Open Access

Original Article

Diagnostic Accuracy of Ultrasound to Differentiate Neoplastic and Non-Neoplastic Causes of Cervical Lymphadenopathy taking Histopathology as the Gold Standard

Aqeel Shafi, Shahla Zameer, Muhammad Nauman Malik, Rabia Liaqat, Bushra Liaqat*, Asiya Liaqat**

Department of Radiology, Pakistan Institute of Medical Sciences, Islamabad Pakistan, *Department of Radiology, Rawalpindi Medical University, Rawalpindi Pakistan, **Department of Radiology, University of Sciences and Technology (NUST), Rawalpindi Pakistan

ABSTRACT

Objective: To evaluate the efficacy of high-resolution ultrasound and colour Doppler in differentiating neoplastic and non-neoplastic causes of cervical lymphadenopathy compared to histopathological diagnosis.

Study Design: Cross-Sectional study.

Place and Duration of Study: Pakistan Institute of Medical Sciences, Islamabad Pakistan, from Jan to Jun 2019.

Methodology: The study included 110 patients with palpable cervical lymph nodes undergoing neck ultrasound and Fine needle aspiration cytology/Biopsy. Certain important sonological features were considered to categorize them into non-neoplastic and neoplastic groups. Colour Doppler imaging was employed along with grey-scale imaging. The histopathology results were compared with sonographic findings to determine the diagnostic accuracy of ultrasound in differentiating neoplastic from non-neoplastic causes of enlarged cervical lymph nodes.

Results: Our study revealed that High-resolution sonography has 94.4% sensitivity and 88.8% specificity, differentiating between neoplastic and non-neoplastic causes of cervical lymphadenopathy. At the same time, the overall accuracy of ultrasound is 90.9%. The most consistent grey-scale feature in the non-neoplastic nodal group was preserved central fatty hilum, while its loss was significantly associated with neoplastic etiologies.

Conclusion: Due to high sensitivity and negative predictive value, high-resolution sonography can be deployed as a first-line investigating tool for enlarged lymph nodes, and invasive procedures like Fine needle aspiration cytology (FNAC) can be abandoned in non-neoplastic lymphadenopathies.

Keywords: Colour doppler**,** Lymph node, Neoplastic, Non-neoplastic, Ultrasound.

How to Cite This Article: *Shafi A, Zameer S, Malik MN, Liaqat R, Liaqat B, Liaqat A. Diagnostic Accuracy of Ultrasound to Differentiate Neoplastic and Non-Neoplastic causes of Cervical Lymphadenopathy taking Histopathology as the Gold Standard. Pak Armed Forces Med J 2023; 73(4): 1024-1027. DOI: https://doi.org/10.51253/pafmj.v73i4.6234*

INTRODUCTION

Cervical lymph node enlargement is a frequently presenting symptom or clinical sign in a diverse group of diseases.[1] Hence, evaluation of these lymph nodes in order to differentiate non-neoplastic from neoplastic causes of cervical lymphadenopathy is paramount in deciding further management. Several causes of cervical lymphadenopathy are recognized, including tuberculosis, reactive, metastatic and lymphomatous.[2,3] Ultrasonography supersedes CT and MRI in assessing cervical lymphadenopathy because of its availability, cost-effectiveness, lack of hazardous radiation and non invasiveness.[4] Since cervical nodes are superficially located, they are accessible for ultrasound, FNAC, or biopsy. In the case of reasonably precise diagnosis on high-resolution sonography, many invas-ive fine needle aspiration cytology can be avoided.[5,6] The colour Doppler to grey scale has further added to ultrasonography's diagnostic accuracy in assessing enlarged cervical lymph nodes.[7] According to a recent study, ultrasound B mode is considered 96.8% sensitive in differentiating non-malignant from malignant causes of cervical lymphadenopathy.[8]

The sonographic criteria in order to distinguish non-neoplastic causes from neoplastic ones takes into account several grey scales and Doppler features. Apart from colour Doppler analysis, spectral Doppler assessment has been considered regarding the resistive index and pulsatility index.[9] However, much variation in cut-off values of RI and PI has been observed, so its role in clinical practice remains limited.[4,7,10] The current study considers the grey scale and colour Doppler features of ultrasound in differentiating non-neoplastic from neoplastic causes of cervical lymphadenopathy and its utility in deciding the need for cytology or histopathology.

