.10% (53) were given Eltroxin 300mgm for TSH suppression. 2 each were given 200mgm, 150mg, 250 MGM. 1 patient was given a dose of 100mgm. 10.45% (7) were not subjected to TSH suppression. The follow up I 131 scan showed a normal study in 67.16% (45) persons and minimal uptake in 1 person. It was observed that 95.52% (64) of the patients were alive and well. Only one patient died of endobronchial metastasis. One due to myocardial infarction and one death was attributed to ageing-related causes.

DISCUSSION

The current study was retrospective case record review of all the thyroid cancer cases diagnosed in the department of oncology, a tertiary care teaching hospital in South India. The study population included all the histopathological confirmed cases of thyroid cancer treated in the study setting between January 2000 to December 2006. A total of 67 subjects were included in the study.

Demographic profile

Majority of the patients (37.31%) belonged to the age group between 21-30, followed by 32.84% in the age group of 41 to 50 years, and 13.43% each in the age groups between 51-60 and more than 60 years. A similar study was done by Karkuzhali et al.[12] which showed that the majority of the cases belonged to ages less than 45 years (73.7%) and the remaining 26.3% of the patients were more than 45 years.

Among the study participants, it was observed that females (68.66%) were more commonly affected than males (31.34%). This sex preference has been proven in studies world over which shows that women being affected three times more than men with an estimated 77% of the total cases occurring in women.[1] A similar study undertaken in a tertiary care center in South India for papillary carcinoma showed that out of 377 cases, the majority that is 81.4% (307) were found among females.[12] The reason for this gender preference is not known, but it is thought to be due to the effect of estrogen on the tumor cells.[13]

Type of presentation and previous history

91.05% that is, 61 patients presented with swelling in the neck, which is considered the usual performance. Of the remaining, there was one person each in the other forms of performance that is cardiac tamponade, compression fracture, cystic mass in the neck, rib swelling thyroglossal cyst and right tonsillar enlargement. Similarly, a study undertaken in Italy showed (98.7%) presented initially with swelling in the neck, cervical nodes were additionally involved in 31 (13%). Among those without clinical evidence of disease in the neck presented with metastasis to the lungs(2), and bones(1).[14]

A study by Mehrotra PK et al. showed that cervical lymphadenopathy was found in 59%, mediastinal lymphadenopathy in 7.2%, extra thyroid invasion in 10% and distant metastasis in 4.2%.[11]

Final diagnosis and associated features

In the present study, the histopathology results show the most common type of papillary in 70.6% (48), followed by follicular type in 17.9% (12), medullary in 4.5% (3), papillary and follicular 4.5% (3), and papillary and medullary 1.5% (1). A study undertaken among children and adolescents in the Himalayan region of India showed that majority of the

type was papillary(85%) followed by follicular(15%) which is the same as our study.[15]

82.09% (55) had the primary disease, 13.43% (9) had recurrent disease, 4.48% (3) had metastatic disease in our present study. In the study by Bal CS et al., distant metastasis presented in 29%.[15]

Surgical procedures in the study population

40.3% (27) of the total participants had a total thyroidectomy, 5 had total thyroidectomy with FND, four each had complete thyroidectomy and left hemithyroidectomy. Three each had right hemithyroidectomy, and total thyroidectomy with bilateral FND. 2 each had undergone total thyroidectomy with right FND and total thyroidectomy with left FND. In 2 persons, total thyroidectomy was done with a frozen section. The other procedures were complete thyroidectomy with left-sided FND, excision recurrent nodal with right supra omohyoid neck dissection, left radical neck dissection, recurrent nodule excision with left FND, rib resection, total thyroidectomy with bilateral paratracheal dissection, total thyroidectomy with excision of thyroglossal cyst, total thyroidectomy with left paratracheal dissection, total thyroidectomy with left RND, total thyroidectomy with tracheal resection to name a few.

The study was undertaken among 71 patients with medullary carcinoma thyroid also showed that total thyroidectomy was performed in 92.6% of patients, central compartment lymph node dissection in 67.6%, lateral cervical lymph node dissection 62.3%, and trans-sternal mediastinal lymph node dissection in 7.2%.[11]

Elizabeth et al. have recommended it that total thyroidectomy is the treatment of choice, and prophylactic lymph node dissection is not mandated unless the patient presents with clinically palpable lymphadenopathy.[16]

I131 ablation among the study participants

I131 ablation was not given in 37.31% (25). Among those who were given, 30 mci was the most commonly administered dose in 52.24% (35). 7.46% (5) were administered a dose of 50 mci and one each was administered doses of 100mci and 35 mci respectively. The study undertaken by Ruegemer JJ et al.[17], using Cox regression models showed that the radioiodine ablation did not have significantly improve the survival. Another author recommends the use of radioactive iodine thyroid ablation in the following circumstances tumor multicentricity, positive lymph nodes, or capsular or vessel invasion.[16]

The American Thyroid Association recommends the use of RAI for high-risk patients following total thyroidectomy. This functions a method of ablation for remnants of macroscopic as well as microscopic disease.[3]

TSH suppression

79.10% (53) were given Eltroxin 300mgm for TSH suppression. 2 each were given 200mgm, 150mg, 250 MGM. 1 patient was given a dose of 100mgm. 10.45% (7), were not subjected to TSH suppression. The ATA guidelines recommend the TSH suppression of less < 0.1 µU/L for distant metastasis.[3]

