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Original article

ULTRASONOGRAPHY AND COLOUR DOPPLER CHARACTERISATION OF CERVICAL LYMPHADENOPATHY WITH PATHOLOGICAL CORRELATION: A PROSPECTIVE STUDY.

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Abstract

Aim:

The purpose of this study is to evaluate the efficacy of ultrasonography and Doppler in differentiating between benign and malignant cervical lymphadenopathy, and to correlate the results with those of other diagnostic procedures, such as fine needle aspiration cytology (FNAC) / histopathology.

Methods :

This was a cross-sectional study with diagnostic test evaluation as its methodology. All suspected cases of cervical lymphadenopathy referred to the Department of Radiodiagnosis at IMS and SUM Hospital, Bhubaneswar for sonological evaluation were included in the study. In the study, approximately 70 patients underwent grayscale and colour Doppler sonography of cervical lymphadenopathy.

Results:

In our research, we observed that out of a total of 128 lymph nodes, 11 exhibited matting, which were all identified as tubercular in nature. For predicting malignant lymph nodes, our study had a high sensitivity of 98.75%, Specificity of 85%, positive predictive value of 81.44%, and negative predictive value of 99.03%.

Conclusion :

Grey scale ultrasonography can be supplemented by colour Doppler ultrasonography (USG) in patients presenting with cervical lymphadenopathy in order to differentiate between benign and malignant lesions, thereby minimising the number of unnecessary biopsies.

Keywords: Grey Scale Ultrasonography, Malignant, Benign Lymph Nodes, Histopathology, cervical lymph nodes Introduction:, Submitted: 2023-06-23 Accepted: 2023-06-26

1. Introduction:

Cervical lymphadenopathy is a prevalent clinical manifestation and physical finding for a diverse array of pathologies, encompassing inconspicuous infections to grave neoplasms affecting the Head & Neck region [1, 2, 3]. It is widely acknowledged in the medical community that relying solely on clinical examination is insufficient for diagnosing the involvement of cervical lymph nodes, particularly those that are deep or small. Numerous pathological mechanisms entail the involvement of lymph nodes, thereby rendering the identification of lymph node participation of significant therapeutic and prognostic consequence

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[4]. In the medical and academic context, imaging modalities such as Computed Tomography (CT) scan, Magnetic Resonance Imaging (MRI), and Ultrasonography are crucial in identifying lymph nodes that are not clinically detectable [5, 6]. Histological examinations, including biopsies and other pathological analyses, are invasive procedures that require a significant amount of time to perform. Computed tomography and magnetic resonance imaging, both cross-sectional imaging modalities, are viable options for evaluating lymphadenopathy. However, ultrasound, specifically utilising high-resolution probes ranging from 7.5 to 15 MHz, has long been regarded as a potent technique for assessing enlargement of lymph nodes in the neck [7, 8]. Furthermore, it is a readily accessible, economically feasible, non-invasive, devoid of radiation, and secure diagnostic procedure. The discrimination between benign and malignant lymphadenopathy holds paramount significance in devising treatment strategies and predicting outcomes [9].

The identification of nodal metastasis is a crucial and prevalent indication for neck imaging in the medical field. The existence of a solitary metastatic lymph node is known to reduce the patient's five-year survival rate by 50% according to medical research. Sonography is an established diagnostic imaging modality utilised for the staging of head and neck tumours. Its diagnostic sensitivity surpasses that of clinical examination and even computed tomography (CT) scan [10, 11]. The integration of Doppler sonography into the established modality of grey-scale sonography augments the diagnostic yield of sonography, resulting in a substantial improvement in spatial and contrast resolution and the ability to visualise the internal architecture of lymph nodes [12].

The sonographic criteria utilised to differentiate between benign and malignant lymph nodes have been extensively researched and include factors such as number, location, morphology, dimensions, echotexture, presence of hilum, matting, nodal contour, long-to-short axis ratio, intranodal necrosis, and angioarchitecture [13].

The ultrasonographic characteristics that aid in the identification of anomalous nodes and provide indications of malignant nodes include heterogeneous echogenicity, the absence of echogenic hilus, architectural loss, extracapsular spread, and intranodal necrosis. Morphology represents the optimal approach to initiate the differentiation process between benign and malignant lymph nodes [14]. The lymph nodes' long/short axis diameter ratio is a reliable criterion for discriminating between benign and malignant enlargement in cervical lymphadenopathy [15].

