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Diagnostic efficacy of ultrasonography-guided fine needle aspiration cytology on thyroid swellings

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Abstract

Introduction: Patients presenting with a thyroid nodule, if malignant, may call for removal. A good screening tool with high diagnostic value for preoperative evaluation is preferred. Through real-time visualization of the needle to aspirate from the suspicious site, ultrasonography-guided fine-needle aspiration cytology could be an excellent screening tool.

Materials and method: A cross-sectional descriptive study was conducted at Ganesh Man Singh Memorial Academy of Ear Nose Throat–Head and Neck Studies, Kathmandu, Nepal, from September 2018 to November 2019. We included 59 subjects of 15–72 years meeting the inclusion criteria. All study participants underwent preoperative ultrasonography-guided fine-needle aspiration cytological evaluation of thyroid nodule, which was correlated with their histopathological findings to determine diagnostic values.

Result: The sensitivity, specificity, and accuracy of ultrasonography-guided fine-needle aspiration cytology of thyroid nodule was 96.96%, 61.53%, and 81.35%, respectively. On stratification according to size, high sensitivity of 100% was observed in evaluating lesions of size < 2 cm and > 4 cm. There was a good inter-rater agreement between findings of ultrasonography-guided fine-needle aspiration cytology and histopathology with a kappa coefficient of 0.607.

Conclusion: Ultrasonography-guided fine needle aspiration cytology is a reliable procedure to evaluate thyroid lesions with high diagnostic value. It is an excellent tool for evaluating small, non-palpable nodules.

Keywords: Accuracy, Cytology, Fine needle, Thyroid nodule, Ultrasonography

Introduction

The thyroid nodule is an important clinical entity to investigate as it leads to anxiety in patients. It can cause thyroid dysfunction, compression symptoms, and potential malignancy risk, which is why an investigation is needed at the earliest [1]. If the nodule is large or has an

index of clinical risk of malignancy based on diagnostic grounds, the nodule should be removed. Thus, surgeons take it as a major conundrum. It is one of the common incidental findings worldwide and one of the most common swellings consulted in Ear, Nose, Throat–Head & Neck Surgery Outpatient Department [2].

Ultrasonography-guided fine needle aspiration cytology (USG-FNAC) is widely advocated as an effective investigation method for analyzing thyroid nodules. Ultrasonography (USG) and fine-needle aspiration cytology (FNAC) are effective preoperative diagnostic tools in analyzing thyroid nodules. USG provides real-time images of thyroid nodule [3] and FNAC offers a direct

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identification of cytology [4]. But both procedures come with certain limitations. Inadequate sampling and inability to aspirate from non-palpable lesions limits FNAC [5]. USG findings are affected by overlapping features of benign and malignant lesions and the operator dependency. Thus, a combination of USG and FNAC helps counter each other's deficiencies to some extent [6]. Adding a real-time visualization to guide the needle to aspirate from a suspicious site provides a more accurate diagnostic method to evaluate thyroid nodules. A highly accurate diagnostic test is needed for surgeon to adopt a surgical strategy and literature has shown the high diagnostic ability of USG- FNAC [7, 8].

However, in Nepal, data on the correlation of findings of USG-guided FNAC with histopathology in thyroid nodule is limited. Therefore, this study aimed to correlate preoperative ultrasonography-guided fine-needle aspiration cytology (BETHESDA SYSTEM) [9] with histopathology in a thyroid nodule

Materials and method

This was a cross-sectional study conducted at Ganesh Man Singh Memorial Academy of ENT - Head and Neck Studies (GMSMA-HNS) from September 2018 to November 2019. Ethical clearance was obtained from the Institutional review committee of the Institute of Medicine, Nepal, with the reference number of 88 (6-11-E)2/075/076. The study protocol was as per the Declaration of Helsinki, revised in 2013 on human experimentation. We used patients with the following criteria to include in the study.

1. Age over 15 years

Patients who underwent USG-guided FNAC and were reported as per The Bethesda Reporting of Thyroid Cytology (TBSRTC) [9] and had final histopathology report available. Exclusion criteria were:

1. Hemorrhagic thyroid swellings
2. Patients who came for completion thyroidectomy

In all patients, a radiologist did USG-guided fine-needle aspiration of thyroid nodule. Under aseptic conditions, the needle was oriented either parallel or perpendicular to the USG probe. The subject was then requested not to move or swallow and remain silent. The operator was preferably positioned at the contralateral side of the lesion with adequate lightning. A needle was targeted at the lesion; the sample was collected by multiple back and forth movements of needles over 5–10 s. However, if insufficient, negative pressure was applied. Negative pressure was then released before withdrawing

the needle. The aspirate was used to prepare the smear. The cytology was evaluated under a light microscope by the same pathologist throughout the study, and the results were classified as per TBSRTC. We considered TBSRTC category II benign and TBSRTC category III-VI malignant [8]. We excluded TBSRTC category I from the study because it does not yield any diagnosis.

