

# Diagnostic Accuracy of Color Doppler Ultrasonography and Fine Needle Aspiration Cytology (FNAC) in Differentiating Benign and Malignant Cervical Lymphadenopathies at Birat Medical College Teaching Hospital, Morang, Nepal

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## ABSTRACT

### Introduction:

Among various imaging modalities useful in diagnosis of cervical lymphadenopathies, Color Doppler ultrasound (CDUS) is useful to evaluate and determine the presence of vascularity, resistance, direction, and velocity of blood flow in lymph nodes. It can determine the morphological and vascular nature of lymphadenopathies which will further help in the differentiation between benign and malignant nodes.

### Methods:

This study was conducted on 61 patients referred to the Department of radiodiagnosis and imaging of Birat Medical College for an ultrasound of cervical lymphadenopathy. These patients had subsequently undergone FNAC examination. Color Doppler sonographic procedures were done with an 11L linear probe with a frequency of 4.5-12MHz and CDUS evaluation of lymph nodes for Resistive Index and Peak systolic velocity were carried out and correlated with FNAC findings.

### Results:

Among 61 lymph nodes, 52 were benign and 9 were malignant in the Color Doppler study where the final diagnosis by FNAC showed 53 benign and 8 malignant nodes. RI above the cutoff value of 0.5 had 83.3% sensitivity, 79.6% specificity, 50% PPV and 95.1% NPV. PSV above the cutoff value of 16cm/sec had 66.6% sensitivity, 95.9% specificity, 80.0% PPV and 92.2% NPV with diagnostic accuracy of 91.8%.

### Conclusion:

Morphological features of the nodes such as shape, absence of echogenic hilum, abnormal vascular pattern, and Doppler indices cutoff values of 0.5 and 16cm/s respectively for RI and PSV were sensitive and specific for the diagnosis of malignant lymph nodes.

**Keywords:** Lymphadenopathy; Lymph Nodes; Ultrasonography, Doppler, Colour

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## INTRODUCTION

Cervical lymphadenopathies are the most common findings in head and neck disorders. The common causes of lymphadenitis are viral, bacterial, protozoal, fungal, malignancy, autoimmune disorders, drugs such as phenytoin, and certain vaccines.<sup>1</sup> Majority of patients have benign reactive lymphadenitis. However, in a few cases, it may be a serious disease.<sup>2</sup> So, it is important to differentiate patients with serious illnesses from benign lymphadenopathies.

Early detection of metastatic lymph nodes is of immense importance. The diagnosis of malignant lymphadenopathy is crucial for therapeutic planning in patients with suspected malignant neoplasms and pretreatment staging in patients with primary malignant tumors.<sup>3</sup>

There are various imaging modalities to differentiate benign and malignant cervical lymph nodes. Color doppler ultrasound (CDUS) is used to evaluate and determine the presence of vascularity, resistance, direction, and velocity of blood flow in lymph nodes. Inflammatory or benign nodes have dilated intranodal vascular alteration due to local humoral agents whereas in malignant or metastatic nodes blood vessel morphology is deranged as internal nodal architecture is destroyed by neoplastic infiltration.<sup>1</sup> Using spectral waveform the vascular resistance in terms of the resistive index (RI) can be calculated. The value of RI in differentiating malignant and benign lymph nodes is unclear. Few studies show higher RI value in metastatic nodes whereas other studies showed lower vascular resistance in metastatic lymph nodes as compared to benign lymph nodes.<sup>4,5</sup> The different cut-off values of RI are suggested with different sensitivities and specificities ranging from 47-81% and 81-100% respectively.<sup>6,7</sup>

There are various advantages of CDUS examination and its importance over conventional methods of clinical examination and fine-needle aspiration as shown in the study by Dangote et al.<sup>1</sup> Very few studies are conducted to determine the efficacy of CDUS in the diagnosis of cervical lymphadenopathy. Therefore, this study is aimed to differentiate between benign lymph nodes from malignant/metastatic nodes using CDUS and

to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of CDUS using fine-needle aspiration cytology as the gold standard.

