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Original Article

Comparison of Fine Needle Aspiration Followed By Histopathology and Sonographic Features of Thyroid Nodule To Formulate A Diagnosis: A Cross-sectional Study

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ABSTRACT

Thyroid nodules are solid lumps filled with fluid that develop inside the thyroid gland. Due to their small size, the majority of them go undetected and are asymptomatic. However, some of them are cancerous. **Objectives:** To compare the diagnostic accuracy of Fine needle aspiration followed by histopathology and sonographic features of thyroid nodule **Methods:** In this study, 274 participants were included. All of them were detected with the solitary euthyroid nodule. All the patients considered in the present study had normal values of T4 and TSH as euthyroid nodules were supposed to be studied. All the participants were subjected to undergo a USG as per the TIRADS system and FNAC wherever it was applicable. The biopsy report of the excised sample was considered a gold standard. **Result:** The classification of FNAC was more specific than the TIRADS system, however, the sensitivity of both the classification was the same. Micro-calcification was most specific and sensitive in the individuals that underwent a USG. Irregular margins had a specificity of 88% and nodules taller-than-wider in shape were 91% specificity. A total of 7 patients had shown benign features on cytology, whereas, they were suspiciously malignant on USG(TIRADES 4 and 5)and showed malignancy in final evaluation after the surgery. **Conclusion:** The sensitivity of both FNAC and USG in the diagnosis of malignancy of thyroid nodule is equal, however, the specificity of FNA is more (90%). FNAC is a minimally invasive procedure that can be opted for the differentiation of benign and malignant lesions with an accuracy of 86%. Patients showing high-risk features on sonography are subjected to repeat the FNAC and they should also be referred for a surgical biopsy to make a definitive diagnosis.

INTRODUCTION

Thyroid nodules are fluid-filled solid lumps that are formed inside a thyroid gland. Most of them are asymptomatic and left unnoticed because of their small size. Whereas, some of them are malignant. Most of them are small in size and are noticed on examination by a surgeon. Some of them are large enough to be visible. The mode of the treatment is dependent on the size and type of the nodule [1]. On the global level, the prevalence of the thyroid nodule is higher in the general population with an estimation of 4 to 8% on palpation and 19 to 67% through an ultrasound examination [2]. The prevalence of thyroid nodule in the population of US is around 68% [3]. The main challenge of clinicians regarding thyroid nodule is its differentiation from a malignancy [4]. The incidence of occurrence of carcinoma of the thyroid gland is seen to be increasing in the last decade which has made marked improvements in the ultrasonography (USG) guided fine needle aspiration (FNAC) as well as USG surveillance of thyroid nodules [5, 6].

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Most of the nodules appeared to be benign, however, 5 to 15% of the cases are found to be malignant. Population with high-risk factors such as advanced age, gender, exposure to radiations in history, and a positive family history of malignancy, need further evaluation of the thyroid nodule [7]. According to various epidemiological studies, it is evident that thyroid nodule is more common in females, whereas, the risk of malignancy in such nodules is higher in the male population [8]. A detailed clinical history, examination, and imaging are required for the evaluation of a thyroid nodule patient. The first line of investigations for Euthyroid nodule patient is USG. A risk stratification system TIRADS is used for risk determination. It is similar to the BIRADs scoring system used for breast lesions [9, 10]. Initially, this system was reported by Horvath et al., [9]. It was subsequently proposed by Park et al., [11] and Kwak et al., [10]. According to the descriptors of the lesions, the thyroid nodules are categorized in categories of TIRADS. The descriptors include the composition, shape, calcification foci, echogenicity, and margins of the lesion. Each descriptor carries on point. All the points are added and TIRADS scores are calculated numerically [12]. The USG findings which are suggestive of a malignant nodule are it being solid, having irregular margins, hypo-echogenic, and presence of micro calcifications view. A rational approach for the management and choosing suitable surgical procedures can be achieved by FNAC. It should provide a higher degree of specificity and sensitivity [13]. Bethesda classification is used as a standard for deciding the mode of treatment, either palliative or surgical. Data regarding TIRAD risk stratification is available abundantly, however, data related to FNAC is scarce. The present study aims the comparison of USG by TIRADS scoring with the cytological diagnosis made by FNAC by Bethesda scoring. At the end of the study, an excisional biopsy was done on all the patients for comparison as excisional biopsy is a gold standard investigation for the evaluation of the presence of malignancy. The specificity, sensitivity, positive predictive value, and negative predictive value of Bethesda scoring and TIRADS scoring are used for the confirmation comparing them to biopsy.