The surgical specimen was fixed in 10% formalin, fixed with hematoxylin and eosin stains. Raw data were collected on proforma and entered on Microsoft Excel 2016 through the data validation tool. IBM-SPSS 16 (Statistical Package for Social Sciences) was used to analyze data. The findings of USG-guided FNAC were compared against histopathological findings. The findings were expressed in terms of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Further evaluation of diagnostic indices of USG-guided FNAC was done for nodules of different sizes viz. <2 cm, 2–4 cm, and >4 cm.

The agreement between findings of USG-FNAC and gold standard histopathological evaluation was tested using Cohen Kapa inter-rater agreement. The strength of USG-FNAC to diagnose a pathology while analyzing thyroid nodule will be based on the Kappa coefficient value. A p -value ≤ 0.05 was considered to be significant [10].

In each Bethesda category, we calculated the risk of malignancy (ROM) by dividing the number of malignant findings found in HPE by the number of cases in that category.

Results

We recruited 59 patients in the study. The patients included in the study ranged from 15 to 72 years, with a mean age of 41.017 ± 13.69 years. There was notable female preponderance (88.1%) among subjects presenting with a suspicious thyroid nodule.

The age group distribution shows most of the patients were in 30 to 60 years (Fig. 1).

Most of the thyroid nodules in our study had a maximal diameter of 2–4 cm ($n = 38$). Most nodules belonged to Bethesda category VI ($n = 21$), followed by Bethesda category II ($n = 17$).

Cross-tabulation of guided FNAC findings with histopathological findings of different thyroid swellings was done and diagnostic indices were calculated (Table 1).

Overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were 96.96%, 61.53%, 76.19%, 94.11%, and 81.35% respectively.

When stratified according to sizes, we observed the highest sensitivity in the lesion of less than 2 cm and over 4 cm. Likewise, specificity was lowest for less than 2 cm and highest for lesion size greater than 4cm (Table 2).

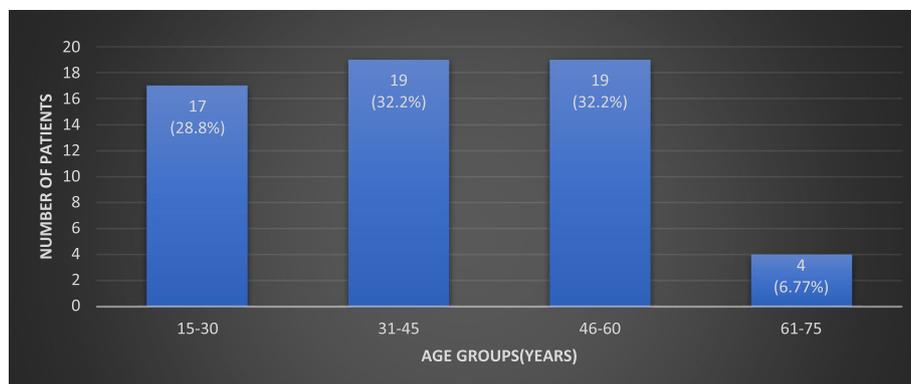


Fig. 1 Age distribution

Table 1 Cross-tabulation of guided FNAC findings with histopathological findings of different thyroid swellings (n = 59)

USG-guided FNAC findings	Histopathology findings		Total
	Malignant (P)	Benign (N)	
Malignant (P)	32 (TP)	10 (FP)	42
Benign (N)	1 (FN)	16 (TN)	17
Total	33	26	59

P positive, N negative, TP true positive, TN true negative, FP false positive, FN false negative

Table 2 Diagnostic indices of USG-FNAC in different thyroid swellings according to their size

Size (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
<2	100	25	78.57	100	80
2–4	94.11	66.67	69.56	93.3	78.94
>4	100	100	100	100	100

Table 3 Cohen Kappa’s coefficient for inter-rater agreement between USG-guided FNAC findings and histopathological findings according to different sizes of nodules

Size	Kappa’s coefficient	p-value	Interpretation
Overall	0.607	0.000	Good agreement
<2 cm	0.328	0.086	Fair agreement
2–4 cm	0.588	0.000	Moderate agreement
>4 cm	1	0.14	Almost perfect agreement

The inter-rater agreement concluded as a good agreement for the overall study and was an almost perfect agreement for >4 cm thyroid nodule (Table 3).

In our study, we calculated the risk of malignancy (ROM) in each category (Table 4).

Table 4 Risk of malignancy in each category found in our study

Bethesda classification	Histopathological findings		
	Malignant	Benign	Risk of malignancy (%)
II	1	16	5.9
III	1	1	50
IV	3	3	50
V	10	3	76
VI	18	3	85

Discussion

A thyroid nodule is one of the commonly encountered lesions in the Ear Nose Throat–Outpatient Department, with a prevalence of 4–7% [2]. It is an important clinical entity for clinicians because of its malignancy potential, which is about 5% [10]. Works of literature have shown that a visual aid as ultrasonography added to guide the needle to aspirate cytology from the lesion site shows promising diagnostic ability. Studies have shown that it reduces inadequacies, and impalpable lesions are also easily aspirated [6–8, 11, 12].