The superior diagnostic precision of Colour Doppler Sonography is predicated upon the examination of vascularity and angioarchitecture. Lymph nodes can be classified as benign, reactively enlarged, tubercular, or malignant. The benign reactive nodes exhibit augmented central hilar vascularity with radial symmetry, whereas metastatic lymph nodes demonstrate displaced or absent hilar vascularity and heightened peripheral vascularity [16]. Although histopathology is considered the definitive diagnostic modality for metastatic lymph nodes, it is an invasive procedure that poses a risk of malignant cell dissemination and is associated with potential complications such as haemorrhage, vascular injury, patient discomfort, and, in certain cases, necessitates general anaesthesia. The prudent utilisation of Colour Doppler Ultrasonography (CDUS) assessment of nodal vascularization presents a prospect to assess the necessity for Fine Needle Aspiration Cytology (FNAC) or biopsy in reactive nodes [17].

The present investigation was undertaken to assess the effectiveness of ultrasonography and Doppler in distinguishing between benign and malignant cervical lymphadenopathy. The obtained results were subsequently correlated with other diagnostic modalities such as fine needle aspiration cytology (FNAC) and histopathology.

1.1. The objectives of this study include:

To detect and characterize cervical lymphadenopathy with Grey scale ultrasound and Colour Doppler.

To differentiate between Malignant and Non Malignant cervical Lymphadenopathy on the basis of imaging features.

To categorize the cervical lymphadenopathies into various etiologies based on imaging characteristics.

To correlate the radiological findings with cytological/pathological diagnosis.

2. Materials and methods:

Our research is a cross-sectional study that involves the evaluation of diagnostic tests. This study was a prospective descriptive investigation conducted at the Outpatient Department of Radio diagnosis, IMS and SUM Hospital, Bhubaneswar, Odisha, India over a period of 18 months from February 2021 to August 2022. The study enrolled a minimum of 70 patients who provided informed and written consent within the designated study period. Clinical information, encompassing pertinent demographic characteristics, was documented for all subjects.

2.1. Inclusion criteria:

- Patients of all ages and sexes
- Patients with clinically palpable neck lump referred for ultrasonography neck
- Patients diagnosed as cervical lymphadenopathy by other imaging modalities.

2.2. Exclusion criteria:

- Patients with clinically palpable neck lump not showing cervical lymphadenopathy on ultrasonography.
- Patients in whom histopathology correlation is not available.
- Patients already under treatment for any infective or malignant causes of cervical lymphadenopathy

2.3. Data collection:

A dataset was gathered from a cohort of 70 patients who were referred for neck ultrasonography. The sampling method employed was purposive, and a standardised data collection form was utilised. The imaging procedures were conducted utilising the "VOLUSON 730 PRO" and "LOGIQ E-9" systems, both manufactured by GE Healthcare. A linear array high frequency transducer (7-12 MHz) was employed for the imaging process.

2.4. Statistical Analysis:

The statistical analysis of descriptive measures will be conducted utilising either the SPSS version 17.0 software or the STATA 9.0 software. Continuous variables shall be presented as mean plus or minus standard deviation or median if the data exhibits skewness. The categorical variables shall be presented in terms of frequencies and percentages, as per the standard medical and academic practise. The study analysed nominal categorical data among the groups using appropriate statistical tests such as the Chi-squared test or Fisher's exact test. In all medical statistical analyses, a significance level of 0.05 will be used to determine the presence of a statistically significant difference between groups or conditions. The present investigation has employed various statistical analysis techniques. The outcomes for every parameter (quantitative and proportional) for categorical data are exhibited in tabular and graphical formats. The statistical significance of the proportions was evaluated using the Chi-square test.

3. Results:

A total of 98 cases were initially included for this study. However, based on exclusion criteria, only 70 patients were included as the final sample population.

The age of the patients ranged from 5-75 years. Majority of the patients belonged to the age group of 40-70 years, with, the average age being 49 years (Table 1). Of the 70 cases, 51 were males (73%) and 19 females (27%) (Table 2).

Table 3 shows that majority of nodal level affected was level II showing maximum of 39 nodes out of 128 of which majority are malignant and most of tubercular nodes are noted in level V (posterior triangle), majority of benign lymph nodes are distributed in level I, whereas majority of reactive lymph nodes are noted in level III.

