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The Efficacy of Colour Doppler Ultrasound in Differentiating Malignant and Nonmalignant Head and Neck Lymph Node Enlargement

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Abstract Cervical lymphadenopathy is a common presenting symptom for a variety of disorders. Differentiation of malignant and non- malignant lymphadenopathy has important clinical and therapeutic implications. The purpose of our study was to assess the efficacy of colour Doppler ultrasound (CDUS) in differentiating malignant and non-malignant cervical lymphadenopathy. 30 patients with clinical evidence of Head and Neck lymph node enlargement 15 patients with clinically suspected malignant/metastatic head and neck lymph node enlargement and 15 patients with clinically suspected reactive/non-malignant head and neck lymph node enlargement] were evaluated with ultrasound and the largest or most prominent node was subjected to CDUS examination. CDUS was performed for 30 out of 126 head and neck lymph nodes. Histopathological/Cytological confirmations were obtained by fine needle aspiration cytology or excisional biopsy. To assess the efficacy of CDUS, a comparison between clinical features, CDUS features and cytological/histological features of the lymph nodes was done. The results thus obtained were statistically analyzed. Clinical examination identified 99 lymph nodes in 30 patients. Ultrasonogram additionally detected 27 lymph nodes. The statistically significant 'p' value ($p < 0.01$) was obtained for sonographic features like S/L ratio > 0.5, loss of echogenic hilum, sharp border and hypoechogenicity. Correlation of vascular pattern of CDUS with pathological diagnosis showed that peripheral and mixed flow pattern for malignant nodes were highly significant with 'p' value of 0.000 ($p < 0.01$). The sensitivity and specificity was 93% and 93%, respectively. The hilar vascular pattern if taken as a criteria for identification of non-malignant nodes then the specificity was 100% and the sensitivity was 46.6%. Thus nodal vascular pattern can be used to differentiate malignant and nonmalignant lymph node enlargement. The presence of avascular flow pattern needs further evaluation. CDUS examination along with clinical examination and grey scale sonography can obviate the need for biopsy/FNAC of lymph nodes.

Keywords: *head and neck lymph node enlargement, colour doppler ultrasound, histopathology, cytology, vascular pattern*

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1. Introduction

Cervical lymphadenopathy is a common presenting symptom and sign for a variety of diseases, ranging from subtle infections to life threatening Head & Neck malignancies [1]. It is well accepted that clinical examination alone cannot be considered as a diagnostic tool to justify the involvement of cervical lymph nodes especially deep or small nodes. Many pathologic processes involve lymph nodes so that detection of lymph node involvement has great therapeutic and prognostic implications. It is in this context that imaging modalities such as Computed Tomography (CT) scan, Magnetic Resonance Imaging (MRI) and Ultrasonogram play a major role in detecting clinically undetectable lymph nodes. Though MRI and CT scan are very useful in detection of cervical lymph node pathology, ultrasound, particularly by using high resolution probes (7.5 to 15 MHz) has always been considered as a powerful tool for assessment of head and neck lymph node enlargement [3]. Although CT scan and MRI are valuable diagnosis aids, both are expensive and not universally available. Moreover CT scan exposes the patient to relatively large doses of radiation, and MRI is expensive, time-consuming and not suitable for every patient.

Ultrasound is a useful imaging modality in assessment of soft tissue lesions. Ultrasonography is an easy, reproducible, non-invasive, no risk procedure, radiation free imaging modality to examine the lymph nodes. Sonography is a known modality for staging head and neck tumors and its sensitivity is greater than clinical examination and even

CT scan. The addition of Doppler sonography to the well-established practice of grey-scale sonography increases the amount of information obtained by sonography, with significant increase in sensitivity and specificity.

Ultrasonography can not only locate LNs, but it also characterizes them by assessing their number, shape, dimension, margins and internal structure [2]. By displaying their vascularity and internal structure, Doppler sonography is more accurate than CT scan, MRI and clinical examination for lymph node characterization.