METHODOLOGY

The cross-sectional study was carried out at the Radiology Department of Pakistan Institute of Medical Sciences, Islamabad Pakistan, from January 2019 to June 2019. The sample size was calculated by comparing ultrasound sensitivity (88%) with FNAC (99%).[2]

Correspondence: Dr Aqeel Shafi, House No 20, Street No 13, Sector G-13/3, Islamabad, Pakistan

Received: 31 Jan 2021; revision received: 08 Mar 2021; accepted: 31 Mar 2021

Inclusion Criteria: Patients aged above 13 years and of both genders with clinically palpable cervical lymph nodes and undergoing ultrasound and FNAC /biopsy were included.

Exclusion Criteria: The study excluded the paediatric age group, those patients who were not willing to undergo FNAC or biopsy, and those already diagnosed through earlier biopsy.

Two senior radiology residents performed neck ultrasonography on all patients fulfilling the inclusion criteria. The Ultrasound examination was performed using Toshiba Xario 500 high-frequency linear probe (7.5MHz) with the patient lying supine and the neck in the extended position by placing a pillow below the shoulder. After adequate gel application, various cervical nodal groups were examined. The following important criteria were taken into account during the sonography of cervical lymph nodes: Number, site, Size, long/short axis ratio, echogenic hilum (present or absent), borders (sharp or un-sharp), echotexture (hypoechoic, mixed or hyperechoic), intranodal necrosis (present or absent), matted or discrete, the vascular pattern on colour Doppler. Considering these features, two broad categories of cervical lymph nodes were made: Neoplastic and Non-neoplastic. The neoplastic versus non-neoplastic sonological features are summarized in the Table–I. Colour Doppler imaging was employed to look for intranodal vascularity, spectral Doppler tracings were acquired and resistive index within the node was measured utilizing the formula: RI=peak systolic velocity–end-diastolic velocity/peak systolic velocity. The ultrasonography was proceeded by ultrasound guided biopsy of the most accessible and suspicious node. The histopathology results were obtained and compared with the sonographic findings to determine the diagnostic accuracy of US in differentiating neoplastic from non-neoplastic causes of enlarged cervical lymph nodes.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quanti

tative variables were expressed as Mean±SD and quali-tative variables were expressed as frequency and percen-tages. Diagnostic parameters were calculated using a 2x2 table. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were determined by using the standard formulae.

RESULTS

The study included 110 untreated, previously un-diagnosed patients of clinically palpable cervical lymph nodes, amongst which 64(58.2%) were males and 46(41.8%) were female. The histopathological reports of all included patients were analyzed, and approxi-mately 2/3 were diagnosed as non-neoplastic. Out of 110 cases, 72(65.5%) were sonological labelled as non-neoplastic and amongst them, 68(61.8%) were non-neoplastic on histopathology as well (Table-I). Sim-ilarly, out of 38(34.5%) sonological labelled cases of neoplastic aetiology, 32(29%) were true positive, while 6(5.5%) had no neoplastic aetiology histopathologically (false positive). The false positive non-neoplastic cases, which were 4 in the count, had histopathological features of lymphoma in 3 of them, and one was diag-nosed as metastasis from Squamous cell carcinoma of the tongue. A comparison between sonological and histopathological findings was made, and ultrasound came out to have a sensitivity and specificity of 94.4% and 88.8%, respectively, in differentiating neoplastic from non-neoplastic causes. The overall diagnostic acc-uracy came out to be 90.9%. The PPV and NPV were 94% and 84%, respectively (Table-II). The various sonological features in the neoplastic and non-neoplastic groups are summarised in Table-III.