## METHODS

This was a prospective cross-sectional study conducted in the Department of Radiodiagnosis and imaging of Birat Medical College for six months from 1<sup>st</sup> October 2020 to 30<sup>th</sup> March 2021. The study group consists of 61 patients with cervical lymphadenopathy. All patients referred for ultrasound evaluation with clinical suspicion of cervical lymphadenopathies were included in the study. Patients not willing to participate in the study and postoperative and histopathological proven cases were excluded from this study. Ethical clearance was taken from the institutional review committee and informed consent was taken for the enrollment in this study. Colour doppler sonographic procedures were done with an 11L linear probe (GEvolution S10 ultrasound system) with the frequency of 4.5-12 MHz and CDUS evaluation of the cervical lymph nodes for RI and Peak systolic velocity was carried out.

All sonographically detectable lymph nodes were first scanned in the longitudinal plane (L) and the transverse plane (T). To measure the size of each lymph node L/T ratio is considered. The presence or absence of hilar structure was also recorded. The vascular pattern and displacement of vascularity of the lymph nodes were assessed by CDUS. After the Color Doppler, flow in the lymph node was stabilized and the color flow pattern was determined. The vascular pattern of the enlarged lymph nodes with long-axis diameters >10 mm was classified into the following four groups according to CDUS findings:

- Central - Flow signals branching radially from the center and the signals are not the periphery of the nodes
- Peripheral - Flow signals along the periphery of the lymph nodes, with branches perforating the periphery of the node and not arising from the hilar vessels
- Mixed- Presence of central and peripheral flow signals

- No flow or avascular - Absence of vascular signals within the lymph nodes.

In the color Doppler study, if the lymph node shows central color flow, then it was considered benign, and if the lymph node shows peripheral or mixed color flow then it was considered malignant. The RI value of more than 0.5 was considered malignant, whereas the RI value of less than 0.5 was considered benign. The color doppler findings were classified into benign and malignant groups. The patients were then sent for fine-needle aspiration cytology (FNAC). The ultrasound findings were then compared with FNAC reports. The data were collected and analyzed using the Statistical Package for the Social Sciences version 25. Following parameters including sensitivity, specificity, and diagnostic accuracy were calculated.

### RESULTS

In total 61 patients were included who met the inclusion criteria. Among them 43.3% were male and 55.7% were female. The age of the patients ranged from one to 71 years with 34.33 being the mean age. A total of 52 nodes were benign and nine were malignant on color Doppler study where final diagnosis by FNAC showed 53 benign and eight malignant. The most common cause of

lymphadenopathy was reactive (67.2%), followed by tuberculosis (19.7%), metastasis (9.8%), and lymphoma (3.3%) keeping FNAC as a gold standard. The USG characteristics of the benign and malignant lymph nodes are shown in Table 1. Similarly, the doppler findings of the benign and malignant nodes are shown in Table 2.

The mean values of RI and PSV for benign and malignant lymph nodes are shown in Table 3. The sensitivity and specificity combination points for various indices were derived from the coordination of the ROC curve to determine the cut-off values. (Figure 1) RI above the cutoff value of 0.5 had 83.3% sensitivity, 79.6% specificity, 50.0% PPV and 95.1% NPV. Similarly, peak systolic velocity above the cutoff value of 16 cm/s had 66.6% sensitivity, 95.9% specificity, 80.0% PPV, and 92.2% NPV with a diagnostic accuracy of 91.8%.

### DISCUSSION

Ultrasonography is the first investigation of choice for cervical lymphadenopathies. The use of color Doppler Ultrasonography in cases of cervical lymphadenopathies can give extra information regarding the vascularity of the lymph node which might help in narrowing the differentials.

