DIAGNOSTIC ACCURACY OF COLOR DOPPLER ULTRASONOGRAPHY IN DIFFERENTIATING BENIGN AND MALIGNANT CERVICAL LYMPH NODES KEEPING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

OBJECTIVE

This study aimed to assess the diagnostic accuracy of Color Doppler Ultrasonography (CDUS) for differentiating benign from malignant cervical lymph nodes, with histopathological correlation.

METHODOLOGY

A prospective cross-sectional study was conducted at the Department of Radiology, MTI–Hayatabad Medical Complex, Peshawar. A total of 235 consecutive patients with clinically suspected cervical lymphadenopathy underwent Color Doppler ultrasonography followed by histopathological confirmation, where clinically indicated. Diagnostic performance measures, including sensitivity, specificity, PPV, NPV, and diagnostic accuracy, along with their 95% confidence intervals, were calculated.

RESULTS

CDUS classified 87 (37.0%) lymph nodes as malignant and 148 (63.0%) as benign. The histopathological results showed 94 (40.0%) malignant and 141 (60.0%) benign lymph nodes. The diagnostic performance of CDUS showed 87.2% sensitivity, 96.5% specificity, 94.3% PPV, 91.9% NPV, and 92.8% diagnostic accuracy. The participants' mean age was 44.40 ± 15.65 years, with a female predominance (54.0%). Exploratory stratified analysis demonstrated numerically comparable diagnostic performance across age and gender categories; these observations were descriptive and not formally compared statistically.

CONCLUSION

CDUS demonstrated high diagnostic performance and may serve as a useful first-line imaging modality for evaluation of cervical lymphadenopathy, particularly in resource-limited settings; however, histopathological confirmation remains necessary in equivocal cases.

KEYWORDS: *Cervical Lymphadenopathy, Color Doppler, Diagnostic Accuracy, Histopathology, Sensitivity, Specificity*

INTRODUCTION

Cervical lymphadenopathy, or swelling of the neck lymph nodes, is one of the most prevalent clinical manifestations in primary care, otolaryngology, and oncology settings. There are several causes of the illness, ranging from benign, self-limiting conditions such as reactive hyperplasia caused by bacterial or viral infections to more severe pathological processes such as lymphoma, metastatic carcinoma, and TB lymphadenitis.[1] Accurate diagnosis of the type of enlarged lymph node is more difficult than just identifying them. Prognostic categorization is crucial for providing appropriate follow-up care and preventing invasive procedures.[2] In oncology and in general head and neck tumors, the presence of malignant cervical lymphadenopathy is crucial for staging, planning management, and predicting the patient's prognosis.[3] The diagnosis of cervical lymphadenopathy involves tissue diagnosis, various imaging modalities, and clinical examination. Although the clinical examination provides initial insight, its subjectivity and low sensitivity for detecting deeply embedded or slightly enlarged nodes diminish its reliability.[4] Cross-sectional imaging techniques, such as MRI (magnetic resonance imaging) and CT (computed tomography), provide excellent anatomical detail. However, their usefulness is often limited by considerable drawbacks, e.g., cost, limited availability in low-resource or remote settings, and exposure to ionizing radiation from CT.[5] Furthermore, they primarily offer morphological data, with little ability to detect the nodal vascularity, a crucial difference between benign and malignant processes.[6] In this diagnostic landscape, Ultrasonography (US) has become a very useful diagnostic tool. It is widely accessible, non-invasive, reasonably priced, and radiation-free.[7] It provides outstanding high-resolution real-time imaging of superficial organs, such as cervical lymph nodes, permitting an extensive assessment of morphological

