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DIAGNOSTIC ACCURACY OF DOPPLER RESISTIVE INDEX IN DIFFERENTIATING MALIGNANT FROM BENIGN THYROID NODULES TAKING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Background: Thyroid nodules are common, with some risk of malignancy. FNAC is the standard diagnostic tool but has limitations. Doppler Resistive Index (RI) offers a non-invasive alternative. This study assesses its accuracy using histopathology as the gold standard.

Materials and Methods: This cross-sectional study, conducted at the Punjab Institute of Neurosciences, Lahore (August–December 2024), included 111 grayscale ultrasound-confirmed

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thyroid nodule patients. Non-probability consecutive sampling was used. Resistive Index (RI) was measured from the nodule. Nodules with RI ≤ 0.7 were benign, while RI ≥ 0.71 indicated malignancy. SPSS version 22 analyzed sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy.

Results: Among 111 patients, 31.5% were male and 68.5% female. The mean age was 49.68 ± 7.14 years, lower in malignant cases (46.86). Malignant cases also had a lower BMI (18.46 vs. 23.42). Mean RI was higher in malignant (0.77) than benign nodules (0.56). DDUS showed 81.1% sensitivity, 89.2% specificity, 78.9% PPV, and 94.5% NPV for malignancy detection. The ROC curve yielded an AUC of 0.955, indicating excellent accuracy.

Conclusion: Doppler Resistive Index (RI) accurately differentiates malignant from benign thyroid nodules. It serves as a non-invasive, cost-effective FNAC adjunct, especially in resource-limited settings.

Keywords: Thyroid nodules; Doppler ultrasound; Resistive Index; Histopathology; Thyroid neoplasm; Diagnostic accuracy

INTRODUCTION

Thyroid is an endocrine gland which plays an important role in metabolism by its hormones. Thyroid nodules or nodular thyroid disease is the most common pathological condition in the population having diet deficient in iodine.[1] In Pakistan approximately 70% of population is at risk of developing thyroid disease due to deficiency of iodine in diet.[2]According to clinical presentation, the prevalence can range from 4–7%. When discovered by USG or autopsy, non-palpable thyroid nodules can be found up to 50% of the time.[3] Thyroid nodules are mostly benign and only 5-15% are malignant.[4] Papillary thyroid carcinomas is the most common malignancy of thyroid, ranging from 55% to 80%.[5-7] According to American Thyroid Association (ATA) a nodule is characterized by a separate lesion in the thyroid gland which is distinguishable from the surrounding thyroid parenchyma radiologically. Fine needle aspiration cytology FNAC is the test of choice to differentiate benign from malignant thyroid nodules, however it is not an unchallenging and feasible to perform FNAC on every single nodule.[8] The resistive index is a measure of fluctuating blood flow in a vessel that reflects the resistance to flow in the vessels distal to the site of measurement. It is calculated by the formula:[9]

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$$RI = \frac{Peaksystolicvelocity(PSV) - Enddiastolicvelocity\ (EDV)}{Peaksystolicvelocity\ (PSV)}$$

Currently there are many investigations in practice which are carried out to diagnose the nodular thyroid disease such as Gray-scale ultrasound, Thyroid function tests and thyroid scan. But none of them can differentiate between benign and malignant thyroid nodules alone. As 10-15% of FNAC are non-diagnostic and repeat biopsy is needed which is a cumbersome procedure and extortionate for patients in due to limited resources of our country. By measuring resistive index (RI) on Duplex Doppler ultrasound (DDUS) is an important adjunctive to differentiate between benign and malignant thyroid nodules. A lot of studies have been conducted worldwide illustrating the accuracy of resistive index (RI) on Doppler ultrasound in differentiating malignant and benign thyroid nodules. Local data is lagging behind and it is requisite to conduct such researches on Pakistani population. If the accuracy becomes comparable with the results of internationally conducted researches then this will be an important and significant alternative to FNAC, with other sonographic features in the coming time and an invasive procedure like biopsy and anxiety of patients will be avoided.[1] Therefore, the objective of this study is to find out the accuracy of resistive index on Duplex Doppler ultrasound to differentiate between malignant and benign thyroid nodules.