A similar study supported female predilection in our study. We also found the age demographics to be like existing literature [7, 8].

As per TBSRTC, most lesions belonged to TBSRTC category VI as they are the most likely candidates for the surgery, which is a prerequisite for the final histopathology report.

Koo et al. also reported the higher prevalence of malignancy, notably TBSRTC VI. The referred cases reviewed by the hospital’s pathologist were included in the study [13].

Only 3% prevalence of TBSTRC III “grey zone” finding in our study could be because of imaging advantage while

performing FNAC, as shown in the study by Kumari et al. [8] The low number in our study could be because of including only operated patients.

Our study showed a different percentage of ROM than the implied ROM for TBSRTC categories. The variations are probably because of the smaller sample size in our study. Categories III and IV showed an increased percentage of ROM in our study than the implied ROM percentage of the TBSRTC system. Thus, including TBSRTC categories III and IV in the malignancy category seems sensible. Kumari et al. reported similar ROM in categories III and IV. Our TBSRTC category VI showed a less risk of malignancy percentage. Since TBSRTC is a relatively adapted system for reporting thyroid pathology, institutional experience in using TBSRTC plays a role in proper diagnosis. So, some overlapping features between benign and malignant lesions, such as pseudo inclusions and nuclear grooves, might have misguided the cytopathologist in reporting cytology. The ROM in TBSRTC VI in the study by Kumari et al. was 100% [8].

The high sensitivity and high NPV of USG-FNAC of a thyroid nodule of our study are broadly in line with previous literature studies, and reporting of cytology report may or may not be based on TBSRTC [8, 13–15]. Similar to our study, the sensitivity was above 90% and better than specificity, mainly when cytological reporting was as per TBSRTC [8, 15, 16].

Thus, USG-FNAC finding as per TBSRTC could be an excellent tool for screening thyroid lesions as negative findings in USG-FNAC are more likely to be negative and rule out disease.

Our study's findings differed from the study by Said et al. [17] probably because the study did not report cytological findings according to TBSRTC.

The specificity, PPV, and accuracy of our study were not satisfactorily high. Most of the false-positive findings were seen in small lesions. An explanation could be because all the lesions might have been aspirated that no pathology remained behind. Similarly, liberal diagnoses made by cytopathologist for lesions with overlapping features could have an increased number of false positives. USG-FNAC presents itself with the limitation of inability to distinguish between follicular adenoma and Hashimoto adenoma with their malignant counterpart, leading to high false positives in the current study. Also, including TBSRTC categories III and IV as malignant lesions could have accounted for high false positives.

Contrary to findings by existing studies, sensitivity did not increase or decrease with size [14, 18–20]. This study showed that USG-guided FNAC has high sensitivity in less than 2 cm or greater than 4 cm. In minor lesion, USG help in locating the nodule and thus accurate sampling. In a more significant lesion, it can

accurately sample the part of the lesion with the suspicious feature, increasing the sensitivity.

Specificity, however, increased with size, which is similar to the study by Kim et al. but at odds with Aydogan et al. where specificity decreased with size [18, 19]. Zhong et al. proffered that size did not influence specificity with the highest specificity reported at size 1–2 cm [20]. Size did not affect accuracy in our study and is consistent with previous studies. Also, our study validated claims by Aydogan et al. that ROM decreased with size, but it may be because of selection bias as we included only suspicious small lesions in the study [14, 18–20].

When the Cohen Kappa inter-rater agreement was applied, the Kappa coefficient increased with size > 4cm, having an almost perfect agreement. However, lesion < 2cm also had a fair agreement; hence, for small thyroid lesion, USG-FNAC can be advocated if not for diagnostic but for screening as our study revealed high sensitivity.

Our study has a limitation of a smaller sample size and not having a comparison group. The data were collected at a tertiary care referral center, thus carrying a risk of sampling bias.

Conclusion

USG-FNAC is a reliable procedure to evaluate thyroid lesions with high diagnostic value. The USG-FNAC reported as per TBSRTC rendered excellent sensitivity, making it an excellent preoperative screening tool to assess thyroid nodule. The specificity provided by USG-FNAC reported as per TBSRTC was, however, not satisfactory. Thus, we do not recommend it to make a definitive diagnosis. Hence, we recommend more extensive use of USG-FNAC for the evaluation of thyroid nodules.

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Authors' contributions

MG did the manuscript writing and along with KA did the conception and design of the study, data gathering, and analysis and interpretation of data. AJ helped with the interpretation of data. PT, BRG, and AKP were involved in the critical revision of the work, while NB analyzed the data and did the manuscript drafting procedure. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets generated during our study are available from the corresponding author upon request from the journal.

Declarations

Ethics approval and consent to participate

We have obtained the necessary ethical committee approval (88(6-11-E)2/075/076) from the Institutional Review Committee of Tribhuvan University Teaching Hospital, IOM for the study and it is included in the manuscript. Consent to participate: informed written consent was obtained from patients/ next of kin to participate in the study.

Consent for publication

Informed written consent was obtained from patients/ next of kin to participate in the study.

Competing interests

The authors declare that they have no competing interests.

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