METHODS

In this cross-sectional study initially, 300 patients were included. However, on examination, 274 patients were found to have thyroid nodules. Informed consent was taken from all of the participants. Permission was taken from the ethical review committee of the institute. Clinical and demographic data were collected from all of the participants. Standard protocols were followed in the collection of the data. All the patients had already undergone thyroid function tests (TFTs). The chemiluminescence technique (CLIA) was used for the estimation of serum TSH and serum-free T4. The value of analytical sensitivity was 0.01 µIU/ml and the total precision value was 2.2% for the TSH. Similarly, the value of analytical sensitivity was 0.35 µIU/ml and the total precision value was 2.7% for the free T4. 12.0µg/dL was reference range of T4, and 0.5-5 µIU/ml was the reference range of TSH. All the patients considered in the present study had normal values of T4 and TSH as euthyroid nodules were supposed to be studied. All the patients were subjected to undergoing a high-resolution USG as well as USG-guided FNAC. Radiology consulted were involved for expert reporting regarding the thyroid USG. They were trained to perform the USG of the thyroid gland. The reports of the scans were given as per the TIRADS score. In Table 1, the indications of malignancy are given.

TIRAD Score	Chances of malignancy	FNAC needed or not
1	Not suspicious	Not needed
2	Not suspicious	Not needed
3	Mildly suspicious	FNAC is needed (if more than 2.5 cm, follow-up if more than 1.5 cm)
4	Moderately suspicious	FNAC is needed (if more than 1.5 cm, follow-up if more than 1 cm)
5	Highly Suspicious	FNAC is needed (if more than 1 cm, follow-up if more than 0.5cm)

Table 1: TIRADS scoring

The reports of the cytopathology were prepared as per Bethesda classification. The Bethesda classification, in Type 1 is non-diagnostic, type 2 is benign, type 3 is AUS/FLUS, Type 4 is a follicular neoplasm, Type 5 is considered suspicious for malignancy, and Type 6 is confirmed malignancy. All the slides of FNAC were studied by a single expert pathologist keeping in view the nature of the study and the protocols of cytopathology. Surgical biopsy and histopathology were done on `the participants. All slides were seen and evaluated by single pathologist to avoid any kind of bias or human error. Out of those 122 participants, 42 had Bethesda 2 cytology. Hence, the nodules were benign. However, surgery was done on them for either compressive symptoms or cosmetic reasons. For statistical analysis, the Chi-square test and Fischer exact tests were applied. The analysis was done in IBM SPSS version 26.

RESULTS

A total of 274 participants were added to the study. The Bethesda score, TIRADS score, and results of surgical histopathology of the participants are shown in table 2.

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Clinical Features	Frequency	Percent
TIRADS Score		
1(Benign)	No FNA	
2(Not suspicious)	No FNA	
3(Mildly suspicious)	182	66.42
4(Moderately suspicious)	58	21.4
5(Highly suspicious)	34	12.4
Bethesda Score		
1(Non-diagnostic)	8	2.92
2(Benign)	170	62.04
3(AUS/FLUS)	40	14.59
4(Follicular neoplasm)	26	9.49
5(Suspicious for malignancy)	28	10.22
6(Malignant)	2	0.73
Surgical Histopathology (n=122)		
Benign	72	59
Malignant	50	41

Table 2: Bethesda score, TIRADS score, and surgical histopathology of the patients

The mean age of the participants was 40.69 ± 12.96 years. The age and gender distribution of the participants are given in table 3.