Cervical nodal involvement in head and neck malignancies influences therapeutic decision. The use of ultrasound has proven effective in detecting nodes and in analysing some morphologic features that are frequently associated with malignancy, such as roundness, absence of echogenic hilum, loss of architecture, extra capsular spread and presence of central tubular structures representing small arteries encased in neoplastic tissue [2]. Moreover, CDUS analysis of vascular pattern and other parameters can add considerable information compared to routine grey scale sonographic features which helps in accurate diagnosis. Though histopathology is the gold standard for diagnosis of metastatic lymphnodes it is invasive, carries risk of dissemination of malignant cells and has its own complications like hemorrhage, injury to vessels, patient discomfort and in some cases requirement of general anaesthesia. Thus, the need for FNAC/biopsy can be obviated by combining clinical, ultrasonographic and CDUS examination of lymph nodes. The judicious use of CDUS examination of nodal vascularity provides an opportunity to evaluate the need for FNAC/biopsy in reactive nodes. Though many studies have evaluated the vascular pattern of malignant nodes only very few have evaluated the efficacy of CDUS in differentiating malignant and nonmalignant lymph nodes. Hence this study has been conducted to assess the efficacy of CDUS in differentiating malignant and non-malignant head and neck lymphadenopathy.

2. Aim and Objectives

To assess the efficacy of colour doppler ultrasound in differentiating malignant and non-malignant head and neck lymph node enlargement. Objectives of the study are:

• To evaluate head and neck lymph node enlargement through ultrasonography.

• To identify the ultrasonographic and colour doppler features in head and neck lymph node enlargement.

• To correlate the Clinical, Colour doppler ultrasound and FNAC/Biopsy findings of the head and neck lymph node enlargement.

• To assess the difference between malignant and nonmalignant lymphnode enlargement using ultrasound and colour doppler ultrasound.

• To substantiate the use of colour doppler ultrasound in diagnosis of head and neck lymph node enlargement.

3. Materials and Methods

This is a prospective study performed during the year 2008-09. This study was conducted in the Department of Oral Medicine and Maxillofacial Radiology and Oral Pathology, Rajah Muthiah Dental College & Hospital, Radiology Department, Rajah Muthiah Medical College & Hospital, Annamalai Nagar.

3.1. Patient Selection Criteria

The patients were categorized based on clinical diagnosis. The study group consisted of 30 patients of both sex and different age groups:

- Non malignant group (15 patients).
- Head & neck malignancy group (15 patients).

3.1.1. Inclusion Criteria

All untreated subjects with clinically enlarged one or more head and neck lymph nodes were included in the study.

3.1.2. Exclusion Criteria

Patients already on treatment were excluded.

3.1.3. Procedure

All selected participants were explained the need and design of the study. A written, well-informed & duly signed consent was obtained from each patient. After a detailed history, Clinical examination of submental lymph nodes, submandibular lymph nodes and cervical lymph nodes was performed. Detailed intraoral, extraoral and relevant systemic examination was done. Examination of drainage areas was done. The clinical findings were noted on the specially designed proforma. Morphological aspects like shape, consistency, mobility etc. were noted Ultrasonography and CDUS examination of the cervical lymph nodes was performed with a high resolution, real time multiplanar diagnostic ultrasound system, manufactured by PHILIPS Systems, India. A linear, high frequency 3-12 MHZ transducer, having a scan head of 30 mm was used for performing the ultrasound. The patients were positioned with the neck extended; a pillow was placed behind their shoulders and the lower neck to allow them to adopt a comfortable position. The distribution of lymph nodes was studied and classified into eight levels namely submental, submandibular, parotid, upper cervical, middle cervical lower cervical, posterior triangular, supraclavicular lymph nodes. Characteristics of lymph nodes including Size, Shape, Location, Number, S/L ratio, Border, Visibility of hilum, Echogenicity, Necrosis, Matting, Calcification were noted. The largest and most prominent node in each patient was subjected to color doppler examination of vascular pattern and classified into four categories [4]:

- Hilar - Flow signal branching radially from the center.
- Capsular - Flow signal along the periphery of the lymph nodes with branches perforating the periphery of the node and not arising from the hilar vessels.
- Hilar and Capsular (Mixed) - Presence of central and peripheral signals.
- Avascular - Absence of vascular signals within the lymph nodes.

After the Ultrasound evaluation, all the patients underwent FNAC or Excision biopsy of the lymph node. The specimens were submitted for pathological examination and a definitive diagnosis was made. The lymph nodes were then classified into malignant or non malignant lymph nodes based on the histopathology report.

The results of color doppler Ultrasound were correlated with clinical and histological or cytological findings and were statistically analyzed by statistical package for social sciences (SPSS). 'p' value is obtained by Pearson Chi-Square Test and statistical significance was calculated. Descriptive data regarding the Clinical, Ultrasonographic, Colour Doppler Ultrasonographic and Histopathological features are presented as percentages. Diagnostic validity tests (Sensitivity and Specificity) were performed to know the diagnostic value of Colour Doppler Ultrasonography comparing with histological diagnosis.