Treatment outcome

It was observed that 95.52% (64) of the patients were alive and all. Only one patient died of endobronchial metastasis. One due to myocardial infarction and one death was attributed to ageing-related causes. A study undertaken by Ruegemer JJ et al.[17] estimated that distant metastasis would occur in 10%, which is higher than is found in the present study. It showed that 78% of all deaths occurred due to thyroid cancer and most commonly within the five-year period. Thyroid cancer deaths mainly occur due to distant metastasis with a mortality of 65% at five years and 75% at ten years. Another study on medullary carcinoma thyroid patients shows a five-year survival of 74% and ten-year survival of 58%.[11]

It has been proven that complete thyroidectomy followed by radioactive iodine ablation is proven to increase the survival rates.[18]

In the present study, as well the one cancer-related death was due to endobronchial metastasis. This study by Ruegemer JJ et al.[17] was undertaken in 1988, and hence the vast improvement in the life expectancy due to better treatment modality is seen. With regard to the site involved, the present study showed an involvement of the endobronchial region. In the study by Ruegemer JJ et al.[17] also it was observed that lungs were most primarily involved in 53%, bones in 20%, multiple organ involvement in 16%. A study by Carlos et al. showed that n 45.5% of the patients presented with distant metastasis along with the primary tumor and lungs was the most common site affected followed by bone, lung and bone.[18]

CONCLUSION

In conclusion, the study bears evidence to the fact that papillary carcinoma is the most commonly occurring form of differentiated thyroid cancer (70.6%). The prevalence of distant metastasis is 4.48% and most commonly found in the lung. The disease is more prevalent among women than men. The currently used regimen of surgical management, radioactive iodine ablation technique remains the recommended choice of treatment. The use of systemic therapy is recommended in inoperable tumors and cases of distant metastasis. Further research is required to identify biomarkers predictors of advanced disease, explore the newer treatment modalities like Sorafenib and Lenvatinib, immunotherapy, and reduce the morbidity associated with these cancers.

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REFERENCES

1. IARC Cancer. World Cancer Report 2014. Bernard W. Stewart and Christopher ed. P. Wild. 2014.
2. Agarwal S, Jain D. Thyroid Cytology in India: Contemporary Review and Meta-analysis. J Pathol Transl Med. 2017;51:533-47.
3. Tumino D, Frasca F, Newbold K. Updates on the Management of Advanced, Metastatic, and Radioiodine

Refractory Differentiated Thyroid Cancer. Front Endocrinol (Lausanne). 2017;8:312.
4. Brose MS, Nutting CM, Jarzab B, Elisei R, Siena S, Bastholt L, et al. Sorafenib in radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer: a randomised, double-blind, phase 3 trial. The Lancet. 2014;384:319-28.
5. Schlumberger M, Tahara M, Wirth LJ, Robinson B, Brose MS, Elisei R, et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med. 2015;372:621-30.
6. Tavarelli M, Sarfati J, Chereau N, Tissier F, Golmard JL, Ghander C, et al. Heterogeneous Prognoses for pT3 Papillary Thyroid Carcinomas and Impact of Delayed Risk Stratification. Thyroid. 2017;27:778-86.
7. Ito Y, Miyauchi A, Kihara M, Higashiyama T, Kobayashi K, Miya A. Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation. Thyroid. 2014;24:27-34.
8. Falchook GS, Millward M, Hong D, Naing A, Piha-Paul S, Waguespack SG, et al. BRAF Inhibitor Dabrafenib in Patients with MetastaticBRAF-Mutant Thyroid Cancer. Thyroid. 2015;25:71-7.
9. Hyman DM, Puzanov I, Subbiah V, Faris JE, Chau I, Blay JY, et al. Vemurafenib in Multiple Nonmelanoma Cancers with BRAF V600 Mutations. N Engl J Med. 2015;373:726-36.
10. Carr LL, Mankoff DA, Goulart BH, Eaton KD, Capell PT, Kell EM, et al. Phase II study of daily sunitinib in FDG-PET-positive, iodine-refractory differentiated thyroid cancer and metastatic medullary carcinoma of the thyroid with functional imaging correlation. Clin Cancer Res. 2010;16:5260-8.
11. Mehrotra PK, Mishra A, Mishra SK, Agarwal G, Agarwal A, Verma AK. Medullary thyroid cancer: clinico-pathological profile and outcome in a tertiary care center in North India. World J Surg. 2011;35:1273-80.
12. Karkuzhali P, Yogambal M, Kumar M. An Indian Tertiary Care Hospital Scenario of Papillary Carcinoma of Thyroid. J Clin Diagn Res. 2017;11:EC26-9.
13. Yao R, Chiu CG, Strugnell SS, Gill S, Wiseman SM. Gender differences in thyroid cancer: a critical review. Expert Rev Endocrinol Metab. 2011;6:215-43.
14. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid. A clinicopathologic study of 241 cases treated at the University of Florence, Italy. Cancer. 1985;55:805-28.
15. Bal CS, Padhy AK, Kumar A. Clinical features of differentiated thyroid carcinoma in children and adolescents from a sub-Himalayan iodine-deficient endemic zone. Nucl Med Commun. 2001;22:881-7.
16. Pearce EN, Braverman LE. Papillary thyroid microcarcinoma outcomes and implications for treatment. J Clin Endocrinol Metab. 2004;89:3710-2.
17. Ruegemer JJ, Hay ID, Bergstralh EJ, Ryan JJ, Offord KP, Gorman CA. Distant metastases in differentiated thyroid carcinoma: a multivariate analysis of prognostic variables. J Clin Endocrinol Metab. 1988;67:501-8.
18. Benbassat CA, Mechlis-Frish S, Hirsch D. Clinicopathological characteristics and long-term outcome in patients with distant metastases from differentiated thyroid cancer. World j surg. 2006;30:1088-95.

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