Age range (Years)	Number of participants	Percentage
18-20	10	3.65
21-40	148	54.01
41-50	48	17.52
51-60	68	24.82
Gender Distribution		
Female	212	77.37
Male	62	22.63

Table 3: Age and gender distribution

The final diagnosis of histopathology in different categories according to the TIRADS scores are given in table 4.

TIRADS Score	Histopathology		Total	Risk of malignancy (%age)
	Malignant	Benign		
3	10	34	44	23
4	14	34	48	30
5	26	4	30	87
Total	50	72	122	41

Table 4: Occurrence of malignancy according to TIRADS Score

The sonographic features of the patients and the occurrence of malignancy is represented in Table 5. According to table 5, ultra-sonographic features are suggestive of lesser observation of taller than wider morphological changes. Micro-calcification was seen more in malignant tumors compared to benign tumors. Hypo-echogenicity was predominant in malignancy. However, more cases of benign tumors were seen with irregular margins compared to malignant ones.

Major Ultrasound Features	Histopathology (n=122)		Total	P-value
	Malignant (n=50)	Benign (n=72)		
Taller than Wider				
Present	18	6	24	0.01
Absent	32	66	98	
Micro-calcification				
Present	40	10	50	<0.0001
Absent	10	62	72	
Hypoechogenicity				
Present	34	16	50	<0.01
Absent	16	56	72	
Irregular Margin				
Present	14	8	22	0.17
Absent	36	64	100	

Table 5: Occurrence of malignancy according to the USG feature

Table 6 shows presence of malignancy on fine needle aspiration. There were 28 cases suspicious for malignancy. However, 24 were diagnosed with malignant tumors and 4 were not detected with any malignancy in Bethesda 5,6. Likewise, there were total 42 cases with Bethesda 2 out of which 6 were diagnosed with malignancy and 36 had benign tumors.

Fine-needle aspiration assay	Malignant Frequency (Percentage)	Benign Frequency (Percentage)	Total Frequency (Percentage)
BETHESDA 5,6	24(86%)	4(14%)	28(39%)
BETHESDA 2	6(14%)	36(86%)	42(60%)
Total	30(43%)	40(57%)	70(100%)

Table 6. Fine needle aspiration findings according to BETHESDA

DISCUSSION

The main challenge to the clinician is determination of presence of malignancy in a thyroid nodule. The overall ratio of malignancy is lower in the indeterminate thyroid nodules, whereas, benignancy can be expected more after a surgical procedure [14-15]. In the present study, it has been observed that thyroid nodules are more commonly present in women as compared to men. It suggests a predominance of euthyroid nodules in women and it is as large as 77.37%. Another similar study conducted by Taddesse et al., also shows female predominance. The percentage of female patients in their study was 88% [16]. The present study suggests that thyroid nodules were more predominant in the participants in the age range of 21 years to 40 years. The percentage of participants in this age range was 54%. A total of 24% of the participants were from an age range of 51 years to 60 years. According to the study by Muthu et al., 80% of the participants were from an age group of 21 years to 40 years [17]. The study of Kwak et al., gave TIRADS scores by an analysis of thyroid nodules retrospectively, in FNAC and USG which are in accordance with our study [6]. In the present study, 23% of participants had malignancy for TIRADS 3. For TIRADS 4 was 30% and TIRADS 5 was 87%. According to the study by Barbosa et al.,

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23.3% of participants were detected with malignancy in TR 3 [18]. The present study had similar findings. According to the TIRADS criteria, there are four scenarios of TR 3; (1) solid and isoechoic, (2) solid and hyperechoic, (3) mixed solid cystic and hypoechoic, (4) mixed solid cystic and hyperechoic with macro-calcification. Hence, higher chances of malignancy should be expected in TR 3. According to the study by Handa et al., the sensitivity of FNAC was 97% [19]. In a similar study by Mundasad et al., the sensitivity of FNAC was 52.6% [20].

CONCLUSION

It can be concluded that both TIRADS and FNAC are highly sensitive, however, the specificity of FNAC is higher. The suspicion in the results of either of them can be ruled out by excisional biopsy as that is a gold standard investigation.

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