4. Results

Total sample size for the study was 30. The patients were categorized based on clinical diagnosis. The Malignant group and Non malignant group comprised of 15 subjects each. The age ranged from 19 to 65 yrs.

• Malignant group of patients were in the age group of 35 to 65 yrs with mean age 52.53 yrs.

• Non malignant patients were in the age group of 19 to 50 yrs with mean age of 33.66 yrs. The obvious difference is due to high incidence of malignancy in the older age (Table 1).

Table 1. MEAN AGE DISTRIBUTION OF THE STUDY

Study Group	N	Mean	Std. Deviation	Minimum	Maximum
Non Malignant Patients	15	33.66	8.91	19	50
Malignant Patients	15	52.53	8.83	35	65
Total	30	43.09	8.99	19	65

In nonmalignant group majority of the patients (11) had nonspecific infection of upper aerodigestive tract and four patients had tuberculosis. The analysis of spectrum of diseases show that the majority of patients in malignant group had Squamous Cell Carcinoma of upper aerodigestive tract (13), one patient had Carcinoma of parotid and in one patient the primary could not be identified (Table 2 & Table 3).

Table 2. SPECTRUM OF DISEASES IN NON MALIGNANT

Diseases	Number of patients
Specific infection - Tuberculosis	4
Non Specific infection	11
Total	15

Table 3. SPECTRUM OF DISEASES IN MALIGNANT GROUP

Diseases	Number of patients
Head and neck malignancy	14
Unknown primary	1
Total	15

Totally 99 lymph nodes were detected by clinical examination, 53 nodes in the nonmalignant group and 46 nodes in the malignant group. Ultrasonogram detected an additional 27 nodes (total 126 nodes). Of these 68 were non-malignant and 58 were proven malignant by histological /cytological examination (Table 4& Table 5).

Table 4. TOTAL NUMBER OF LYMPH NODES DETECTED BY ULTRASOUND AND CLINICAL EXAMINATION

Study group	Clinical Examination	Percentage	USG Examination	Percentage
Non malignant	53	77.95%	68	100%
Malignant	46	79.31%	58	100%
Total	99		126	

Table 5. CLINICAL DETECTION OF NUMBER OF LYMPH NODES IN THE STUDY GROUPS

Clinical detection of lymphnodes	Non- malignant Patients	Malignant Patients
Palpable	53	46
	77.95%	79.31%
Non Palpable	15	12
	22.05%	20.69%
Total = 126	68	58
	53.97%	46.03%

Region wise distribution of lymph nodes showed that in the nonmalignant group by ultrasonographic examination, 2 (2.9%) nodes were in the Submental group, 19 (27.94%) nodes in submandibular region, 2 (2.9%) nodes in parotid region, 19 (27.94%) nodes in upper cervical, 7 (10.29%) nodes in mid cervical, 3 (4.41%) nodes in lower cervical, 3 (4.41%) nodes in supraclavicular, 13 (19.11%) nodes in posterior triangle (Table 6).

Table 6. LOCATION OF LYMPH NODES BASED ON CLINICAL &ULTRASONOGRAPHIC EXAMINATION IN NON MALIGNANT GROUP

Location number	Location of Lymph nodes	Number of regions of lymph nodes detected by	
		Clinical Examination	Ultrasonographic Examination
1	Sub Mental	2	2
2	Sub Mandibular	15	19
3	Parotid	1	2
4	Upper Cervical	16	19
5	Middle Cervical	5	7
6	Lower Cervical	2	3
7	Supra Clavicular	2	3
8	Posterior triangular	10	13
Total		**53**	**68**

Region wise distribution of lymph nodes showed that in the Malignant group, by ultrasonographic examination, 2 (3.45%) nodes were located in the Submental region, 15 (25.86%) nodes in submandibular region, 2 (3.45%) nodes in the parotid region, 14 (24.14%) nodes in the upper cervical, 5 (8.62%) nodes in the middle cervical, 5 (8.62%) nodes in the lower cervical region, 4 (6.4%) nodes in the supraclavicular region, 11 (18.96%) nodes in the posterior triangle (Table 7).

