### **ORIGINAL ARTICLE**

# DIAGNOSTIC ACCURACY OF THYROID ULTRASOUND IN DETECTION OF MALIGNANCY IN THYROID NODULES

Sadia Nawaz, M Babar Khan, Bushra Parveen\*, M Asif\*, M Rashid\*\*, M Azeem, M Nawaz Department of Radiology, \*Pathology, CMH, Muzaffarabad, \*\*Department of Radiology, CMH, Peshawar, Pakistan

**Background:** Occurrence of thyroid nodules is a common clinical problem in Pakistan being endemic area for hypothyroidism. This study was carried out to evaluate the diagnostic accuracy of thyroid ultrasound in detection of malignancy in thyroid nodules keeping Fine Needle Aspiration Cytology (FNAC) as a gold standard. Methods: A descriptive cross-sectional validation study was conducted at Departments of Radiology and Pathology, Shaikh Khalifa Bin Zayed Al-Nahyan Hospital/ CMH, Muzaffarabad from Dec 2014 to Jun 2015. Patients referred for evaluation of thyroid nodules were included in the study. Ultrasound guided FNAC was performed under direct imaging guidance. The imaging findings and FNAC were compared to access the diagnostic accuracy of ultrasound in predicting malignancy in thyroid nodules. **Results:** A total of 175 patients were studied with age range between 20-70 years. Mean age of the patients was 44.05±14.8 years. Of these, 35.4% were males and 64.6% were females. On FNAC, 27.4% cases were positive and 72.6% cases were negative while on thyroid ultrasound 26.3% cases were positive and 73.7% cases were negative. True positive were 24.0%, false positive 2.3%, false negative 3.4%, and true negative were 70.3%. Thyroid ultrasound showed sensitivity 87.5%, specificity 96.8%, diagnostic accuracy 94.2%, positive predictive value 91.3% and negative predictive value 95.3%. Conclusion: High resolution ultrasound is a very useful tool in accessing and selecting thyroid nodules for biopsy with a high diagnostic accuracy.

**Keywords:** Thyroid, Ultrasound, FNAC, Malignancy, Thyroid nodule, Tumour, Diagnosis Pak J Physiol 2018;14(3):11–3

### INTRODUCTION

The incidence of thyroid nodules has increased in the recent years. This has been attributed to increased use of imaging modalities, mainly ultrasound. Malignancies have been found in up to 15% of the nodules that were evaluated with Fine Needle Aspiration Cytology (FNAC).<sup>2,3</sup> In evaluation of thyroid nodules, highresolution ultrasound is being increasingly used to detect malignancy and guide fine needle aspiration for cytological analysis.<sup>4</sup> In addition, ultrasonography (USG) can evaluate the size and characteristics of nonpalpable nodules and it may diagnose lymph node metastasis.<sup>5</sup> According to Lingam et al<sup>6</sup>, a nodule should have at least one of the following findings to be subjected to FNAC: markedly reduced echogenicity. irregular or micro lobulated margins, presence of micro calcifications, length greater than the width.<sup>6</sup> Other investigators have highlighted the sensitivity of intranodular vascularity as being relatively high in predicting neoplastic nodules ranging from 66.7% to 91.7%. According to the Society of Radiologists in Ultrasound, FNAC should be performed on a nodule 1 Cm in diameter or larger with micro calcifications, 1.5 Cm in diameter or larger that is solid or has coarse calcifications, and 2 Cm in diameter or larger that has mixed solid and cystic components or is associated with abnormal cervical lymph nodes.<sup>8,9</sup>

Based on these criteria sensitivity and specificity of ultrasound has been reported at 89.2% and 85.2% respectively. Worldwide, USG is becoming the

mainstay for detection and evaluation of thyroid nodules as well as in providing guidance for FNAC. 11,12 Occurrence of thyroid nodules is a common clinical problem in Pakistan being endemic area for hypothyroidism. The careful evaluation of thyroid nodules for malignant potential and targeted approach to avoid unnecessary intervention should prove useful.

There is lack of local scientific data showing the importance of thyroid USG in detecting malignancy in thyroid nodules. The incidence of malignancy has been reported as 28.97% in this endemic area. There was high incidence of papillary carcinoma mainly in middle aged female patients while majority of the thyroid enlargements were benign.<sup>13</sup>

Several studies done in urban centres of Pakistan have shown that USG has overall good sensitivity in detecting thyroid cancer. <sup>13–18</sup> The use of ultrasound in selecting patients for biopsy is a useful screening tool as the availability of USG is almost universal even in our remote areas and may help screen patients in need for referral to higher centre for FNAC or follow up. This study was carried out to evaluate the diagnostic accuracy of thyroid ultrasound in detection of malignancy in thyroid nodules keeping FNAC as a gold standard.

