



## A Clinicopathological Study Of Thyroid Lesions And A Correlation Between Pre-Operative Cytology And Post-Operative Histopathology

Dr. Vipin Ekhar, Dr. Lal Ramnghaki, Dr. Ritesh Shelkar, Dr. Jeevan Vedi.

Department of Otorhinolaryngology, Indira Gandhi Govt. Medical College, Nagpur (MS).

\*Corresponding Author:

Dr. Vipin Ekhar

Flat No. 303, Vasundhara Enclave, Near Narendra Nagar flyover Narendra Nagar (Nagpur)

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### Abstract

**Background:** The evaluation of a thyroid lesion is a common clinical predicament and this study aimed to know the magnitude of a clinical diagnosis presented as thyroid swellings in our region and to correlate the preoperative radio-pathological diagnosis with final post-operative histopathological reports, to comprehend the nature and diagnostic accuracy of the thyroid lesions.

**Methods:** A prospective study of 80 cases of thyroid lesions were carried out in the Department of ENT, Indira Gandhi Government Medical College and Hospital, Nagpur; a tertiary care centre in Central India from August 2016 to October 2018. Data were collected and analysed.

**Results:** The mean age was  $41.93 \pm 12.378$  years. Males constituted 12.50%, while females were 87.50% giving a Male: Female ratio of 1:7. The Thyroid lesions are common in the females between 31-40 years with the most common symptom was swelling in the anterior neck. On clinical assessment, the majority (58.75%) had solitary thyroid nodule, 85 % were clinically benign and 15% were malignant. When correlated with the final histopathology, the clinical diagnosis, USG and FNAC have a sensitivity of 100%, 88.9% and 88.9%; specificity of 95.7%, 88.7% and 100%; diagnostic accuracy of 96.25%, 88.75% and 98.75% respectively. Surgical management depends on the nature of the lesion and the risk group classification.

**Conclusion:** Differentiating benign and malignant thyroid lesions at the earliest may radically alter the prognosis and management protocols. Apart from the clinical evaluation, the use of USG and FNAC definitely improves the diagnostic accuracy to a privileged level and help in prudent management. Therefore, a combination of scrupulous clinical examination, USG and FNAC as diagnostic modalities, will give paradigmatic results and preclude mismanagement.

**Keywords:** Thyroid lesions, clinical diagnosis, Ultrasonography(USG), Fine Needle Aspiration Cytology(FNAC), Histopathological examination(HPE).

### Introduction

Thyroid gland lesions remains a behemoth problem all over the world and are one of the most common conditions encountered in ENT clinical practice. The prevalence of thyroid swelling ranges from 4% to 10% in adults and 0.2% to 1.2% in children. Of these, only 5% to 30% are malignant and require surgical intervention<sup>1</sup>. Others are benign conditions, which can cause significant cosmetic deformity and occasionally pressure symptoms necessitating

surgery. Thyroid cancer comprises 1% of all malignancies<sup>2</sup>. The thyroid gland is one of the endocrine glands which is amenable to direct physical examination because of its superficial location. It's having a wide spectrum of diseases ranging from functional/immunologically mediated enlargements to neoplastic lesions. This clinicopathological study of thyroid lesion is of special interest both because of the unique feature of the thyroid gland and thyroid tumours. Albeit superficial

and easily visible, the clinical diagnosis of the thyroid nodule is many a time like a tip of the iceberg. The problem in clinical practice is to discriminate the few malignant tumours from the many harmless benign lesions. At one extreme, the diagnosis of malignancy may be strongly suspected on clinical grounds, on the other hand, one finds many patients in whom the history and clinical findings are confusing and not diagnostic.

The application of Ultrasonography (USG) and Fine needle aspiration cytology (FNAC) in the preoperative evaluation has enhanced the armamentarium of the head and neck surgeons, however there are limitations of each technique and the final answer is still elusive. Rapid evolution in sonographic technology helps to identify benign from malignant lesions and its application in the preoperative evaluation has made ultrasound an important adjunct to the practice of head and neck surgery. On the other hand, FNAC is a simple, minimally traumatic, speedy, safe, cost-effective and an accurate technique being used worldwide. Since the introduction of Bethesda classification<sup>3</sup>, FNAC of the thyroid gland became the first line diagnostic tool for the evaluation of thyroid lesions. Its use, combined with high resolution ultrasound, has allowed the design of surgical algorithms that have been incorporated in the recently published American and British Thyroid Association Guidelines and simultaneously diminished the number of surgeries done for benign lesions and increased the proportion of malignancies in surgically resected thyroids.