Table 7. LOCATION OF LYMPH NODES BASED ON CLINICAL &ULTRASONOGRAPHIC EXAMINATION IN MALIGNANT GROUP

Location number	Location of Lymph nodes	Number of regions of lymph nodes detected by	
		Clinical Examination	Ultrasonographic Examination
1	Sub Mental	1	2
2	Sub Mandibular	12	15
3	Parotid	0	2
4	Upper Cervical	12	14
5	Middle Cervical	4	5
6	Lower Cervical	4	5
7	Supra Clavicular	3	4
8	Posterior triangular	10	11
Total		**46**	**58**

Assessment of Size of lymph nodes showed that the average long axial diameter of lymph nodes in the Nonmalignant group was 16.31mm (ranged from 10 mm to 28 mm), with standard deviation of 4.02mm. In the Malignant group longest axial diameter was 20.83mm (ranged from 12 mm to 30 mm), with standard deviation of 4.62mm (Table 8).

Table 8. DESCRIPTION OF LYMPH NODES BASED ON SIZE (LONG AXIS DIAMETER) IN THE STUDY GROUPS

Size	Average	Maximum size	Minimum size	Standard deviation
Non malignant	16.31mm	28mm	10mm	4.02mm
Malignant	20.83mm	30mm	12 mm	4.62mm

Assessment of shape of lymph nodes showed that majority of Malignant nodes 42 (72.41%) were round while 16 (27.59%) were oval in shape. In the Nonmalignant group, only 11 (16.28%) were round in shape while 57 (83.82%) were oval in shape (Table 9). 'p' value was 0.0000 ($p<0.01$) which is statistically significant.

Table 9. DESCRIPTION OF LYMPH NODES BASED ON SHAPE IN THE STUDY GROUPS

Shape	Non Malignant Patients	Malignant Patients	Total
Oval	57	16	73
	83.82%	27.59%	57.94%
Round	11	42	53
	16.28%	72.41%	42.06%
Total	68	58	126
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		**0.0000 (p<0.01)**	

Assessment of lymph nodes based on S/L ratio in the nonmalignant group showed an average of 0.479 (range 0.285 to 0.667) with a standard deviation of 0.129 and in the malignant group the average was 0.761 (range 0.429 to 0.923) with a standard deviation of 0.103. The 'p' value was 0.000 ($p < 0.01$), which proves that it is statistical significant, as the S/L ratio more than 0.5 is indicative of malignancy (Table 10).

Table 10. COMPARISON OF LYMPH NODES BASED ON S/L RATIO IN THE STUDY GROUPS

Study Group	N	Mean	Std. Deviation	Min	Max	'p' value	'F' value
Non Malignant Patients	15	0.479	0.129	0.285	0.667	0.000 (P<0.01)	2.32
Malignant Patients	15	0.761	0.103	0.429	0.923		

Assessment of border in the study groups showed that 46 (79.31%) of malignant nodes had sharp border while 12 (20.69%) had unsharp borders. In the nonmalignant group 30 (44.12%) had sharp border while 38 (55.88%) of nodes had unsharp border. The 'p' value was 0.0000 ($p<0.01$) which proves that it is statistical significant (sensitivity 79% and specificity 55%) (Table 11).

Table 11. DESCRIPTION OF LYMPH NODES BASED ON BORDER SHARPNESS IN THE STUDY GROUPS

Border sharpness	Non Malignant Patients	Malignant Patients	Total
Unsharp	38	12	50
	55.88%	20.69%%	39.68%
Sharp	30	46	76
	44.12%	79.31%	60.32%
Total	68	58	126
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		**0.0001 (p<0.01)**	

Assessment of Hilum in malignant nodes showed that only 13 (22.41%) nodes had visible hilum while 45 (77.59%) had no visible hilum. In the Nonmalignant group hilum was present in 46 (67.64%) nodes and absent in 22 (32.36%) nodes. The 'p' value was 0.000 ($p < 0.01$), which proves that it is statistical significant (sensitivity 70% and specificity 67%) (Table 12).

Table 12. DESCRIPTION OF LYMPH NODES BASED ON HILUM IN THE STUDY GROUPS

Hilum	Non Malignant Patients	Malignant Patients	Total
Present	46	13	59
	67.64%	22.41%	46.83%
Absent	22	45	67
	32.36%	77.59%	53.17%
Total	68	58	126
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		**0.0000(p<0.01)**	

Assessment of Echogenicity of lymph nodes showed that 38 (65.52%) malignant nodes were hypoechoic while 20 (34.48%) had mixed echogenicity. In the nonmalignant group 60 (88.23%) were hypoechoic while 8 (11.77%) were hyperechoic. The 'p' value was 0.000 ($p < 0.01$), which proves that it is statistical significant (sensitivity 100% and specificity 11%), (Table 13).