## **MATERIAL AND METHODS**

This descriptive, cross-sectional validation study was conducted at Departments of Radiology and Pathology, Shaikh Khalifa Bin Zayed Al-Nahyan Hospital/CMH, Muzaffarabad from 24 Dec 2014 to 23 Jun 2015

following approval from Institutional Ethical Review Committee. Patients referred to radiology and pathology departments for solitary or multiple thyroid nodules evaluation or FNAC of thyroid nodules, were included in the study. The patient population was from Muzaffarabad and surrounding areas. Referrals from non-residents of the region, already diagnosed cases and patients taking radioactive iodine were excluded from the study. A total of 175 adult (18-70 years) patients with no gender discrimination were included in the study. Patients fulfilling inclusion and exclusion criteria were enrolled by non-probability consecutive sampling method after describing the study protocol and informed verbal consent. Demographic, clinical, and sonographic information of the patients was recorded on a predesigned proforma.

To characterize the nodules as malignant we selected solid or predominantly solid nodule with greater than 50% solid component that showed hypo echoic echo texture described as being lower than the surrounding normal thyroid tissue or being lower than the strap muscles where normal gland was replaced by multiple nodules, irregular or micro lobular margins, taller than wider shape and the presence or absence of micro calcification. The same were accessed irrespective of number, however in multiple nodules without above features the largest was biopsied.

Ultrasound guided FNAC was performed with patient lying supine having extended neck position and single pass per nodule was made with the help of 23 gauge needle and 5 or 10 cc syringe. Philips USG HD3 and Logic 200 (3.5/7.5 mHz probes) machine was used to characterize the thyroid nodule and to provide guidance for aspiration. Confirmation of placement of the needle in the targeted nodule was done by Ultrasound. The sample was taken from solid portion of the nodule; aspirate was spread on glass slides. Wet and dry fixed smears were made for cytology and the results were compared. The data was analyzed for estimation of sensitivity and specificity using SPSS-10.

### RESULTS

A total of 175 patients, during the study period of six months, 18–70 years of age were included in the study. Mean age of the patients was 44.05±14.8 years. Out of 175 patients, 62 (35.4%) were males and 113 (64.6%) were females. Forty-seven (26.9%) patients were having thyroid nodule <1 Cm, and 128 (73.1%) patients were having thyroid nodule >1 Cm in size. On FNAC, 48 cases were positive and 127 cases were negative, and on thyroid ultrasound 46 cases were positive and 129 cases were negative. True positive were 42, false positive 4, false negative 6, and true negative were 123 (Table-1). Thyroid ultrasound showed sensitivity 87.5%, specificity 96.8%, diagnostic accuracy 94.2%, positive predictive value 91.3% and negative predictive value 95.6%.

Table-1: Comparison of thyroid ultrasound and FNAC (n=175)

Thyroid	FNAC		
Ultrasound	Positive	Negative	Total
Positive	42 (TP)	4 (FP)	46 (26.3%)
Negative	6 (FN)	123 (TN)	129 (73.7%)
Total	48 (27%)	127 (72.6%)	175

TP= True positive, FP= False positive, TN= True negative

### **DISCUSSION**

Many benign and malignant thyroid conditions commonly present in the form of thyroid nodules. <sup>19,20</sup> In Pakistan, thyroid disease is a concerning health issue mainly because of dietary iodine deficiency. According to the estimates given by UNICEF, 70% of our total population is at risk of developing thyroid diseases because of deficiency of iodine. <sup>21,22</sup> Moreover, there is a higher incidence of differentiated thyroid malignancy, mainly papillary cancer, in the geographical location of our study.<sup>13</sup> Thyroid cancer is responsible for 1.2% cases of all malignant tumours in Pakistan.<sup>22</sup> With this background, the need for a useful screening tool for early detection of thyroid cancer becomes significant. Several studies have been done demonstrating the usefulness of USG in detecting thyroid malignancy. Several guidelines have been proposed using ultrasound as a screening tool. These have used various sonographically detectable morphological parameters like echogenicity of the nodule, its margins, the presence or absence of micro calcifications, size, taller than wider shape, solid content, central vascularity, extra thyroid extension, calcification and abnormal neck lymph nodes.<sup>23</sup> Because of its simplicity we mainly applied Kim et al<sup>24</sup> criteria in our study with assessment of nodal status which was negative in all cases. Using this approach yielded a higher diagnostic accuracy than reported in their original study, probably because of the higher incidence of papillary carcinoma in our setting.<sup>13</sup>