The main aim of this study is to evaluate the usefulness of clinical features, FNAC and USG in diagnosis and management of thyroid lesions, and correlate preoperative diagnosis with the postoperative histopathological findings.

## Material And Methodology

**Study design and setting** - It was a prospective analysis of 80 cases of thyroid lesions, which underwent clinical and radiological examination, followed by fine-needle aspiration and surgery, from August 2016 to October 2018. The study was conducted in the Department of ENT, in collaboration with the Department of Pathology and Radiology, at Indira Gandhi Government Medical College and Hospital, Nagpur a tertiary care centre in Central India; after obtaining permission from the

Institutional Ethics Committee. A proper informed consent was taken from the patient, both for enrolling in the study and for further treatment, before participating in the study.

**Inclusion criteria:** All age patients of either sex with complaints of neck swelling, confirmed to be of thyroid lesion on clinical examination and investigations and subjected to thyroid surgery were included in this study.

**Exclusion criteria:** Those who were considered inoperable or patients with anterior neck swelling of non-thyroid origin and also those not willing for surgery were excluded.

**Plan of study:** A detailed clinical history and examination regarding thyroid swellings including the consistency, fixity, vocal cord movements, symptoms and signs suggestive of hypo/hyperthyroidism, factors that increase the risk of malignancy like rapid growth, symptoms of compression or invasion such as dysphagia, dysphonia and hemoptysis, male sex, pain, age younger than 20 or older than 60, family history of thyroid cancer or multiple endocrine neoplasias, previous head and neck irradiation was noted in all cases and findings were meticulously recorded in the case proforma. Depending on the history and clinical examination, the patients were clinically differentiated as Benign and Malignant.

USG of the thyroid lesions were evaluated for various sonological parameters to differentiate between benign and malignant lesions like nodularity, echotexture, presence of micro-calcifications, heterogeneity, etc. The overall impression was recorded as benign, suspicious or malignant. Also, the presence of lymphadenopathy and extra-thyroidal spread were noted. T3, T4, TSH was estimated and guided FNAC was done only in euthyroid patients. The results were reported based on Bethesda system nomenclature as Bethesda Type I to VI {Non-diagnostic (ND), Benign (B), Atypia of undetermined significance (AUS)/ follicular lesion of undetermined significance (FLUS)/Follicular Neoplasm/Suspicious of Follicular Neoplasm (FN), suspicious for malignancy (SM) and malignant (M)}<sup>3</sup>. CT scans (neck+thorax) were done in all the cases of malignancy of the thyroid to know about the extent of the lesion, extra-thyroidal spread, nodal/ distant metastases and suspected retrosternal / intra-thoracic

extension. After anaesthetic fitness, all patients included in the study underwent thyroidectomy ± neck dissection, depending upon the clinico-cytological diagnosis, and the surgical specimen was sent for final histopathological examination (HPE). The histopathology reports were recorded and correlated with the clinical examination, USG and FNAC findings. Statistical analysis was done to know the sensitivity, specificity, diagnostic accuracy and other values of each with the final histopathology, considering histopathology as the gold standard for diagnosis. All statistical calculations were analysed by P value using  $\chi^2$  tests with 2×2 contingency table by using Epi Info™ version 7.2.2.6.

**Results**

Thyroid lesions are common in the females of age group 31-40 years. Mean age at which patients

presented was 41.93±12.378 years. Males constituted 12.50% of patients while 87.50% were females. Male: Female ratio was 1:7 showing significant female preponderance. The commonest presenting complaint was swelling in the anterior neck, although few patients presented with pressure symptoms on first presentation (Table 1). In the majority of the patients, duration of swelling before the presentation was between 3 months to 5 years although patients with rapid growth and pressure symptoms presented early. On clinical evaluation, the majority (58.75%) had solitary nodule of the thyroid. Clinically the patients were diagnosed to have either benign or malignant lesions depending on history and various characteristics. On clinical grounds 85 % appeared benign and 15% malignant. When correlated with histopathology, the clinical diagnosis has a sensitivity of 100% and specificity of 95.7% with diagnostic accuracy 96.25%