**Table 1: USG characteristics**

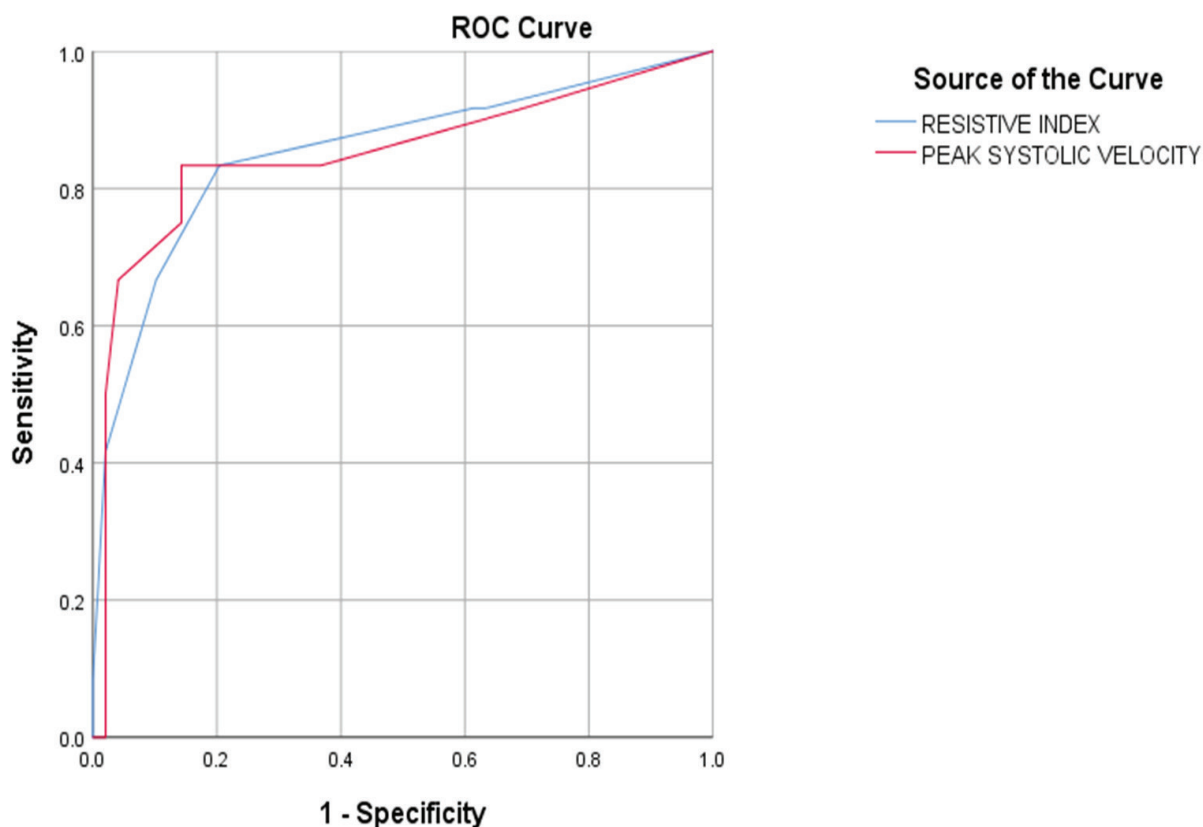
| USG Characteristics |               | Frequency |           |
|---------------------|---------------|-----------|-----------|
|                     |               | Benign    | Malignant |
| Shapes              | Oval          | 43(70.5%) | 2(3.3%)   |
|                     | Round         | 6(9.8%)   | 10(16.4%) |
| Texture             | Homogenous    | 40(65.6%) | 3(4.9%)   |
|                     | Heterogeneous | 9(14.8%)  | 9(14.8%)  |
| Hilum               | Present       | 37(60.7%) | 2(3.3%)   |
|                     | Distorted     | 4(6.6%)   | 1(1.6%)   |
|                     | Absent        | 8(13.1%)  | 9(14.8%)  |
| Margins             | Regular       | 44(72.1%) | 3(4.9%)   |
|                     | Irregular     | 5(8.2%)   | 9(14.8%)  |
| Calcifications      | Present       | 0         | 5(8.2%)   |
|                     | Absent        | 49(80.3%) | 7(11.5%)  |
| Matting             | Present       | 9(14.8%)  | 2(3.3%)   |
|                     | Absent        | 40(65.6%) | 10(16.4%) |