Our results support the usefulness of this simplified method as reported by Frates  $et\ al^5$ . The missed cases on ultrasound in our study warrant a thorough follow up of all cases labelled as negative using these criteria and a 3 to 6 months and 12 month follow up was suggested to look for any increase in size or alteration in sonographic appearance and reassessment of the nodal status of the neck region. Our results follow already reported diagnostic accuracy further consolidating the usefulness of USG being an essential part of FNAC of thyroid nodules.

Ultrasound being readily available, cheap, safe without radiation hazards and the ease with which it can access and aid fine needle aspiration cytology of thyroid nodules is conveniently the most commonly employed modality compared to CT, MRI, or an isotope scan. Our study like others reaffirms this point and the pivotal role it has played in the evaluation of patients with thyroid diseases. <sup>14,27–31</sup>

#### **CONCLUSION**

The results highlight the usefulness of USG as diagnostic tool for screening patients with thyroid nodules for suspected malignancy and selecting thyroid nodules for biopsy with a reasonably high diagnostic accuracy.

## REFERENCES

- Moon WJ, Baek JH, Jung SL, Kim DW, Kim EK, Kim JY, et al. Ultrasonography and the Ultrasound-Based Management of Thyroid Nodules: Consensus Statement and Recommendations. Korean J Radiol 2011;12(1):1–14.
- Kwak JY, Kim EK, Kim HJ, Kim MJ, Son EJ, Moon HJ. How to combine ultrasound and cytological information in decision making about thyroid nodules. Eur Radiol 2009;19(8):1923–31.
- Taddesse A, Yaqub A. Clinical, sonographic and cytological evaluation of small versus large thyroid nodules. J Pak Med Assoc 2011;61(5):466–9.
- Baier ND, Hahn PF, Gervais DA, Samir A, Halpern EF, Mueller PR, et al. Fine-Needle Aspiration Biopsy of Thyroid Nodules: Experience in a Cohort of 944 Patients. Am J Roentgenol 2009;193(4):1175–9.
- 5. Frates MC, Langer JE. Biopsy of Thyroid Nodules: Comparison of three sets of guidelines. Am J Roentgenol 2010;195:W472.
- Lingam RK, Oarib MH, Tollev NS. Evaluating thyroid nodules: predicting and selecting malignant nodules for fine-needle aspiration (FNA) cytology. Insights into Imaging 2013;4(5):617– 24
- Ahn SS, Kim EK, Kang DR, Lim SK, Kwak JY, Kim MJ. Biopsy of Thyroid Nodules: Comparison of three sets of guidelines. Am J Roentgenol 2010;194(1):31–7.
   Yunus M, Ahmed Z. Significance of ultrasound features in
- Yunus M, Ahmed Z. Significance of ultrasound features in predicting malignant solid thyroid nodules: Need for fine-needle aspiration. J Pak Med Assoc 2010;60(10): 848–53.
- Vinayak S, Sande JA. Avoiding unnecessary Fine-Needle Aspiration Cytology by accuractely predicting the benign nature of thyroid nodules using ultrasound. J Clin Imaging Sci 2012;2(1):23.
- Frates MC, Benson CB, Doubilet PM, Charboneau JW, Cibas ES, Orlo HC. Likelihood of thyroid cancer based on sonographic assessment of nodule size and composition [abstract]. In Radiological Society of North America Scientific Assembly and Annual Meeting Program. Oak Brook, IL: 2004.p. 395.
- Annual Meeting Program. Oak Brook, IL: 2004 p. 395.