**Table 1: Distribution of the study subjects based on clinical features**

Clinical features	Frequency	%
1. Anterior neck swelling over thyroid region	80	100
2. Fixity to surrounding structures	5	6.25
3. Dysphagia	4	5
4. Pain	4	5
5. Dyspnoea	3	3.75
6. Dysphonia	3	3.75
7. Vocal fold paralysis	3	3.75
8. Retrosternal extension	2	2.5
9. Cervical Lymphadenopathy	2	2.5
10. Hypo/hyper- thyroidism	1	1.25
11. Abnormal Eye signs	0	0

**Table 2: Correlation of clinical diagnosis with histopathology**

Clinical diagnosis	Frequency(%)	Histopathology	Frequency(%)	
Benign	68(85%)	Colloid goitre	61	71(88.75%)
		Benign Follicular adenoma (FA)	4	
		Hashimoto’s Thyroiditis	2	

		Lymphocytic Thyroiditis	1	
		Benign follicular adenoma (FA)	3	
Malignant	12(15%)	Anaplastic carcinoma (ACT)	2	9(11.25%)
		Follicular Carcinoma(FC)	1	
		Medullary Carcinoma(MCT)	2	
		Papillary Carcinoma(PCT)	4	

When we look at the correlation between clinical diagnosis and the final histopathology (Table 2), all the 68 lesions which were considered benign clinically, were benign on histopathology as well. However, of the 12 lesions which were reported to be malignant clinically, 9 were reported as malignant and 3 turned out to be benign and all were reported as follicular neoplasm(benign). On statistical analysis, the sensitivity was 100%, specificity 95.7%, positive predictive value 75.0%, negative predictive value 100% and the diagnostic accuracy was 96.25%.

**Table 3: Correlation of USG with histopathology**

USG	LESION	Frequency	HISTOPATHOLOGY					
			Benign		Malignant			
Benign n=64 80%	Cystic	1	Colloid Goitre	1	0			
	Multinodular goitre (MNG)	28	Colloid Goitre	27	n=28	0		
			Lymphocytic Thyroiditis	1				
Hyperechoic nodule (HN)	35	Colloid Goitre	29	n=34	Anaplastic Carcinoma Thyroid	1		
		Follicular Adenoma	4					
		Hashimoto's Thyroiditis	1					
Suspicious Malignant n=11 13.75%	Suspicious Mixed Echogenic Nodule (SMN)	11	Colloid Goitre	4	n=8	Medullary Carcinoma Thyroid	2	n=3
			Follicular Adenoma	3				
			Hashimoto's Thyroiditis	1		Papillary Carcinoma Thyroid	1	
Malignant n=5 6.25%	Mixed echogenic nodule(MN)	5	0		Papillary Carcinoma Thyroid	3	n=5	
					Anaplastic Carcinoma Thyroid	1		
					Follicular Carcinoma Thyroid	1		

Out of 64 lesions that were reported benign on USG (Table 3), 63 came out to be benign on histopathology as well and interestingly, 1 case turned out to be anaplastic carcinoma. 11 lesions were reported as suspicious for malignancy, of these 8 were benign and 3 were malignant on final histopathology. At the same time, all 5 reported as malignant on USG were also malignant on histopathology. On statistical analysis, the sensitivity

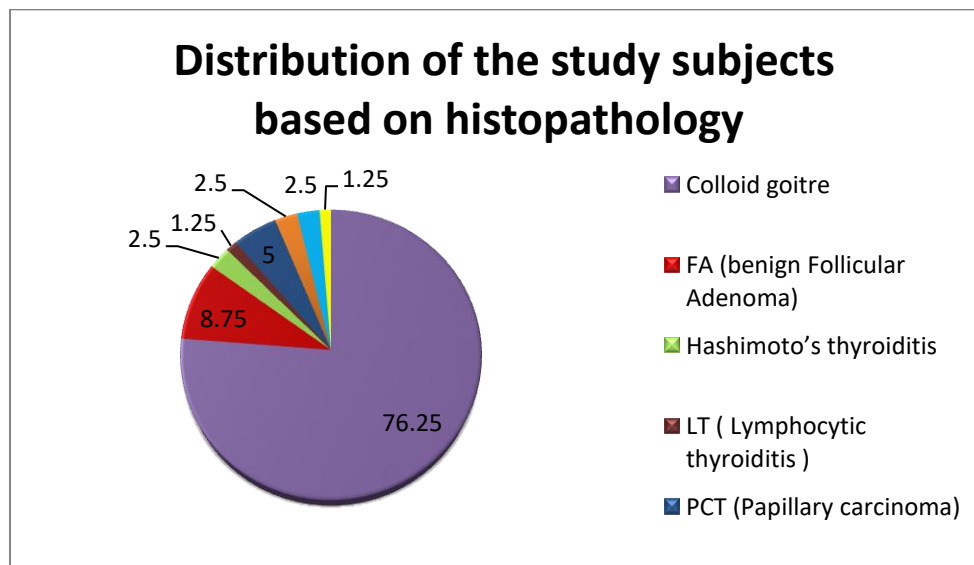
was 88.9 %, specificity 88.9 %, positive predictive value 50%, negative predictive value 98.4% and the diagnostic accuracy was 86.75%.