features, including size, shape, cortical hypertrophy, hilum preservation, margin contour, and echogenicity. Due to the advancement of Color Doppler Ultrasonography (CDUS), this structural evaluation now includes a functional component. As a reflection of their distinctive physiological design, benign reactive nodes typically demonstrate preserved hilar vascularity. In contrast, abnormal vascular patterns, such as peripheral or mixed vascularity, are often seen in malignant nodes, whether caused by lymphoma or metastatic deposits. This is because the neo-vascularization associated with tumor growth affects the normal hilar blood supply.[8] Additional malignant findings on CDUS include a round shape, increased cortical thickness, and loss of the echogenic fatty hilum.[9] The reported diagnostic performance of CDUS in the literature has demonstrated significant inconsistency despite these well-described features. According to research by Khanal et al. (2021), CDUS has 83.3% sensitivity and 79.6% specificity compared with fine-needle aspiration cytology (FNAC).[10] Another study revealed differences in how CDUS results were interpreted, demonstrating inter-observer variability and the lack of widely established diagnostic standards.[4] This discrepancy presents a clinical challenge and emphasizes the necessity of continuing, methodologically sound research to confirm the diagnostic accuracy of CDUS, particularly in a variety of patient demographics and clinical settings. Tissue diagnosis remains the gold standard for lymph node pathology, as it provides a definitive histologic diagnosis. Though FNAC is a less invasive option, sample errors and equivocal results are common, especially in nodes with fibrosis or cystic degeneration.[2] Excisional biopsy is the gold standard for diagnosis because it provides a detailed architectural assessment, albeit at the cost of greater invasiveness. Consequently, this indisputable benchmark must be used to assess the accuracy of each new diagnostic test. The availability of modern imaging techniques such as CT and MRI is frequently limited in health care settings with the least resources, as seen in many deprived nations.[5] There is an urgent need for a precise and accessible diagnostic tool. With its affordability and portability, CDUS has immense potential to close this gap by serving as a valuable triage tool to determine whether patients actually need more expensive imaging or invasive biopsy.[5] Hence, using histological validation as the gold standard, the main purpose of this study was to establish the diagnostic accuracy of Color Doppler Ultrasonography in differentiating benign from malignant cervical lymph nodes. This study aims to provide high-quality evidence on the clinical value of CDUS using a robust cross-sectional design with a sufficient sample size and blinding of radiologists and pathologists. The results are anticipated to support diagnostic procedures, enhance patient care pathways, and validate CDUS's function as a first-line imaging modality in the assessment of cervical lymphadenopathy, particularly in situations where access to healthcare resources is crucial.

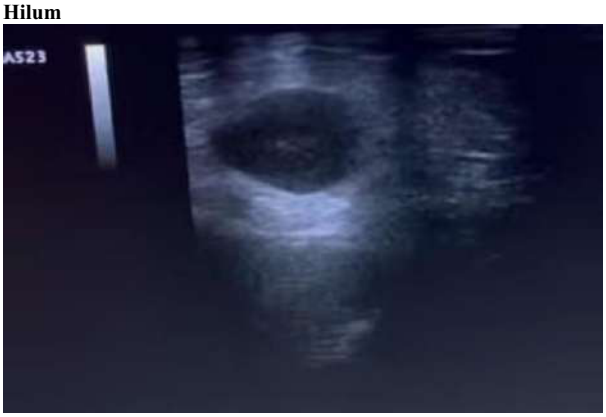
METHODOLOGY

The study employed a cross-sectional design and was conducted at the Diagnostic Radiology Department, MTI-Hayatabad Medical Complex, Peshawar. The study duration was 6 months following ethical approval (IRB Ref: 1784**).** A total of 235 consecutive patients aged 18–70 years presenting with clinically suspected cervical lymphadenopathy were enrolled using a non-probability consecutive sampling technique. The sample size was calculated using the WHO sample size calculator, assuming an expected prevalence of 23%, a sensitivity of 83.3%, a specificity of 79.6%, and a 10% margin of error. CDUS examination is performed for each participant, followed by histopathological examination of the lymph nodes, to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. Participants with a history of known malignancy under treatment, previous neck surgery, or radiotherapy were excluded. Socioeconomic status was recorded as a demographic variable based on participants' reported monthly household income and categorized into low, middle, and high groups according to predefined study categories. After obtaining informed consent, all participants underwent Color Doppler ultrasonography (CDUS) examination performed by experienced radiologists blinded to histopathological results. All ultrasound examinations were performed using a GE LOGIQ S8 ultrasound machine equipped with a 7-12 MHz high-frequency linear transducer, and a structured reporting pro forma was used for all examinations. Lymph nodes were assessed for morphology, including size, short-axis diameter, long-to-short axis ratio, shape, margins, echogenic hilum, cortical thickness, nodal borders, internal necrosis, calcification, and vascularity pattern, classified as hilar, peripheral, mixed, or avascular. Benign lymph nodes were generally characterized by oval morphology and preserved echogenic hilum (Figure 1). Nodes were classified as malignant when at least three predefined suspicious sonographic features were present, including round configuration (L/S ratio <2), absent echogenic hilum, peripheral or mixed vascularity, cortical thickening >3 mm, irregular margins, or intranodal necrosis (Figure 2). Two consultant radiologists with more than five years of head and neck imaging experience independently