MATERIALS AND METHODS

This cross-sectional study was conducted from 1st August to 31st December 2024 at the Department of Diagnostic Radiology, Punjab Institute of Neurosciences, Lahore, Pakistan. A total of 111 patients with nodular thyroid disease confirmed by grayscale ultrasound were selected through non-probability consecutive sampling. Inclusion criteria included patients aged 15–60 years of either gender. Patients with comorbidities such as diabetes, hypertension, or thyroiditis, as well as those who were non-cooperative or had previous thyroid surgery, were excluded. Clinical data were collected, and grayscale and Doppler ultrasonography were performed using a GE LOGIQ S8 ultrasound machine. Doppler studies measured the resistive index (RI) of thyroid nodules by evaluating arterial flow either at the periphery or center of the nodules. RI values were calculated as an average of three readings per nodule. Histopathological evaluation served as the gold standard. Data were analyzed using SPSS version 22 to calculate diagnostic accuracy,

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sensitivity, specificity, positive predictive value, and negative predictive value. Ethical approval from Institutional review board and informed consent were obtained.

OPERATIONAL DEFINITIONS

Benign Nodule On Doppler Ultrasound: The nodules having RI ≤ 0.7 was considered benign. Figure below shows the grey-scale, color Doppler and Duplex Doppler images of a benign thyroid nodule **(Figure 1).**

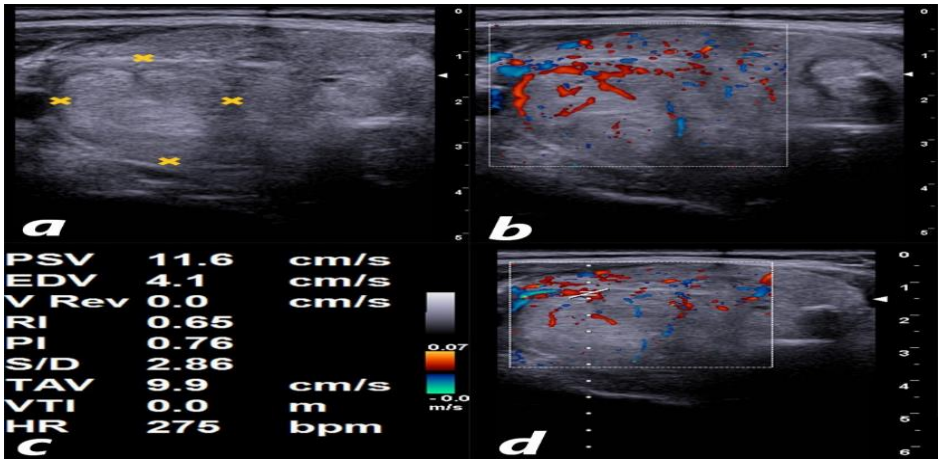

Figure 1. (a) Grey scale image of right lobe of thyroid gland showing a hyperechoic solid nodule (yellow cursors). **(b)** Color Doppler image of the same nodule showing intense peripheral and mild internal vascularity. **(C & d)** Duplex Doppler image showing the RI of 0.65 (consistent with the benign nodule).

Malignant Nodule On Doppler Ultrasound: The nodules having RI ≥ 0.71 was considered malignant.

RESULTS

The study involved 111 participants, with an average age of 49.68 ± 7.14 years and an average BMI of 21.77 ± 3.02. The gender distribution was 31.5% male and 68.5% female. Male participants had a slightly higher mean age of 51.89 years compared to females, who had a mean age of 48.67 years. The mean BMI for males was 21.74 ± 0.54, while for females, it was 21.78 ± 0.33 **(Table 1)**.