**Table 4: Correlation of FNAC (Bethesda system) with histopathology**

Bethesda system	No. of cases	Histopathology		Malignancy risk %
		Benign	Malignant	
I(Nondiagnostic or Unsatisfactory)	1 (1.25%)	1	0	0
II( Benign)	66 (82.5%)	66	0	0
III(Atypia of undetermined significance or follicular lesion of undetermined significance)	3 (3.75%)	2	1	33.3
IV(Follicular neoplasm or suspicious for a follicular neoplasm)	2 (2.5%)	2	0	0
V(Suspicious for Malignancy)	0	0	0	0
VI ( Malignant)	8 (10%)	0	8	100
<b>Total</b>	80	71	9	

FNAC (Bethesda System) was also analyzed with histopathology (Table 4). We found that all the 66 lesions reported as benign (type II) on the Bethesda system were benign on final histopathology. Similarly, all the 8 lesions reported malignant (type VI) on FNAC turned out to be malignant on histopathology. 3 lesions were reported as atypia of undetermined significance (type III) on FNAC, of these 2 turned out to be benign and 1 was malignant on histopathology. 2 lesions reported as suspicious for a follicular neoplasm (type IV) on FNAC, proved to be benign follicular adenoma on histopathology. On statistical analysis, the sensitivity was 88.9%, specificity was 100 %, positive predictive value 100%, negative predictive value 98.6%, and diagnostic accuracy was 98.75%.

**Fig 1: Distribution of the study subjects based on histopathology**



**Table 5. Comparison of the percentage of distribution of fine needle aspiration diagnosis and malignancy risk of the present study with other studies.**

Diagnostic category	Present study		Jo <i>et al</i> <sup>10</sup> (2010)		AlmondalSK <i>et al</i> <sup>13</sup> (2016)		YassaEt <i>al</i> <sup>11</sup> (2007)		Yang <i>et al</i> <sup>14</sup> (2007)		Nayar and Ivanovic <i>et al</i> <sup>12</sup> (2009)	
	Distribution %	Malignancy risk %	Distribution %	Malignancy risk %	Distribution %	Malignancy risk %	Distribution %	Malignancy risk %	Distribution %	Malignancy risk %	Distribution %	Malignancy risk %
I (Nondiagnostic Unsatisfactory)	1.25	0	18.6	8.9	1.2	-	7	10	10.4	10.7	5	9
II (Benign)	82.5	0	59.0	11	87.5	-	66	0.3	64.6	0.7	64	2
III (Atypia of undetermined significance or Follicular lesion of undetermined significance)	3.75	33.3	3.4	17	1	-	4	24	3.2	19.2	18	6
IV (Follicular neoplasm or suspicious of a follicular neoplasm)	2.5	0	9.7	25.4	4.2	-	9	28	11.6	32.2	6	14
V (Suspicious Malignancy)	0	0	2.3	70	1.4	-	9	60	2.6	64.8	2	53
VI (Maligna)	10	100	7.0	98.1	4.7	-	5	97	7.6	98.4	5	97



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Depending on the pre-operative diagnosis, various surgical procedures were done. Hemithyroidectomy was the most common surgery done which constituted 71.25% followed by total thyroidectomy which was performed in 15 % of the study subjects. Subtotal thyroidectomy (7.5%) and total thyroidectomy with functional neck dissection (2.5%) were also done. Postoperative period was uneventful most of the time except in few (3) cases where there was transient postoperative hypocalcaemia which was managed conservatively. Since the study mainly consists of diagnosis of the thyroid lesions and the usefulness of clinical examination, radiology and FNAC in diagnosis, we have not statistically analyzed the surgical procedure and complication in further details.