reviewed 30 randomly selected cases to improve observer calibration. Concordance between reviewers was assessed during calibration through case-wise comparison of final classifications, and discordant interpretations were resolved by consensus discussion before final analysis. Formal interobserver agreement statistics (e.g., Cohen's kappa) were not performed because quantitative reproducibility assessment was beyond the predefined objectives of the present study. The same nodes were then sent to a senior pathologist who was blinded to ultrasound findings and clinical radiology reports to minimize interpretation bias. Histopathological diagnosis was established using either core needle biopsy or excisional biopsy, according to routine clinical indications and the treating clinician's preference rather than the study protocol, and all specimens underwent histopathological evaluation. Benign-appearing lymph nodes were biopsied because all enrolled patients had persistent cervical lymphadenopathy with clinical suspicion requiring tissue diagnosis as part of routine clinical management. For statistical analysis, SPSS version 23.0 was used. Continuous variables were reported as mean ± standard deviation, and categorical variables as frequencies and percentages. Diagnostic accuracy measures, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy, and corresponding 95% confidence intervals, were calculated using a 2×2 contingency table. As the study used dichotomous classification rather than continuous probability outputs, receiver operating characteristic (ROC) analysis was not performed. Multivariable adjustment was not undertaken because the study objective focused on estimating diagnostic performance rather than identifying independent predictors. Stratified analyses by age and gender were exploratory and descriptive.

Figure 1: Sonographic Appearance of a Benign Cervical Lymph Node Demonstrating Preserved Fatty Hilum and Oval Morphology

Figure 2: Sonographic Appearance of a Malignant Cervical Lymph Node Showing Rounded Morphology and an Absent Fatty Hilum



RESULTS

This study included 235 patients in the final analysis with a mean age of 44.40 ± 15.65 years. The cohort demonstrated a slight female predominance (54.0%), and the majority of participants (60.4%) were under 50 years of age.

Table 1: Baseline Demographic and Clinical Characteristics of Study Population (n=235)

Variable	Category	Value
Age (Years)		44.40 ± 15.65 (Mean ± SD)
Duration of Symptoms (Months)		12.83 ± 7.11 (Mean ± SD)
Age Group	< 50 Years	142 (60.4%)
	≥ 50 Years	93 (39.6%)
Gender	Male	108 (46.0%)
	Female	127 (54.0%)
Socioeconomic Status	High	20 (8.5%)
	Middle	121 (51.5%)
	Low	94 (40.0%)

Table 2: Contingency Analysis and Diagnostic Performance of Color Doppler Ultrasonography Versus Histopathology (n=235)

2A. Contingency Table			
	Histopathology		Total
	Malignant	Benign	
CDUS Malignant	82	5	87
CDUS Benign	12	136	148
Total	94	141	235

2B. Diagnostic Performance Measures		
Diagnostic Parameter	Estimate(%)	95% Confidence Interval
Sensitivity	87.2	78.8-93.2
Specificity	96.5	91.9-98.8
Positive Predictive Value (PPV)	94.3	87.1-98.1
Negative Predictive Value (NPV)	91.9	86.3-95.7
Diagnostic Accuracy	92.8	88.7-95.7

Abbreviations: CDUS = Color Doppler Ultrasonography; PPV = Positive Predictive Value; NPV = Negative Predictive Value

Table 3: Stratified Analysis of CDUS Diagnostic Accuracy

Subgroup	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Age < 50 Years (n=142)	88.2%	96.7%	93.8 %	93.6 %	93.6%
Age ≥ 50 Years (n=93)	86.0%	96.0%	94.9 %	88.9 %	91.4%
Male (n=108)	84.4%	91.3%	95.0 %	75.0 %	86.7%
Female (n=127)	89.8%	96.1%	93.6 %	93.7 %	93.7%