Table 4 shows that metastatic lymph nodes predominantly present with more of central (cogulative) necrosis and tubercular lymph nodes show

Table 1: **Age distribution**

	Frequency	Minimum	Maximum	Mean	Std deviation
Age	70	5.00	75.00	49.6571	17.95476

Table 2: **Sex distribution**

Sex	**Frequency**	**Percentage**
Male	50	71.43%
Female	20	28.57%

Table 3: **Distribution of Lymph Node level**

Lymph Node level		Usg D B	M	T	Total
1	Count	5	22	0	27
	%	18.5%	81.5%	.0%	100.0%
2	Count	3	35	1	39
	%	.7.7%	89.7%	2.6%	100.0%
3	Count	6	16	2	24
	%	.25%	66.7%	8.3%	100.0%
4	Count	3	5	2	10
	%	30.0%	50.0%	20.0%	100.0%
5	Count	3	7	6	16
	%	18.8%	43.8%	37.5%	100.0%
6	Count	0	1	0	1
	%	.0%	100.0%	.0%	100.0%
2-3	Count	0	9	0	9
	%	.0%	100.0%	.0%	100.0%
3-4	Count	0	2	0	2
	%	.0%	100.0%	.0%	100.0%

Table4: **Distribution of necrosis**

Usg D		Necrosis Nil	Central Necrosis	Cystic Necrosis	Total
B	Count	20	0	0	7
	%	100.0%	.0%	.0%	100.0%
M	Count	62	5	30	97
	%	63.9%	5.2%	30.9%	100.0%
T	Count	7	0	4	11
	%	63.6%	.0%	36.4%	100.0%

cystic necrosis. The p value for this criterion was 0.083,which showed the association to be insignificant. In our study 31% of malignant nodes showed cystic necrosis which were all malignant on FNAC correlation. Whereas 37% of tubercular nodes showed cystic necrosis. Benign and reactive nodes showed no necrosis.

Table 5 displays a comparison between USG and FNAC diagnosis. The comparative study of USG and FNAC lymph node diagnosis revealed that 18% of lymph nodes were malignant, 16% were benign, and 15% were reactive. FNAC study does not correlate with USG diagnosis. For predicting malignant lymph nodes, our study had a high sensitivity of 98.75%, Specificity of 85%, positive predictive value of 81.44 %, and negative predictive value of 99.03%. The p value of 0.001 in the table above is considered to be extremely significant. The study demonstrated that there are no distinctions between primary and secondary nodal malignancies.

4. Discussion:

To differentiate benign, reactive, tuberculous, lymphomatous, and malignant cervical lymphadenopathy, high resolution Sonographic examination was performed on seventy patients referred for neck ultrasonography to the department of Radio diagnosis, IMS and SUM Hospital, Bhubaneswar. The mean age was 49.6 ± 17.9 years, and they ranged from 5-75 years. The examination was conducted methodically from superior to inferior, with no nodes missed. The purpose of this study is to demonstrate the efficacy and utility of high resolution ultrasonography and to assess the utility of Colour Doppler Sonography in differentiating between malignant, tuberculous, reactive, and benign cervical lymphadenopathy.

The presence of metastatic lymph nodes plays a crucial role in the therapeutic planning of patients with a malignancy suspicion [18]. The presence or absence of these metastases has a significant impact on treatment, recurrence risk, and survival. Ultrasound is more sensitive than CT and MRI for evaluating lymph nodes in the cervical region [18]. The primary drawbacks of CT and MRI are:

Reliance on size criteria: Size alone is not a reliable criterion for distinguishing benign lymph nodes from malignant ones. With a specificity of 95% to 100%, the presence of central nodal necrosis is believed to be the most specific indicator of metastatic involvement. It is referred to as central low attenuation in CT. The process of fatty nodal metaplasia resulting from infection and a variety of other causes resembles CT [19] central nodal necrosis. Under 0.5 centimetres in diameter, cervical lymph nodes may not be accurately detected by CT. In addition, due to the fact that the majority of cervical lymph nodes have their long axis parallel to the long axis of the body and because CT demonstrates only the transverse plane of the lymph nodes, in which plane all lymph nodes appear to be round, all lymph nodes appear to be round. Increased lipid deposition is a normal occurrence in the lymph nodes of the elderly, which stimulates the development of central nodal necrosis in the CT. Lastly, CT and MRI are costly and not readily available for repetitive use during patient follow-up. Ultrasonography is readily available, cost-effective, non-invasive, secure, and radiation-free; it is the investigation of choice for differentiating between malignant, lymphomatous, tuberculous, reactive, and benign cervical lymphadenopathy [20]. It enables examination of lymph nodes in all planes, enabling precise evaluation of nodal size and morphology.