**Discussion**

The study of the thyroid lesions and its management is an interesting topic yet difficult to understand completely. It requires active participation and coordination of various medical fields (surgeons, radiologists and pathologists) for accurate diagnosis that will benefit the patient and the clinician to the maximum and avoid unnecessary operations and complications during the course of management of the lesion.

In the present study, the maximum numbers of patients were in the age group of 31 to 40 years (32.5%). The mean age group was 41.93±12.37 years. Age distribution of the present study can, to some extent, be compared to that of Handa et al<sup>4</sup> while Afroze et al<sup>5</sup> (2002) gives M: F ratio of 1:2.54, however female preponderance is seen in all available studies. The direct actions of estrogen on the thyroid tissues contribute to the development of thyroid goitre, nodule and cancer in females.

Benign thyroid swelling is usually asymptomatic unless it is accompanied by pressure symptoms due to diffuse enlargement of the gland which may compress the trachea or the oesophagus or the recurrent laryngeal nerve and the patients presented with dyspnoea, dysphagia or change in voice respectively. Pain over the swelling is an uncommon feature of benign thyroid lesion. Hence, patients having thyroid swelling without associated symptoms

often presented late to the clinician. However, the patients having a rapid rise of thyroid swelling with additional signs and symptoms of hyper/hypothyroidism, signs of retrosternal extension, cervical lymphadenopathy or infiltration in the surrounding structures were suspected to have a malignant lesion and usually presented little early. Signs and symptoms of patients in our study correlated well with literature.

In the present study, out of 68 patients clinically diagnosed to have benign swelling of the thyroid, 68(100%) were indeed benign on histopathology too. Out of 12 cases suspected to be malignant on clinical diagnosis, 9(75%) of the cases turned out to be malignant while 3 (25%) turned out to be benign. These were cases which showed pressure symptoms and inflammation mimicking malignancy. Thus benign diseases were diagnosed with much higher accuracy on clinical grounds compared to malignancy. Similarly there are definite chances of missing malignant lesions on clinical examination, especially if the lesion is limited to the gland. In a study conducted by Bamanikar S et al<sup>6</sup> (2014), the majority of clinically diagnosed thyroid nodules were benign in nature and those requiring surgical intervention due to malignant lesions were 5-20% which is comparable to our study. The diagnostic accuracy of 96.25% stressed the fact that in countries with poor medical infrastructure, a thorough and detailed history along with proper clinical examination can help in suspecting malignant lesions with acceptable accuracy and is important adjunct to other diagnostic modalities.

Based on various sonographic features, thyroid lesions were subdivided into three groups- benign, suspicious of malignancy and malignant. Features suggestive of benign diseases are- Halo Sign (transonic uniform rim surrounding the mass), variable echogenicity, multinodularity, large cystic lesion, diffusely nodular in-homogeneous gland and peripheral calcification. Features suggestive of malignancy on USG are- hypoechoic pattern, incomplete peripheral halo, irregular margins, internal micro-calcification, presence of cervical lymphadenopathy and peripheral degeneration in mixed nodules. The lesions that did not show a

benign or malignant characteristic were classified in the suspicious group<sup>7</sup>.

In our study, out of 16 cases diagnosed to be malignant on USG, 8 cases were confirmed on histopathology while the remaining 8 cases turned out to be benign. 1 case in which the USG gave diagnosis as a benign disease, surprisingly histopathology revealed it to be an anaplastic carcinoma (false negative). Thus anaplastic carcinoma of thyroid can show the variable hyperechoic benign nodular pattern on USG and can be tricky to diagnose on ultrasonography. 11 lesions were reported as suspicious of malignancy, of these 8 were benign and 3 were malignant on final histopathology, 2 of them Medullary Carcinoma. Thus suspicious of malignancy, thyroid lesions on USG, are more likely to be benign than malignant; but if malignant highly likely to be medullary carcinoma of the thyroid which has no typical characteristics.

In our study, we found that the sensitivity and specificity of USG in detecting malignancy was 88.9% and 88.7% respectively which is almost comparable to the study conducted by Watters *et al*<sup>8</sup>. Watters *et al*<sup>8</sup> study emphasized that USG has added advantage of allowing the whole gland to be examined rather than the dominant nodule but was limited by the fact that no features were pathognomic for malignancy so that it should be regarded as complementary rather than an alternative investigation to FNAC in the diagnosis of thyroid lesions. It has been a consistent observation according to published literature, that the risk of thyroid cancer is less with multiple nodules than with the solitary nodules. Simeone *et al*<sup>9</sup> stated that the detection of more than one lesion with USG reduces the probability of malignancy to 1-6%.