**Table 2: Vascularity and FNAC findings**

| Vascularity and FNAC findings |            |               |           |           |
|-------------------------------|------------|---------------|-----------|-----------|
| Benign                        |            | FNAC findings |           | Total     |
|                               |            | Malignant     |           |           |
| Vascularity                   | Hilar      | 39 (63.9%)    | 2(3.3%)   | 41(67.2%) |
|                               | Peripheral | 3(4.9%)       | 5(8.2%)   | 8(13.1%)  |
|                               | Mixed      | 5(8.2%)       | 2(3.3%)   | 7(11.5%)  |
|                               | Absent     | 2(3.3%)       | 3(4.9%)   | 5(8.2%)   |
| Total                         |            | 49(80.3%)     | 12(19.7%) | 61(100%)  |

**Table 3: Resistive Index and Peak systolic velocity**

| Doppler indices        | Benign     | Malignant  |
|------------------------|------------|------------|
|                        | Mean±SD    | Mean±SD    |
| Resistive index        | 0.49±0.10  | 0.70±0.17  |
| Peak systolic velocity | 11.00±2.11 | 22.00±3.60 |



Diagonal segments are produced by ties.

**Figure 1:** ROC curve of the resistive index and peak systolic velocity

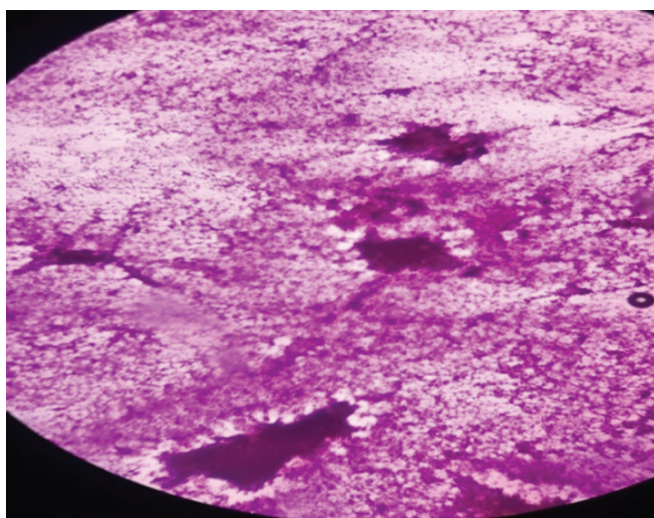
In our study, we have evaluated the accuracy of color Doppler Ultrasonography in differentiating benign and malignant cervical lymphadenopathies by comparing it with the FNAC result.

In our study, the mean age was 34.33. In a study by Jaiswal et al., the mean age was 43.9.<sup>8</sup> In a study by Kamat et al., the mean age was 42.5.<sup>9</sup> In our study, the males were 43.3% and females were 57.7%. A study conducted by Regmi et al. also showed similar results for 56 females and 52 males.<sup>10</sup> In our study, 52 lymph nodes were benign and nine were malignant by color Doppler study whereas the final diagnosis by FNAC showed 53 benign and eight malignant lymph nodes. The most common cause of lymphadenopathy was reactive (67.2%), followed by Tuberculosis (Figure 2a and 2b) (19.7%), metastatic (9.8%) (Figure 4) and

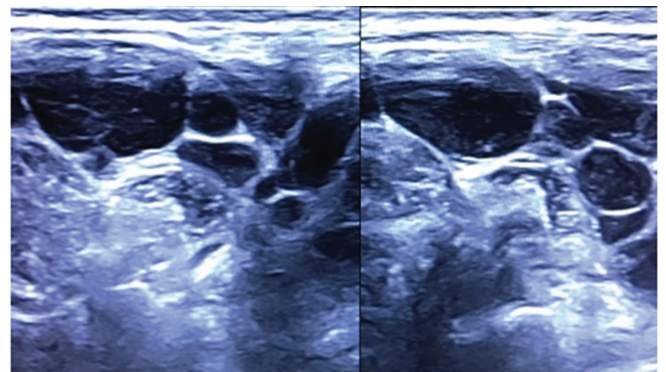
lymphoma (3.3%) (Figures 3a and 3b).