DISCUSSION

Our study demonstrates an overall accuracy of 92.8%, with a sensitivity of 87.2% and significant specificity of 96.5%. The findings indicate that CDUS is a very reliable diagnostic tool. These results validate CDUS as a useful and consistent initial approach for evaluating cervical lymphadenopathy. One of the major findings of this study was the high specificity (96.5%) of CDUS; it is reasonably reliable in correctly identifying benign nodes, thereby reducing the number of false-positive results.[11] CDUS can efficiently triage patients by ruling out malignancy, reducing the number of invasive, expensive biopsy procedures. In addition to reducing procedural morbidity and patient anxiety, this maximizes the use of healthcare resources, which is crucial in any situation, particularly in those with limited resources.[12] This utility is further supported by the high positive predictive value (PPV) of 94.3%, indicating that when CDUS features point to malignancy, there is a very high likelihood of histopathological confirmation, giving clinicians the confidence to proceed with additional management or intervention. Our findings strongly align with the growing body of modern literature. A recent study by reported a sensitivity of 89% and a specificity of 94% for CDUS in the Evaluation of cervical lymphadenopathy, figures that are strikingly consistent with our findings.[13] The authors attributed this outstanding result to a methodical evaluation of vascular patterns, particularly the transition from hilar to peripheral vascularity, which was also an important diagnostic criterion in our study. In addition, a 2019 study by Zuzana Sedlackova et al. that examined the use of ultrasound in assessing head and neck lymph nodes synthesized data from multiple studies and confirmed the high specificity of sonographic features, such as Doppler-identified vascular patterns, in identifying cancerous nodes. The validity and consistency of CDUS's diagnostic performance across a range of populations and practice settings are further supported by the fact that our results fall comfortably within, and in some cases slightly surpass, the performance metrics reported in such thorough reviews.[14] The comparatively higher specificity observed in our study relative to previous reports may reflect differences in study populations, reference standards, ultrasound protocols, and case selection across studies rather than a true difference in diagnostic performance.[15] The high diagnostic value of specific sonographic features observed in our study, particularly vascular patterns, is supported by prior studies. A recent meta-analysis by Jisun Hwang et al. (2025), focusing on pediatric cervical lymphadenopathy, reported abnormal vascularity as one of the most specific ultrasound features for predicting malignancy, with a pooled specificity of 0.91 (95% CI: 0.82-0.97).[16] These findings are generally consistent with our observation of CDUS's high specificity and support the role of vascular assessment in cervical lymph node evaluation across different populations. Exploratory subgroup analyses demonstrated numerical variation in diagnostic performance across demographic categories. However, the present study was not designed or powered to establish subgroup effects, and no formal comparative statistical testing was undertaken. Therefore, these observations should be interpreted cautiously and should not be considered evidence of true biological or clinical differences. Future studies with predefined subgroup analyses are needed to evaluate potential variation in diagnostic performance further. Despite its demonstrated efficacy, it is important to acknowledge the inherent limitations of CDUS. Its operator-dependency remains a significant factor, as the acquisition and interpretation of images are strongly influenced by the radiologist's skill and experience.[18] Moreover, certain clinical conditions remain to pose diagnostic challenges. For instance, Tuberculous lymphadenitis often presents with necrotic or cystic changes that can be indistinguishable from necrotic metastatic lymph nodes on conventional CDUS.

CONCLUSIONS

Color Doppler ultrasonography demonstrated high diagnostic accuracy in differentiating benign from malignant cervical lymph nodes when compared with histopathology. It showed high sensitivity and specificity and may serve as a useful first-line imaging investigation in the assessment of cervical lymphadenopathy. However, CDUS remains operator-dependent, and certain inflammatory conditions, particularly tuberculous lymphadenitis, may exhibit overlapping sonographic appearances with malignant lymphadenopathy. Therefore, histopathological confirmation remains essential in equivocal or clinically suspicious cases.

LIMITATIONS

Although efforts were made to standardize ultrasound acquisition and interpretation, color Doppler

ultrasonography remains operator-dependent and may show variability across different clinical settings. While observer calibration and consensus review were incorporated to improve consistency of image interpretation, formal interobserver agreement statistics were not performed; therefore, reproducibility across observers could not be quantitatively assessed. Receiver operating characteristic (ROC) analysis was not performed, limiting detailed evaluation of discriminatory performance. Subgroup analyses by age and gender were descriptive, and formal inferential statistical testing or multivariable adjustment for potential confounders was not undertaken; therefore, these findings should be interpreted with caution. Finally, overlap in sonographic features between inflammatory conditions - particularly tuberculous lymphadenitis and necrotic reactive lymph nodes-and malignant lymphadenopathy remains a recognized diagnostic challenge.

CONFLICT OF INTEREST: None

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AUTHORS CONTRIBUTION

Jawad Ali - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Critical Revision; Final Approval*
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Faryal Bashir - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Final Approval*
Muhammad Waleed Khan - *Concept & Design; Data Analysis/Interpretation; Drafting Manuscript; Final Approval*
Kiran Zafar - *Concept & Design; Data Analysis/Interpretation; Drafting Manuscript; Final Approval*
The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.