FNAC with Bethesda Classification is supposed to be very useful in the diagnosis of Thyroid Lesions. We compared the results obtained in our study with the studies of Jo *et al*<sup>10</sup>, Yassa *et al*<sup>11</sup> and Nayar & Ivanovic *et al*<sup>12</sup>. We observed that the distribution of the cases as per the six-tier Bethesda system in our study differed from that in the above-mentioned studies, with the percentage of cases in the non-diagnostic, AFLUS and Suspicious Malignant categories being lower and in the benign category being higher. The reason for the number of cases in the benign category being higher can be attributed to

the fact that our institute, despite being a tertiary care centre, not only caters to the need of patients on a referral basis but also patients come directly to the OPD on primary basis. So, a large population, representative of the general population, is encountered in our institute. Therefore, the proportion of benign cases that is a lot higher in the general population was reflected proportionately in our study. According to Jo *et al*<sup>10</sup>, most of the above-mentioned studies have been done in tertiary care centres, where patients come only on a referral basis, and hence is not exactly representative of the general population.

The reason for the lower percentage in the non-diagnostic, AFLUS and Suspicious Malignant categories can be attributed to the fact that, in our institute, usually an ultrasound-guided FNAC is performed for small lesions that appear heterogeneous on palpation so that the aspirate can be procured from the exact pathological site, thereby allowing a more specific cytological diagnosis. Also in case of non diagnostic FNAC reports, re-performance of FNAC by the highly skilled radiologist under ENT surgeon guidance is regularly done at our centre. In a study conducted by Wang and Song *et al*<sup>15</sup> found that, Ultrasound-guided FNAC performed by surgeons provides a number of benefits, including assessment by a surgeon familiar with neck anatomy, reduction of multiple clinical visits, the rates of adequate samples obtained by ultrasound-guided FNAC performed by trained surgeons were similar to those obtained by experienced radiologists but even with higher efficiency, and earlier triage to surgery if needed.

The malignancy risk for the non-diagnostic and suspicious for follicular neoplasm categories is 0% in our study as compared to the higher rates in other studies, similarly higher malignancy risk were seen in AFLUS category as a compared lower rate in Jo *et al*<sup>10</sup> and Nayar and Ivanovic<sup>12</sup>. These findings can be explained by the fact that, in our study, we have a smaller denomination of population for the non-diagnostic and AFLUS categories, as a result of which the malignancy risk cannot be accurately compared.

## Conclusion

Since thyroid swellings are a very commonly encountered condition in ENT practice, a fairly



accurate preliminary diagnosis assisted by cytological confirmation goes a long way in assisting speedy and effective management of the underlying pathology. It is imperative to distinguish between benign and malignant lesions at the earliest as it may radically alter the prognosis and management protocol for the patient. Some take home points from our study are -

1. 75% of the malignant lesions on clinical examination were confirmed by histopathology.
2. USG could diagnose malignancy in 5 patients where FNAC and HPR confirmed the correct diagnosis. Therefore use of ultrasound along with FNAC will improve the diagnostic accuracy to a higher level and help in better management.
3. All malignant lesions on FNAC were confirmed by histopathology indicating its excellence. Therefore FNAC helps in planning the correct management and avoid second surgeries.
4. Nondiagnostic FNAC reports should not be considered benign, and repeat FNAC or selective surgical treatment is recommended.
5. Patients with suspicious thyroid nodules may be evaluated by the head and neck surgeon who perform the FNAC under USG guidance to the same satisfaction as radiologists.

We would like to recommend that larger centres should calculate their own malignancy rates on basis of Bethesda system and should be communicated to the treating surgeons for better interpretation of the results. The management of the patient should be based on the malignancy rate for the centre along with clinical and radiological correlation rather than following the Bethesda guidelines blindly for all the patients. Therefore, a combination of thorough clinical examination, USG and FNAC as diagnostic modalities, will give optimal results and avoid mismanagement.

### Authors Contributions

All named authors played a substantial role in the conception and/or study design, data acquisition and/or analysis, as well as drafting of the manuscript agree the accountability for all aspects of accuracy and integrity of the work.

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**Ethical approval:** The study was approved by the Institutional Ethics Committee.

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