In our study, 100% of benign and reactive lymph nodes were homogenous, as were 62% of malignant lymph nodes and 63% of tuberculous lymph nodes. In a study conducted by Kaji et al. [21], 30 of 33 homogenous lymph nodes (90.9%) were identified as benign. Therefore, the results correspond with the prior investigation. This criterion's p value was 0.013, indicating that the association was significant. In our study, 40 of 128 lymph nodes are heterogeneous, with 36 malignant and 4 tuberculous. FNAC determined that all 36 lymph nodes were cancerous. This criterion's p value was 0.013, indicating that the association was significant. In a study by Toriyabe et al. [22], 17 of 19 lymph nodes exhibited het-

Table 5: **Comparison of USG diagnosis with FNAC diagnosis**

Fnac D		Usg D			Total
		B	M	T	
R	Count	6	16	0	22
	%	30%	16.5%	.0%	17.2%
I	Count	2	2	0	4
	%	10%	2.1%	.0%	3.1%
M	Count	1	79	0	80
	%	5%	81.4%	.0%	62.5%
R	Count	11	0	0	11
	%	55%	.0%	.0%	8.6%
T	Count	0	0	11	11
	%	.0%	.0%	100.0%	8.6%

erogeneous echotexture and were determined to be malignant via FNAC. Our research correlated with this research.

Cystic necrosis is a subtype of coagulation necrosis that occurs when certain microorganisms, such as mycobacterium tuberculosis, cause cell death. Necrosis of the central type is observed in metastasis and primary cancers [23]. 39 out of 128 lymph nodes exhibited necrosis in our study. 34 lymph nodes (87%) exhibited cystic necrosis, of which 30 (88%) were malignant and 4 (12%) were tuberculous. 5 lymph nodes exhibited central necrosis (13%), and they were all malignant (100%). This criterion's p value was 0.083, indicating that the association was not significant.

In our study, only 31 of the 44 benign lymph nodes (diagnosed by FNAC) were identified as such by ultrasound prior to FNAC. FNAC/biopsy revealed that only 84 of 97 potentially malignant lymph nodes identified by ultrasonography were indeed malignant. Our study slightly overdiagnosed malignant lymph nodes, according to the preceding statement. This was primarily attributable to the incorporation of all grey scale and colour Doppler parameters in the diagnosis of benign and malignant cervical lymphadenopathy. Certain parameters, including cystic/central necrosis and Doppler indices RI and PI, were deemed insignificant at the conclusion of the study.

Danninger et al. [25] found that the sensitivity and specificity of ultrasonography for detecting malignant lymph nodes were 96% and 69%, respectively. In a separate study by Ahuja et al. [26], the sonographic sensitivity and specificity for identifying cervical lymph nodes were 95% and 83%, respectively. Ahuja et al. [26] concluded that ultrasound had a sensitivity of 95% and a specificity of 83% for classifying lymph nodes as metastatic or non-metastatic. In our study, the sensitivity, specificity, positive and negative predictive values of Ultrasonography for distinguishing benign and malignant cervical lymphadenopathy are 98%, 85%, 81%, and 99%, respectively. In evaluating sonographically detectable cervical lymph nodes, our research confirmed the reliability of ultrasound sensitivity and specificity.

5. Conclusion:

This investigation reaches the conclusion that High resolution Sonography has proven to be an effective primary investigation for identifying lymph nodes and differentiating benign, tuberculous, and malignant lymphadenopathy. The ultrasonographic evaluation of cervical lymphadenopathy proved to be a cost-effective, non-invasive, radiation-free, and secure method. This sensitive technique can visualise lymph nodes as small as 6 to 7 mm in diameter. The ultrasonographic examination is highly sensitive in distinguishing cystic/necrotic foci from solid growths. In identifying tuberculosis, adjacent

soft tissue edoema and matting are particularly helpful. Colour Doppler Sonography provides additional information on lymph node vasculature and plays a crucial role in distinguishing benign, tuberculous, and malignant cervical lymphadenopathy. Combination of shades of grey Sonographic characteristics and lymph node vascular pattern have a high degree of accuracy, sensitivity, and specificity in distinguishing between malignant and benign cervical lymphadenopathy. All USG diagnoses must be correlated with FNAC/histopathology not only to determine whether the nodes are malignant, tuberculous, or benign, but also to determine the histopathology of the malignancy.

6. Limitations:

In the present investigation, both the number and variety of cases with malignant lymph nodes were limited. Clearly, additional studies with a greater number and variety of cases (of both benign and malignant aetiology) are required to demonstrate the efficacy of ultrasonography in distinguishing benign from malignant lymph nodes.

7. Recommendations:

We recommend that all cervical lymph nodes should be evaluated with combined grey scale and elastographic methods to characterize the lymph nodes as benign or malignant.

8. Acknowledgement:

None

9. List of abbreviations:

FNAC- Fine needle aspiration cytology
USG- Ultrasonography
CT- Computed Tomography
MRI- Magnetic Resonance Imaging
CDUS- Colour Doppler Ultrasonography

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None declared.

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