Table 13. DESCRIPTION OF LYMPH NODES BASED ON ECHOGENICITY IN THE STUDY GROUPS

Echogenicity	Non Malignant Patients	Malignant Patients	Total
Hypoechoic	60	38	98
	88.23%	65.52%	77.78%
Hyperechoic	8	0	8
	11.77%	0%	6.35%
Mixed	0	20	20
	0%	34.48%	15.87%
Total	68	58	126
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		0.0000(p<0.01)	

Assessment of Necrosis of lymph nodes showed that 10 (17.24%) of malignant nodes and 4 (5.88%) nonmalignant nodes showed intranodal necrosis. The 'p' value was 0.0432 ($p < 0.05$), which proves that it is statistical significant (sensitivity 17% and specificity 94%) (Table 14).

Table 14. DESCRIPTION OF LYMPH NODES BASED ON NECROSIS IN THE STUDY GROUPS

Necrosis	Non Malignant Patients	Malignant Patients	Total
Present	4	10	14
	5.88%	17.24%	11.11%
Absent	64	48	112
	94.12%	82.76%	88.89%
Total	68	58	126
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		0.0432 (p<0.05)	

Assessment of Matting of lymph nodes showed that 1 (6.67%) malignant node showed matting and 3 (20%) nonmalignant patients had matting of nodes. The 'p' value was 0.2827 ($p > 0.01$), which proves that it is statistical not significant (Table 15).

Table 15. DESCRIPTION OF LYMPH NODES BASED ON MATTING IN THE STUDY GROUPS

Matting	Study group		Total
	Non Malignant Patients	Malignant Patients	
Present	3	1	4
	20%	6.67%	13.33%
Absent	12	14	26
	80%	93.33%	86.67%
Total	15	15	30
	100.0%	100.0%	100.0%
		p Value	
Pearson Chi-Square		0.2827 (p>0.01)	

Assessment of *Calcification* of lymph nodes showed that calcification was present in 4(6%) of Nonmalignant nodes and none of malignant nodes 0 (0%).

Assessment of Colour doppler ultrasonogram (CDUS) of lymph nodes showed that 9 (60%) malignant nodes showed capsular pattern, 5 (33.33%) showed mixed hilar and capsular pattern and 1 (6.66%) showed avascular pattern. None of the malignant lymph nodes had hilar pattern. In the nonmalignant group, 7 (46.66%) had hilar pattern, 1 (6.66%) had capsular pattern (tuberculous node with necrosis) and 7 (46.66%) had avascular pattern. The 'p' value was 0.000 ($p < 0.01$), which proves that it is statistical significant (sensitivity 93% and specificity 93%) (Table 16).

Table 16. DESCRIPTION OF VASCULAR PATTERN OF LYMPHNODES BY CDUS IN THE STUDY GROUP

Vascular pattern	Non Malignant	Malignant	Total
Hilar	7 (46.66%)	0	7
Capsular	1(6.67%)	9(60%)	10
Mixed	0	5(33.33%)	5
Avascular	7(46.66%)	1(6.66%)	8
Total	15	15	30
		p Value	
Pearson Chi-Square		0.000(p<0.01)	

5.Discussion

Metastasis to cervical lymph nodes is common in head & neck carcinomas. Regional metastasis is one of the most important prognostic factors that influences the treatment of choice in patients with head and neck carcinoma. The presence of metastatic nodes on one side of the neck reduces the 5-year survival rate by 50% & the presence of metastatic nodes on both sides of the neck reduces the survival rate to 25%. Therefore evaluation of cervical lymphadenopathy is important for the patients with head & neck carcinomas as it helps the assessment of prognosis & the selection of treatment method.