Table-I: Sonological features of Neoplastic and Non-Neoplastic Lymph Nodes (n=110)

Ultrasound Features	
Non-Neoplastic	**Neoplastic**
Size	
Small	Comparatively large
Long to Short Axis Ratio (shape)	
Long axis>short axis (oval) <0.5	Long axis ≈ short axis (round) >0.5
Central Fatty Hilum	
Preserved	Absent
Echotexture	
Hypoechoic	Predominantly Heterogenous (Variably hyperechoic or hypoechoic)
Necrosis	
+/- More in tuberculosis	More common
Calcification	
+/-	+/-
Vascularity Pattern	
Central	Peripheral
Resistive Index on Doppler	
High RI	Low RI
Matting/Conglomeration	
+/Tuberculosis	-

Table-II Comparison between Sonological and Pathological Diagnosis of enlarged Cervical Lymph Nodes (n=110)

US Diagnosis	Pathologically Non-Neoplastic	Pathologically Neoplastic
Non- neoplastic	68(61.8%)	4(3.6%)
Neoplastic	6(5.5%)	32(29%)

*Sensitivity= TP/(TP+FN)= 68/(68+6)*100=94.4%*
*Specificity= TN/(TN+FP)= 32/(32+4)*100=88.8%*
*Positive Predictive Value= TP/(TP+FP)*100= 68/(68+4)= 94%*
*Negative Predictive Value= TN/(TN+FN)*100=32/32+6)= 84%*
*Diagnostic Accuracy=(TP+TN)/All patients*100 = (76+5)/84=90.9%*

Table-III: Ultrasonographic features of enlarged Cervical Lymph Nodes (n=110)

Ultrasound Diagnosis	Non-neoplastic	Neoplastic
Echotexture		
Hypo	49	10
Hyper	1	8
Mixed	22	20
Shape		
Oval	66	8
Round	6	32
Central fatty hilum		
+	60	2
-	12	36
Necrosis		
+	14	28
-	58	10
Calcification		
+	24	16
-	48	22
Conglomeration		
+	23	4
-	49	34
Vascularity		
Central	56	0
Mixed	45	4
Peripheral	1	34

The most consistent grey scale feature favouring non-neoplastic aetiology was the preservation of central echogenic fatty hilum. The mean width of neoplastic nodes was 18±2.4 mm, while non-neoplastic was 15±1.6 mm. The spectral analysis with its Resistive index remained another important aspect of Doppler assessment, with non-neoplastic nodes showing an RI ranging from 0.54-0.76 with a mean value of 0.65±0.58. The RI values from the vessels of non-neoplastic nodes ranged from .61-0.93 with the mean value of .87± 0.74.

Of the 68 non-neoplastic, true-positive cases, 42 (61.8%) were reactive, and 26(38.2%) proved to be tuberculous. The true positive neoplastic group of 32 cases turned out to be Lymphoma in 14(43.8%) cases and metastases in 18(46.2%), which were predominantly the metastatic deposits from squamous cell carcinomas of the head and neck region, followed by a few cases of adenocarcinoma.

DISCUSSION

Ultrasound evaluation is paramount in assessing clinically palpable cervical lymph nodes.[11] Individual B mode parameters cannot effectively differentiate neoplastic causes from non-neoplastic ones. Rather the combined utility of the grey scale and Doppler features adds to the diagnostic information.[12] Worldwide literature compliments the cardinal role of Doppler assessment of cervical nodal vascularity in reliably eliminating the need for FNAC/Biopsy.[13]