Table 1. Demographics of study participants. N = 111

Study Parameters	n (%)

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Age (years)	
Mean ± SD	49.68 ± 7.14
Range	28 years – 60 years
BMI	
Mean ± SD	21.77 ± 3.02
Range	16.0 – 28.80
Gender	
Male	35 (31.5 %)
Female	76 (68.5 %)
Gender wise Age and BMI distribution	
Mean age of M ± SD	51.88 ± 1.04 years
Mean age of F ± SD	48.67± 0.84 years
Mean BMI of M ±SD	21.74± 0.54
Mean BMI of F ± SD	21.78 ± 0.33

Legend: M: male, F: female, N: number, BMI: body mass index, SD: standard deviation.

Histopathological analysis classified nodules as either malignant or benign. Malignant nodules were linked to a lower mean age of 46.86 years and a lower BMI of 18.47, compared to benign nodules, which had a mean age of 51.09 years and a BMI of 23.42. The duration of symptoms was also longer for malignant cases, averaging 13.3 months, versus 9.1 months for benign cases. These results indicate that malignant cases tend to occur in younger, leaner individuals and are associated with prolonged symptom duration. Additionally, Resistive Index (RI) values obtained through Doppler sonography were significantly higher for malignant nodules, with a mean of 0.77, compared to benign nodules, which had a mean RI of 0.56**(Table 2).**

Table 2. Demographics of study participants and study parameters on the basis of benign and malignant nodules. N = 111

Study Parameters	n (%)
Total malignant cases	

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Mean age ± SD	46.86 ± 1.28
Mean BMI ± SD	18.46 ± 0.24
Mean duration of symptoms (months ± SD)	13.29 ± 1.19
Mean RI ± SD	0.77 ± 0.005
Total benign cases	
Mean age ± SD	51.09 ± 0.74
Mean BMI ± SD	23.4 ± 0.24
Mean duration of symptoms (months ± SD)	9.08 ± 0.68
Mean RI ± SD	0.56 ± 0.008

Legend: SD; standard deviation.

The evaluation of diagnostic performance metrics highlighted key insights. Doppler ultrasound (DDUS) demonstrated strong accuracy in detecting malignant nodules. According to cross-tabulation analysis, DDUS exhibited a sensitivity of 81.1% and a specificity of 89.2%, accurately identifying 81.1% of malignant cases and 89.2% of benign cases. These findings reflect the actual real-world effectiveness of DDUS within the study population **(Table 3).**

Table 3. Nodule on Doppler ultrasound x Nodule on Histopathology Cross tabulation. N = 111

			Nodule on Histopathology		Total
			Malignant	Benign	
Nodule on DDUS	Malignant	Count	30	8	38
		% within Nodule on Histopathology	81.1%	10.8%	34.2%
	Benign	Count	7	66	73
		% within Nodule on Histopathology	18.9%	89.2%	65.8%
Total		Count	37	74	111

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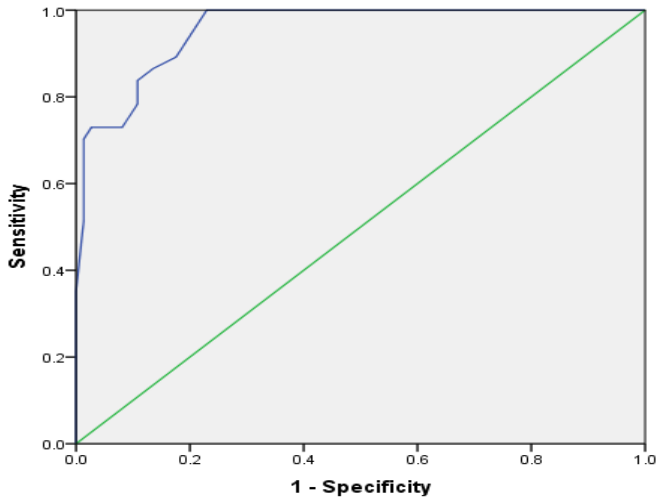
	% within Nodule on Histopathology	100.0%	100.0%	100.0%

Legend: DDUS; Duplex Doppler Ultrasonography.