- Clinical examination is subjective and highly inaccurate in the assessment of cervical lymphadenopathy. This fact is supported by many studies [5] and was proven again in our study. While clinical examination detected only 99 nodes ie., 77.95% (53 Nonmalignant and 46 Malignant) an additional 27 nodes (15 nodes – 22.05% nonmalignant and 12 nodes - 29.69% malignant) were detected by ultrasonography. Thus clinical examination was false negative in 27 (21.42%). Hence it proves that clinically non palpable node - N0 neck can be diagnosed with ultrasonogram.
- Based on the region wise distribution of nodes, the majority of lymph nodes of malignant group were found in submandibular and upper cervical regions (50%, 19 lymph nodes). This could be explained by the fact that majority of patients in the malignant group had oral cavity malignancies which usually

metastasize to submandibular and upper cervical lymph nodes. In the nonmalignant group, majority of lymph nodes were in the submandibular and upper cervical regions (65.5%, 38 nodes). This is because majority of the nonmalignant group had nonspecific infection of the upper aerodigestive tract which drains mainly to submandibular and upper cervical nodes. However in the 4 Tuberculosis patients posterior cervical nodes were predominantly involved.

- Lymph nodes more than 10mm in the longest axial diameter are said to be enlarged. The upper limit in minimal axial diameter of normal node is 9mm for submandibular and upper cervical nodes and 8mm for other cervical nodes [18,19]. In our study mean long axis diameter was 16.31mm ± 4.02mm (range 10mm to 28 mm) for nonmalignant group and 20.83mm ± 4.62mm (range 12mm to 30mm) for malignant group. This is higher compared to older studies [13] in which mean long axis diameter was 14.9 ± 9.2mm for malignant nodes and to other studies [6] in which mean long axis diameter was 15.1 ± 6.6mm for malignant nodes and 12.5 ± 4.2mm for nonmalignant nodes. It is agreed that larger the node greater is the chance of lodging metastasis. However certain benign nodes (e.g., tuberculosis) tend to be large and smaller nodes can harbor metastasis6. So instead of actual size, S/L ratio is now widely being used.
- The mean S/L ratio for nonmalignant nodes was 0.479 ± 0.129 (range 0.285 to 0.667) and for malignant nodes it was 0.761± 0.103 (range 0.429 to 0.923). Reference [7] showed short to long axis ratio (S/L ratio) more than 0.5 had 81% specificity, 75% sensitivity, and 79% overall accuracy rate for detection of metastasis. In our study the p value was 0.0000 ($p < 0.01$), showed statistical significance. The Sensitivity was 94% and Specificity was 64%.
- Malignant nodes tend to be round due to rapid growth whereas nonmalignant nodes tend to be oval in shape [8,9,10,11]. This fact was clearly proven in our study. 42 (72.41%) of malignant nodes were round and 57 (83.82%) of nonmalignant nodes were oval in shape. p value was 0.000 ($p < 0.01$) it is statistically significant.
- Malignant nodes tend to have sharp borders whereas reactive and normal nodes show unsharp borders [12]. In our study, 79.31% (46 nodes) of malignant nodes had sharp borders and 20.69% (12 nodes) had unsharp borders. However only 55.88% (28 nodes) of non malignant nodes had unsharp border while 44.12 % (30 nodes) had sharp border. The 'p' value was 0.000 ($p < 0.01$) and with a sensitivity of 79% and specificity of 55%.
- Metastatic and lymphomatous nodes tend to have sharp borders [9,10,11] whereas reactive and normal nodes usually show unsharp borders. The sharp borders in malignant nodes are believed to be due to tumour infiltration and reduced fatty deposition within the lymph nodes which increase the acoustic impedance difference between the lymph node and the surrounding tissue. Unsharp borders are common in tuberculous nodes and these are due to the edema and inflammation of the surrounding soft tissue.
- An older study showed that 54% of lymph nodes with metastasis were poorly defined, 46% has well defined borders and more than 70% of benign nodes had unsharp border [13].
- In our study echogenic hilus was present in 67.64% (46 nodes) of non malignant nodes and 22.41% (13 nodes) of malignant group. Loss of echogenic hilus was noted in 77.59% (45 nodes) of malignant nodes. The p value was 0.000 ($p < 0.01$). The sensitivity was 70% and the specificity was 67%. This is comparable to an older study [13] which detected hyperechogenic hilum in only 19% of metastatic lymphnodes and to older studies which showed loss of echogenic hilus in 57-91% of malignant lymphnodes. In a study14 loss of hilar echogenicity was 100% specific and 29% sensitive for malignancy.
- In our study 88.23 % (60 nodes) of non malignant nodes and 65.52 % (38 nodes) of malignant nodes were uniformly hypoechoic. 34.48% (20 nodes) of malignant nodes had mixed echogenicity and none of the malignant nodes were hyperechoic. In non malignant group most of nodes 88.23 % (60) were hypoechoic, 11.77% (8) were hyperechoic. The p value was 0.000 ($p<0.01$). The Sensitivity was 100% and Specificity was 11%. In a study3 presence of internal echoes was highly specific for malignancy (93.8% specificity and 60.2 % sensitivity).
- In our study necrosis was found in 4 non malignant (all of which were tuberculosis nodes) and in 10 nodes in malignant group. The 'p' value was 0.0432 ($p < 0.05$). The Sensitivity was 17% and Specificity was 94%. Presence of intranodal necrosis is pathological. Cystic necrosis which appears as intranodal echolucent area can occur in metastatic nodes from squamous cell carcinoma, papillary carcinoma thyroid as well as tuberculosis. So necrosis alone cannot be used as a criterion for diagnosing malignancy.
- In our study 3 tuberculosis patients (20%) had matting while only one patient (6.67%) with malignancy had matting. The 'p' value was 0.2827 ($p > 0.05$), hence it was statistically insignificant. Soft tissue matting and edema is a common feature of tuberculosis but is less common in malignant lymph nodes.
- Several studies have evaluated the usefulness and efficacy of color doppler ultrasonography in the detection of malignant and non malignant lymphadenopathy [3,13,15,16]. Most of the studies agreed that peripheral vascular pattern is associated with malignancy with high specificity and varying sensitivity. This is because tumor cells secrete angiogenic factors. As the hilar vessels get obstructed due to tumor infiltration, revascularization arises from peripheral and adjacent vessels [17]. In our study p value was 0.000 ($p < 0.01$) so it is statistically significant. If peripheral vascularity alone is taken as a criterion for malignancy, sensitivity was 60% and specificity was 93.33% positive predictive value was 90%. This is comparable to a study which showed peripheral vascularity in malignancy had 68.2% Sensitivity and 97.40% specificity [13]. However in a study [16] sensitivity was higher 87.6% and specificity was similar 91.66%.