  11. Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z. Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. J Ultrasound Med 2009;28(7):861–7.
- 12. Romitelli F, Di Stasio E, Santoro C, Iozzino M, Orsini A, Cesareo R. A comparative study of fine needle aspiration and fine needle non-aspiration biopsy on suspected thyroid nodules. Endocr Pathol 2009;20(2):108–13.
- Ejaz R, Salaria SM, Bukhari MH, Ahmed M, Nosheen J, Ejaz U. Histopathological spectrum of surgically treated goiters in Muzaffarabad. Pak J Med Health Sci 2015;9(1)2–4.
- Tarrar AM, Wahla MS, Ilyas S, Khan OU, Waqas A, Raza A. Solitary thyroid nodule; frequency of malignancy at Combined Military Hospital Rawalpindi. Professional Med J 2010;17(4):598–602.
- Alam T, Khattak YJ, Beg M, Raouf A, Azeemuddin M, Khan AA. Diagnostic accuracy of ultrasonography in differentiating

- benign and malignant thyroid nodules using fine needle aspiration cytology as the reference standard. Asian Pac J Cancer Prev 2014;15(22):10039–43.
- Muhammad D, Khan S, Rahman A. Diagnostic accuracy of grayscale and colour doppler ultrasonography in diagnosing malignant thyroid nodules. Pak Arm Forces Med J 2016;66(4):574–8.
- Ram N, Hafeez S, Qamar S, Hussain SZ, Asghar A, Anwar Z, et al. Diagnostic validity of ultrasonography in thyroid nodules. J Pak Med Assoc 2015;65(8):875–8.
- Shah AH, Marfani Ś, Ejaz A. To determine the frequency of malignancy in solitary nodule of thyroid in ENT, Head and Neck Surgery Department at Civil Hospital Karachi. Med Forum 2016;27(4):44–7.
- Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. The American Thyroid Association Guidelines Taskforce. Thyroid 2006;16(2):109–42.
- Akhtar T, Ullah Z, Paracha Pl, Lutfullah G. Impact assessment of salt iodization on the prevalence of goiter in district Swat. Pak J Med Sci 2004;20(4):303–7.
- Sushel C, Khanzada TW, Zulfikar I, Samad A. Histopathological pattern of diagnoses in patients undergoing thyroid operations. Rawal Med J 2009;34(1):14–6.
- Zuberi LM, Yawar A, Islam N, Jabbar A. Clinical presentation of thyroid cancer patients in Pakistan-AKUH experience. J Pak Med Asso 2004;54(10):526–7.
- Asso 2004;54(10):526–7.

  23. Cheng P, Chen ED, Zheng HM, He QX, Li Q. Ultrasound score to select subcentimeter-sized thyroid nodules requiring ultrasound-guided fine needle aspiration biopsy in eastern China. Asian Pac J Cancer Prev 2013;14(8):4689–92.
- Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee T, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. AJR Am J Roentgenol 2002;178(3):687–91.
- Rahimi M, Farshchian N, Rezaee É, Shahebrahimi K, Madani H. To differentiate benign from malignant thyroid nodule comparison of sonography with FNAC findings. Pak J Med Sci 2013;29(1):77–80.
- 26. Shin S, Park SE, Kim Y, Hyun MK, Kim SW, Kwon JW, et al. Effectiveness of ultrasonographic screening for thyroid cancer: Round-table Conference in the National Evidence-based Healthcare Collaborating Agency (NECA) in conjunction with the Korean Thyroid Association. Asian Pac J Cancer Prev 2014;15(12):5107–10.
- Koike E, Noguchi S, Yamashita H, Murakam T, Ohshima A, Kawamoto H, *et al.* Ultrasonographic characteristics of thyroid nodules: prediction of malignancy. Arch Surg 2001;136:334–7.
   Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E.
- Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color doppler sonography aid in the prediction of malignancy of thyroid nodules? J Ultrasound Med 2003;22(2):127–31.
- Mazzaferri EL, Sipos J. Should all patients with subcentimeter thyroid nodules undergo fine-needle aspiration biopsy and preoperative neck ultrasonography to define the extent of tumor invasion? Thyroid 2008;18(6):597–602.
- Accurso A, Rocco N, Palumbo A, Leone F. Usefulness of ultrasound-guided fine-needle aspiration cytology in the diagnosis of non-palpable small thyroid nodules. Tumori 2005;91(4):355–7.
- Lee MJ, Kim EK, Kwak JY, Kim MJ. Partially cystic thyroid nodules on ultrasound: probability of malignancy and sonographic differentiation. Thyroid 2009;19(4):341–6.

## **Address for Correspondence:**

Lt Col Dr M Babar Khan, Assistant Professor Radiology, Shaikh Khalifa Bin Zayed Al-Nahyan Hospital/CMH, Muzaffarabad, Azad Jammu & Kashmir, Pakistan. Cell: +92-345-9907994

Email: babar1967@me.com

Received: 3 Feb 2018 Reviewed: 23 May 2018 Accepted: 8 Jun 2018