Additionally, the Resistive Index (RI), measured through Doppler ultrasound, showed exceptional discriminatory ability, achieving an area under the curve (AUC) of 0.955 in ROC curve analysis. At an optimized RI cutoff of 0.645, the sensitivity rose to 91.9%, with a specificity of 81.1%, a positive predictive value (PPV) of 78.9%, and a negative predictive value (NPV) of 94.5%. These results underscore the potential of RI as a highly accurate and dependable diagnostic tool for differentiating malignant from benign nodules **(Figure 2).**

Figure 2. ROC Curve for Resistive Index (RI).



DISCUSSION

Distinguishing between malignant and benign thyroid nodules continues to be a critical challenge in the fields of endocrinology and radiology. Precise classification is crucial for ensuring timely treatment of malignancies while reducing unnecessary interventions for benign cases. In our study, the Doppler Resistive Index (RI) proved to be a highly dependable, non-invasive diagnostic tool, demonstrating significant value in differentiating malignant from benign thyroid nodules. This finding is consistent with existing research that advocates for the use of RI as a supplementary diagnostic method, particularly in scenarios where invasive procedures such as fine-needle aspiration cytology (FNAC) are not feasible or accessible.

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Our findings demonstrated that malignant thyroid nodules exhibited significantly higher Resistive Index (RI) values compared to benign nodules. Specifically, we recorded mean RI values of 0.77 for malignant nodules and 0.56 for benign ones, with an optimized RI threshold of 0.645 for differentiation. These results align closely with those reported by Chammas et al., who observed mean RI values of 0.75 for malignant nodules and 0.55 for benign nodules, identifying an optimal RI threshold of 0.7.[10] This consistency between our findings and established literature highlights the broad applicability and reliability of RI as a diagnostic tool in the evaluation of thyroid nodules. The diagnostic performance of Doppler Resistive Index (RI) in our study was highly impressive, achieving a sensitivity of 91.9%, a specificity of 81.1%, and an area under the curve (AUC) of 0.955. These metrics highlight the remarkable accuracy of RI in differentiating malignant from benign thyroid nodules. While a study by Nobuhiro et al. suggested that color Doppler evaluation of thyroid nodules does not enhance the risk stratification capability of the ACR TI-RADS ultrasound classification system.[11]Other research has demonstrated that RI can serve as a valuable adjunctive tool when combined with grayscale ultrasound and other standard diagnostic methods. This reinforces the potential of RI to complement existing techniques in improving diagnostic precision.

A 2018 study involving 63 patients revealed that 14% of the nodules were malignant, with these nodules exhibiting a higher resistive index (RI > 0.715) compared to benign nodules (RI < 0.715).[9] Similarly, a 2021 study on 40 patients concluded that malignant nodules had a higher RI than benign ones, suggesting that RI can serve as a valuable non-invasive tool for distinguishing between malignant and benign nodules.[12] Another study identified a significant association between malignancy and an RI threshold of less than 0.715, reporting sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for malignant nodules at 88.9%, 79%, 42%, and 97%, respectively.[9] Additionally, Color-Doppler ultrasound demonstrated impressive diagnostic accuracy, with an overall accuracy of 81.0%, sensitivity of 88.9%, and specificity of 74.2%. These findings highlight the potential of Color-Doppler ultrasound to play a more prominent role in the differential diagnosis of thyroid tumors.[13]

In addition to its diagnostic accuracy, our study revealed notable demographic and clinical differences between patients with malignant and benign thyroid nodules. Malignant nodules were

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associated with younger age and lower body mass index (BMI) compared to benign nodules. These findings align with studies conducted in iodine-deficient regions, which have similarly identified younger age and lower BMI as potential risk factors for thyroid malignancy.[14] For instance, a study by Moon and his colleagues, found that patients with malignant thyroid nodules were significantly younger than those with benign nodules.[15] While studies in iodine-sufficient populations have not consistently reported these associations, the influence of environmental and nutritional factors in regions like Pakistan cannot be ignored.