Figure 1. CDUS of submandibular node-hilar vascular pattern

- When hilar and capsular (mixed) and capsular vascularity were taken as criteria for malignancy specificity was 93.33% and sensitivity 93.33%. Mixed flow of metastatic node might be explained by 2 pathogeneses [16,17,18,19,20]. First as the tumor nests replace the node, preexisting nodal vessels proliferate into aberrant feeding vessels by tumor angiogenesis resulting in central vascularity. Second, advanced tumor infiltration destroys hilar blood supply, induction of vascular supply from peripheral vessels and perinodal connective tissue occurs resulting in combined central and peripheral vascularity.

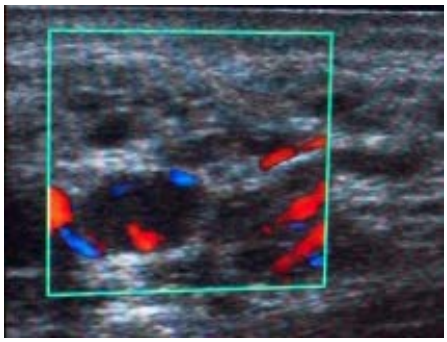

Figure 2. CDUS of left submandibular node-peripheral vascular pattern

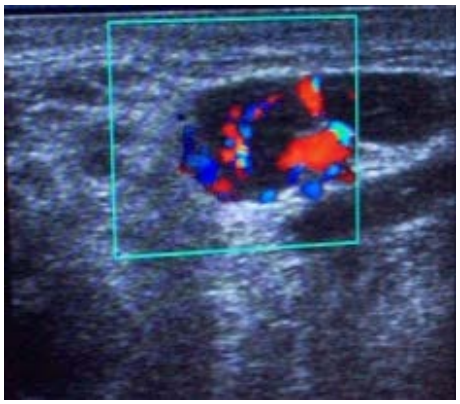

Figure 3. CDUS of left submandibular node-mixed vascular pattern

- In our study one malignant node showed avascular pattern. Many studies suggest that absence of perfusion is an important CDUS feature of malignancy because of total replacement of whole node by necrosed keratinized tumor tissue [20,21,22]. But in our study 46.6% non-malignant nodes also showed avascular pattern. So the presence of avascular pattern in CDUS is not specific for malignancy and needs further evaluation.