A study by Jaiswal et al. showed 40 benign (17 reactive and 23 tubercular) and 30 malignant (9 lymphomas and 21 metastatic).<sup>8</sup> The number of tubercular lymph nodes was less in our study than reactive lymph nodes which are not similar to the results of a study done by Jaiswal et al. This difference might be due to decreased prevalence of tuberculosis as shown by the study done by Dasgupta et al.<sup>11</sup>

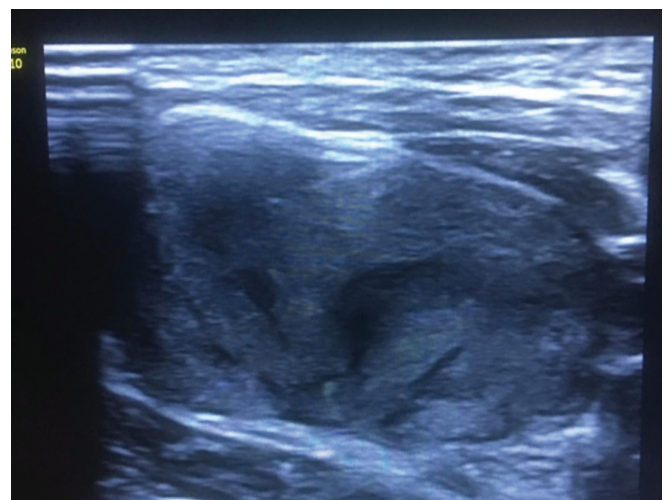
The shape of benign lymph nodes in our study was similar to the study done by Jaiswal et al., in which, oval and round shapes were observed in 94 % and 6% of lymph nodes respectively. Reactive lymph nodes are usually oval or flat whereas metastatic, lymphomatous, and tubercular lymph nodes appear round.<sup>10</sup>



**Figure 2(a):** Caseous necrosis with histiocytes



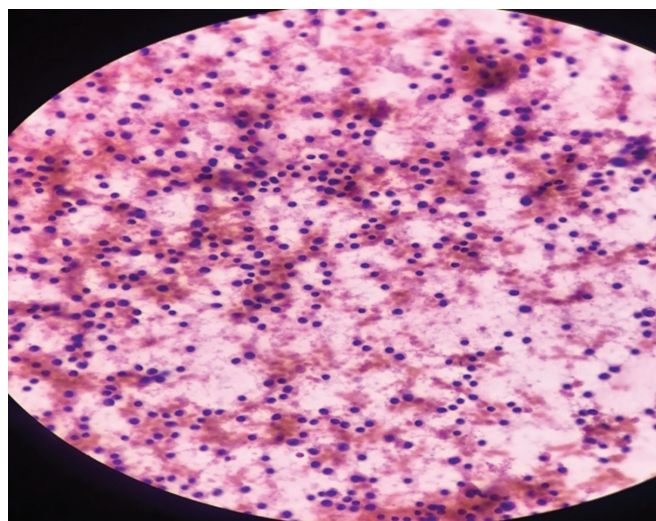
**Figure 2(b):** USG of tubercular lymph node epithelioid



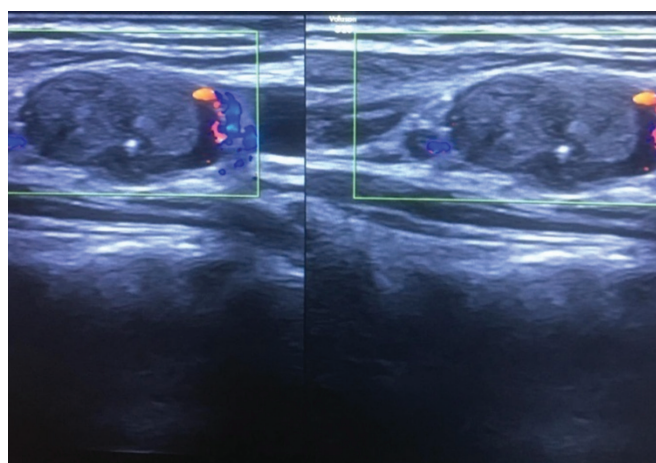
**Figure 3(a):** USG features of lymphoma