One study concluded that high-resolution ultrasound has a specificity of 94.8% and diagnostic accuracy of 92.8%.[14] Another study concluded that B mode alone has a sensitivity of 88% and specificity of 97.3% in making correct differentiation between neoplastic and non-neoplastic cervical nodes.[15] The diagnostic accuracy and specificity of ultrasound in our study were comparably high, measuring 90.9% and 88.8%, respectively. Moreover, a previous study concluded that a central vascular pattern is highly specific for non-neoplastic aetiology, while the peripheral pattern is significantly associated with neoplastic disease. Our study showed similar results, with 55/68(82.3%) confirmed non-neoplastic lymph nodes showing central vascularity. However, the rest of the confirmed non-neoplastic cases had a mixed vascular pattern in them. B mode underdiagnosed three lymphoma cases and one metastasis from tongue SCC, largely due to mixed vascularity with few borderline grey scale features. Likewise, 6 cases were sonologically misdiagnosed as neoplastic, which later on were confirmed to have tuberculous aetiology in most of them with the combination of mixed vascularity and the presence of loss of fatty hilum and intranodal necrosis.[16] The reactive nodal group constitutes the major component of non-neoplastic nodes, followed by tuberculosis in certain developing countries.[17] While the neoplastic nodes in the cervical chain mostly have metastatic origin followed by lymphoma.[18]

In a recent analysis conducted by Rohan *et al.* in 2020, the most sensitive feature favouring neoplastic causation was the loss of central echogenic hilum, while the most specific feature was a high S/L ratio (round shape).[14] In our study, the most consistent feature observed among 99% of the histopathological proven neoplastic nodes was the loss of fatty hilum. Moreover, this study highlighted peripheral vascularity to be significantly associated with neoplastic

disease with a *p*-value of <0.001. In our study, peripheral vascularity was characteristically appreciated in all confirmed cases of neoplastic aetiology (other than lymphoma). In contrast, lymphoma had a mixed vascularity pattern, leading to a few misdiagnoses. Mahyar Gahfoori *et al*. highlighted the role of spectral Doppler in differentiating neoplastic from non-neoplastic with an RI value of 0.75 in non-neoplastic group.[7] Our study showed a similar result with an RI of 0.65 (mean value) in the non-neoplastic group and 0.87 in neoplastic nodes.

CONCLUSION

Due to high sensitivity and negative predictive value, high-resolution sonography can be deployed as a first-line investigating tool for enlarged lymph nodes, and invasive procedures like FNAC can be abandoned in cases of non-neoplastic lymphadenopathies. However, neoplastic diagnosis on high-resolution sonography will still merit further confirmation by Fine needle aspiration cytology.

Conflict of Interest: None.

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

AS & SZ: Conception, study design, drafting the manuscript, approval of the final version to be published.