The clinical implications of our findings are particularly significant in resource-constrained settings. Although fine-needle aspiration cytology (FNAC) remains the gold standard for evaluating thyroid nodules, its limitations are well-documented. Approximately 10–15% of FNAC results are non-diagnostic, often requiring repeat procedures that can be both burdensome and anxiety-inducing for patients. Additionally, the invasive nature of FNAC makes it less appealing, especially for nodules that appear clinically benign but require confirmation. By integrating Doppler Resistive Index (RI) into routine diagnostic protocols, healthcare providers can reduce reliance on FNAC, minimizing patient discomfort and optimizing resource utilization. A study by Moon et al. highlighted the utility of Doppler ultrasound in reducing the need for FNAC, particularly for nodules with definitive RI thresholds indicative of benignity or malignancy.[16]

Our study also underscores the potential of Doppler RI to complement other imaging modalities in thyroid nodule evaluation. While grayscale ultrasound is widely used, its specificity and sensitivity for distinguishing benign from malignant nodules are limited. According to a study grayscale features such as hypoechogenicity, irregular margins, and microcalcifications have sensitivity rates ranging from 60% to 70%, which are lower than those observed for Doppler RI.[17] The inclusion of RI measurements provides a quantitative, less operator-dependent, and more reproducible parameter, thereby enhancing overall diagnostic accuracy. Similar conclusions were drawn by Algin et al., who found that combining Doppler RI with grayscale ultrasound improved the diagnostic performance of thyroid nodule assessments.[18]

The high diagnostic performance of Doppler RI in our study is further supported by ROC curve analysis, which demonstrated an area under the curve (AUC) of 0.955. This reflects the exceptional discriminatory power of RI and is consistent with other studies reporting AUC values ranging from

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0.85 to 0.92. At an optimized RI threshold of 0.645, the sensitivity and specificity observed in our study were 91.9% and 81.1%, respectively, highlighting the reliability of RI as a diagnostic tool. These metrics are particularly valuable in reducing false negatives, ensuring accurate identification of malignant nodules, and minimizing false positives, which could lead to unnecessary biopsies or interventions.

LIMITATIONS

Despite its promising results, our study has certain limitations that should be acknowledged. The relatively small sample size may restrict the generalizability of our findings, particularly to populations with different demographic and clinical characteristics. Larger, multi-center studies are necessary to validate our results and establish standardized RI thresholds that can be applied across diverse patient groups. Additionally, while Doppler RI demonstrated excellent diagnostic performance, it should not be used as a standalone tool. A comprehensive diagnostic approach that includes clinical evaluation, thyroid function tests, and, when appropriate, cytological examination remains crucial to ensure the best possible patient outcomes.

CONCLUSIONS

In conclusion, Doppler Resistive Index (RI) provides a non-invasive, dependable, and economical substitute for fine-needle aspiration cytology (FNAC) by exhibiting remarkable diagnostic accuracy in distinguishing between benign and malignant thyroid nodules. Healthcare professionals can enhance patient care, reduce dependency on invasive procedures, and optimize resource use by incorporating RI into standard diagnostic processes. In order to further improve diagnostic precision, future studies should concentrate on confirming these results in a variety of groups and investigating the incorporation of cutting-edge imaging modalities.

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Consent and Ethics permission: This was a retrospective study and presented no harm to the subjects studied. Ethical approval was obtained from Institutional Review Board of Punjab Institute of Neurosciences, Lahore, Pakistan.

Conflict of interests: None.

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