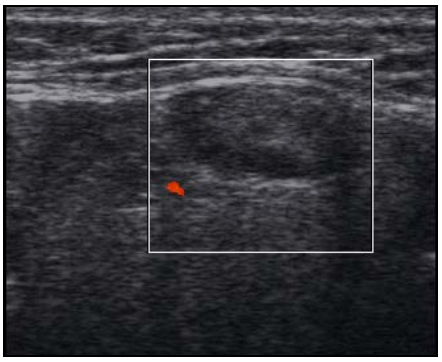

Figure 4. CDUS of left submandibular node-avascular pattern

- In benign group 46.66% showed hilar vascular pattern. This is in accordance with results obtained by several studies. One tuberculous node had capsular pattern similar to study [16]. It may be explained by loss of hilar vascularity from intra cystic necrosis and later inflammation induces new vessel formation from perinodal connective tissue.
- If hilar vascularity is taken as a criteria for identification of non malignant nodes sensitivity was 46.6% and specificity was 100%.
- Thus, it can be understood that a combination of clinical, ultrasonographic and CDUS characteristics of head and neck lymph nodes can differentiate malignant and non malignant nodes.

A summary of results obtained from our study is as follows:

1. Clinical examination is inaccurate and unreliable. Ultrasonogram is superior to clinical examination as it detected 21% of nodes undetected by clinical examination.
2. Malignant nodes tend to be larger as evidenced by high mean long axial diameter.
3. S/L ratio more than 0.5 and round shape are valuable indicators of malignancy with 64% specificity and 94% sensitivity. The p value was 0.000 ($p< 0.01$). This was statistically significant.
4. Most malignant nodes have sharp border, with 55% specificity and 79% sensitivity. The p value was 0.000 ($p < 0.01$). This was statistically significant.
5. Loss of echogenic hilus is a common feature of malignancy showing 70% sensitivity and 67% specificity. The p value was 0.000 ($p < 0.01$). This was statistically significant.
6. Most of malignant nodes were hypoechoic. But hypoechogenicity is not specific for malignancy as most normal and benign nodes are hypoechoic. Sensitivity was 100% and specificity was 11%. However presence of internal echoes (mixed echogenicity) is highly specific for malignancy.
7. Necrosis may be present in both malignant and non malignant nodes. Sensitivity was 17% and specificity was 94%. The p value was 0.0432 ($p < 0.05$). This was statistically significant.
8. In our study matting and edema were present in 3 tuberculosis patients and in 1 malignant patient. The p value was 0.2827 ($p > 0.05$). This was statistically not significant. Hence matting is not specific for malignancy.
9. Intranodal calcifications were present in tuberculosis nodes but absent in malignant nodes in our study.

10. Capsular and mixed (hilar and capsular) vascular pattern if taken as criteria for malignancy, the p value was 0.000 ($p < 0.01$). This was statistically significant. The specificity was 93.5% sensitivity was 93.3%. However presence of avascular pattern needs further evaluation. Presence of hilar vascularity as a criterion for non-malignancy had 100% specificity but only 46.6% sensitivity.

6. Conclusion

Ultrasonography is not routinely being used as a preliminary diagnostic modality in head and neck region. But it is a valuable tool and is showing promising results in the recent years. It is simple, non-invasive, quick and easily reproducible with minimal patient discomfort and expense. Rapid technical strides in ultrasonography and CDUS have led to wider use of USG and CDUS as the primary modality of investigation in head and neck lymphadenopathy. Using clinical examination, ultrasonography and CDUS criteria (S/L ratio, border sharpness, hilum, echogenicity, necrosis, matting and vascular pattern) it is possible to differentiate malignant and non malignant head and neck lymphadenopathy. Ultrasonogram being a bedside and outpatient procedure can be used by radiologists as well as oral physicians for the evaluation of cervical lymphadenopathy. Though histopathological examination is the gold standard for detection of lymphnode metastasis, CDUS can be used alternatively. This needs to be confirmed with studies using bigger sample size.

Competing interest

The authors have no conflict of interest.

List of abbreviations

CDUS	Colour Doppler Ultrasound
cm	Centimeter
CT	Computed tomography
e.g.	Example
et al.,	And others
etc.,	Excreta
FNAC	Fine Needle Aspiration Cytology
i.e.	That is
LNs	Lymphnode
MHz	Megahertz
Mm	Millimeter
MRI	Magnetic Resonance Imaging
P value	Probability value
S/L	Short axis to Long Axis diameter ratio
TB	Tuberculosis
USG	Ultrasonography

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