MNM & RL: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

BL & AL: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Vandana M, Dambar S, Amit J. Role of ultrasonography in evaluation of cervical lymphadenopathy. Med Phoenix 2019;4(1): 59-63. https://doi.org/10.3126/medphoenix.v4i1.25761
2. Pattanayak S, Chatterjee S, Ravikumar R, Nijhawan VS, Sharma V, Debnath J, et al. Ultrasound evaluation of cervical lymphadenopathy: Can it reduce the need of histopathology/cytopathology? Med J Armed Forces India 2018; 74(3): 227-234. https://doi.org/10.1016/j.mjafi.2017.04.005
3. Kumar S, Pande S, Shrivastava G. Ultrasonographic evaluation of cervical lymphadenopathy with cytological correlation. Int J Sci Stud 2017; 4(11): 180-185. https://doi: 10.17354/ijss/2017/74
4. Ahuja AT, Ying M, Ho SY. Ultrasound of malignant cervical lymph nodes. Cancer Imaging 2008; 8(1): 48–56. https://doi.org/10.1102%2F1470-7330.2008.0006
5. Misra D, Panjwani S, Rai S. Diagnostic efficacy of color Doppler ultrasound in evaluation of cervical lymphadenopathy. Dent Res J (Isfahan) 2016; 13(3): 217-224. https://doi.org/10.4103/1735-3327.182180
6. Ghafoori M, Azizian A, Pourrajabi Z, Vaseghi H. Sonographic evaluation of cervical lymphadenopathy; Comparison of metastatic and reactive lymph nodes in patients with head and neck squamous cell carcinoma using gray scale and doppler techniques. Iran J Radiol 2015; 12(3): e11044. https://doi.org/10.5812%2Firanjradiol.11044
7. Vinyaka US, Shivalli S, Rai S, Haris A, Madhurkar R, Hemraj S, et al. Diagnostic accuracy of high resolution ultrasound to differentiate neoplastic and non neoplastic causes of cervical lymphadenopathy. J Clin Diagn Res 2014;8(9): RC05–RC07. https://doi.org/10.7860%2FJCDR%2F2014%2F10431.4913
8. Sathyanarayan V, Bharani SK. Enlarged lymph nodes in head and neck cancer: Analysis with triplex ultrasonography. Ann Maxillofac Surg 2013; 3(1): 35-39. https://doi.org/10.4103/2231-0746.110077
9. Naik RM, Pai A, Guruprasad Y, Singh R. Efficacy of colour doppler ultrasound in diagnosis of cervical lymphadenopathy. J Maxillofac Oral Surg 2013; 12(2): 123-129. https://doi.org/10.1007/s12663-012-0395-1
10. Chan JM, Shin LK, Jeffrey RB. Ultrasonography of abnormal neck lymph nodes. Ultrasound Q. 2007; 23(1): 47-54. https://doi.org/10.1097/01.ruq.0000263839.84937.45
11. Sattar A, Shamim SH, Wahab S, Javed A. Yield and safety profile of ultrasound guided fine needle aspiration cytology (FNAC) of lymph nodes. J Coll Physicians Surg Pak 2016; 26(5): 357-360.
12. Gupta A, Rahman K, Shahid M, Kumar A, Qaseem SM, Hassan SA, et al. Sonographic assessment of cervical lymphadenopathy: role of high-resolution and color Doppler imaging. Head Neck 2011; 33(3): 297-302. https://doi.org/10.1002/hed.21448
13. Rohan K, Ramesh A, Sureshkumar S, Vijayakumar C, Abdulbasith KM, Krishnaraj B, et al. Evaluation of b-mode and color doppler ultrasound in the diagnosis of malignant cervical lymphadenopathy. Cureus 2020; 12(8): e9819.
14. Chammas MC, Macedo TA, Lo VW, Gomes AC, Juliano A, Cerri GG. Predicting malignant neck lymphadenopathy using color duplex sonography based on multivariate analysis. J Clin Ultrasound 2016; 44(9): 587-594. https://doi.org/10.1002/ jcu.22380
15. Dongade SP, Meti M, Ramesh DN. Cervical lymphnode metastasis in oral squamous cell carcinoma: Correlation of manual palpation, ultrasonographic, and histopathological findings. J Indian Acad Oral Med Radiol 2017;29 (3) :170-173
16. Özel D, Özel BD. Evaluation of diagnostic value of conventional and color Doppler ultrasound with elastography strain ratios in differentiation between benign and malignant lymph nodes. Pol J Radiol 2018; 83(4): e32-e36. https://doi.org/10.51 2018. 73293
17. Toriyabe Y, Nishimura T, Kita S, Saito Y, Miyokawa N. Differentiation between benign and metastatic cervical lymph nodes with ultrasound. Clin Radiol 1997; 52(12): 927-932. https://doi.org/10.1016/s0009-9260(97)80226-7
18. Mikami Y, Kamata S, Kawabata K, Nigauri T, Hoki K, Mitani H, et al. Ultrasonographic evaluation of metastatic cervical lymph nodes in head and neck cancers. Nihon Jibiinkoka Gakkai Kaiho 2000; 103(7): 812-820. https: doi: 10.3950/jibiinkoka.103.812