In total 81.6% of benign nodes appeared homogeneous while 75% of malignant nodes were heterogeneous. Metastatic nodes may look homogeneous or heterogeneous.<sup>12,13</sup> Lymph nodes involved with lymphoma usually look homogeneous and tubercular nodes are commonly heterogeneous.<sup>14,15</sup> Presence of the echogenic hilum is long considered a sign of benignity.<sup>10</sup> In a study done by Ahuja et al., over 90% of benign cervical nodes showed echogenic hilum which is comparable to our study.<sup>16</sup>

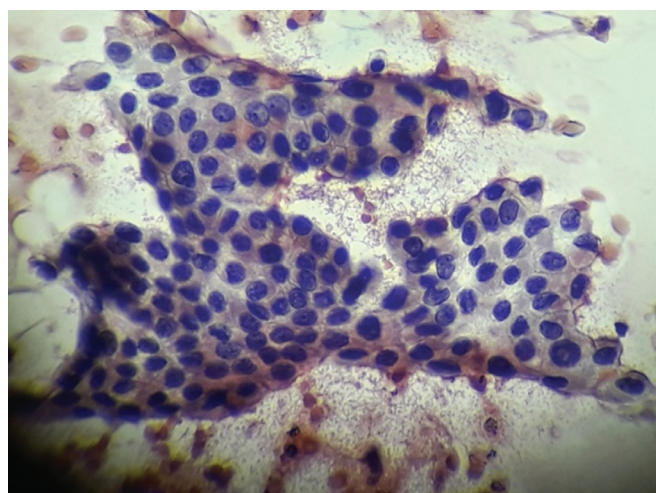
In cases of malignant nodes, the hilum was absent in 75% of cases. This was, in contrast, to a study done by Regmi et al., which showed the presence of echogenic hilum in two cases of the malignant lymph node.<sup>10</sup>



**Fig 3(b):** Small atypical lymphocytes



**Figure 4(a):** USG of metastatic lymph node



**Figure 4(b):** Metastatic papillary carcinoma thyroid

It is possible to see echogenic hilum in early nodal malignancy because the medullary lymphatic

sinuses have not been sufficiently invaded.<sup>16</sup> In studies done by Mazaher et al., and Teng et al., ill-defined margins had a statistical significance with malignant nodes which is similar to our study.<sup>17,18</sup>

Benign lymph nodes showed a predominantly hilar pattern of vascularity (79.5%). This result is similar to the study by Dangote et al., in which 106 nodes out of 108 nodes showing hilar flow were found to be benign.<sup>1</sup> Nearly, 96% of reactive nodes show hilar flow and seldom show peripheral vascularity.<sup>19</sup> Reactive nodes tend to have prominent hilar/ central vascularity due to the increase in vessel diameter and blood flow.<sup>1</sup> Malignant lymph node had a predominance of peripheral vascularity (41.66%). This result is similar to the study done by Regmi et al., in which most of the malignant nodes demonstrated either peripheral or mixed vascularity.<sup>10</sup> Metastatic nodes tend to have peripheral or mixed vascularity and mixed vascularity is also common in lymphomatous nodes.<sup>20</sup> As peripheral vascularity is not found in normal or reactive nodes, the presence of peripheral vascularity, regardless of sole peripheral or mixed vascularity, is highly suspicious of malignancy.<sup>21</sup> About 3.3 % of benign and 4.9% of malignant nodes showed no vascularity. This may be due to necrosis or due to replacement by keratinized tumor tissue.<sup>22</sup>

The predominant vascular pattern of the tubercular node was mixed type (41.6%). This result was similar to that of a study conducted by Regmi et al. which showed 11 cases of mixed vascularity out of 22 cases of tubercular lymphadenitis.<sup>10</sup> In a study by Rohan et al., tubercular lymph nodes showed peripheral/mixed patterns (66.6%).<sup>9</sup> In our study, two cases of tubercular lymph nodes show no vascularity which may be related to extensive intranodal cystic necrosis of tubercular nodes, which destroys the blood vessels of the lymph nodes.<sup>23</sup>

The flow pattern within cervical lymph nodes can be assessed by parameters such as RI, PI, PSV, and EDV. Out of these parameters, RI has been most commonly used. In our study, we have taken RI and PSV for this differentiation of benign and malignant nodes.

In our study, the mean RI and PSV were significantly higher in malignant nodes compared to benign nodes. In a study by Dangote et al., the RI of malignant lymph nodes had a mean value of  $0.73 \pm 0.16$  and that of benign nodes had a mean value of  $0.65 \pm 0.18$ .<sup>1</sup> The theory for increased RI is that with the growth of tumor cells, the normal part of a node is replaced, thus resulting in compression of its blood vessels, increased vascular resistance, and increased RI.<sup>24,25</sup> In a study by Gupta et al. the mean RI values were  $0.74 \pm 0.08$  and  $0.60 \pm 0.1$  in malignant and benign nodes respectively.<sup>26</sup>

In our study, the cut-off value of 0.5 for RI and 16cm/sec for PSV were determined for the differentiation of benign and malignant cervical lymph nodes. These cut-off values were similar to the study done by Van den Brekel et al. which had taken 0.6 and 16.5cm/sec as cut-off values for RI and PSV.<sup>27</sup> In a study by Dangote et al, sensitivity and specificity of RI were 83% and 81% respectively and of PSV were 72% and 81% respectively. (1) The result of RI of this study is similar to that of our results. But, the sensitivity in the case of PSV is less while the specificity is more in our study.

In a study done by Abhuja et al., the optimal cut-off value of RI in differentiating reactive from metastatic nodes was 0.7 with a sensitivity of 86% and specificity of 70%.<sup>16</sup> This cut-off value was higher than our cut-off value with similar sensitivities but less specificity than that of our study. Steinkamp et al had taken a cut-off value of 0.8 for RI which had a sensitivity of 80% and specificity of 94%. This cut-off value was higher than our study with similar sensitivities but more specificity.<sup>28</sup>

A study done by Chang et al reported that lymph nodes affected by the malignant process showed a low RI of less than 0.6.<sup>12</sup> According to Ahuja et al., the reason for the contrasting results of the values of RI between the study by Chang et al and other studies is the differences in methodology and vessel sampling used for RI evaluation.<sup>29</sup> In another study done by Ahuja et al, lowering of RI in malignant lymph nodes may be due to the absence of smooth muscle layer in malignant neoangiogenesis and arteriovenous stunting.<sup>25,29</sup>

## LIMITATIONS

The sample size was small as we only included patients with a confirmatory diagnosis on cytology/histopathology. The deep lymph nodes such as retropharyngeal lymph nodes cannot be assessed which is the first echelon lymph node of the nasopharynx and a common site of metastasis in nasopharyngeal cancers. The inability to detect micrometastasis in the non-enlarged lymph node is another limitation of Ultrasonography.

The results would have been more precise if Pulsatility Index was also added to the study on the differentiation of cervical lymph nodes.

## CONCLUSION

Color Doppler ultrasound is a useful tool that provides an insight into the vascularity of a lymph node. It can act as a surrogate marker for in vivo assessment of neovascularity. The vascular hemodynamics within the lymph node can be assessed by this technique. Color Doppler ultrasound plays an adjunct role to ultrasound in differentiating benign from malignant lymph nodes. It enhances the diagnostic confidence in predicting malignancy in cervical lymph nodes.

The various features like abnormal shape, absence of echogenic hilum, abnormal vascular pattern, and Doppler indices revealed good sensitivity, specificity, and accuracy in differentiating benign from malignant nodes.

## CONFLICT OF INTEREST

None

## SOURCES OF FUNDING

None

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