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## **Original Article**

# Diagnostic Accuracy of Ultrasononography in Detection for Diagnosis of Malignancy of Lymph Nodes in Newly Diagnosed Head and Neck Carcinoma Patients Taking Histopathology as Gold Standard

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#### Abstract

**Objective:** To determine the diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients, taking histopathology as gold standard.

**Methods:** This cross-sectional study was undertaken in Department of Radiology, Jinnah Hospital, Lahore. Total 168 newly diagnosed cases with head and neck carcinoma, 20-80 years of age of both genders were selected. All the patients with history of previous neck surgery, on chemotherapy or any other oncology treatment and recurrent cases were excluded. After taking informed consent, ultrasonography of neck was performed. Each USG findings were interpreted by one consultant radiologist and were looked for malignant lymph nodes as per-operational definition. USG findings were compared with histopathology findings.

**Results:** Age range in this study was from 20-80 years with mean age of  $50.33 \pm 11.98$  years. Majority of the patients 92 (54.76%) were between 20-50 years of age. Out of these 168 patients, 98 (58.33%) were males and 70 (41.67%) were females with ratio of 1.4:1. All the patients were subjected to USG and found that 83 were True Positive and 08 were False Positive. Among 77, USG negative patients, 07 (False Negative) had malignant lymph nodes on histopathology whereas 70 (True Negative) had benign lymph nodes on histopathology (p=0.0001). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients was 92.22%, 89.74%, 91.21%, 90.91% and 91.07% respectively.

**Conclusion:** This study concluded that ultrasound is a highly sensitive and accurate non-invasive modality for detecting malignant lymph node in head and neck cancers.

Keywords: head and neck cancers, lymph node metastasis, ultrasound.

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#### Introduction

The mouth cavity, pharynx, larynx, paranasal sinuses, salivary glands, and thyroid are all part of the head and neck region. The mucosal linings of the upper aerodigestive tract, which include 1) the nasal cavity and paranasal sinuses, 2) the nasopharynx, 3) the hypopharynx, larynx, and trachea, and 4) the oral cavity and oropharynx, evolve into head and neck squamous cell carcinoma (HNSCC). The most common malignant tumour of the head and neck region is squamous cell carcinoma (SCC). HNSCC is the sixth most common

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cancer in the globe.<sup>1,2</sup>

Tobacco use and alcohol abuse are risk factors for malignancies of the oral cavity, oropharynx, hypopharynx, and larynx, and infection with oncogenic viruses is linked to cancers of the nasopharynx, palatine, and lingual tonsils of the oropharynx. The presence or absence of clinically affected neck nodes is the most important prognostic factor in head and neck malignancies.<sup>3</sup> The correct diagnosis of a metastatic lymph node is critical in the treatment of head and neck cancer. Recent alterations in the epidemiology of head and neck cancer have necessitated the development of improved lymph node prognostics. Head and neck cancer staging is critical for directing suitable management strategies and delivering the best radiation therapy and surgery. The determination of T and N stages, stage migration with discovery of metastatic disease, and identification of primary illness in patients with nodal metastasis are the first hurdles in head and neck cancer imaging.<sup>4-6</sup>

Ultrasound, not just of the thyroid but also of the regional neck lymph nodes, is widely used for initial diagnosis and follow-up of patients with thyroid nodules and thyroid cancer, thanks to broad availability and recommendations from specialist organisations.<sup>7</sup> The prevalence of lymph nodes has been observed to be 18.65% in individuals with head and neck cancers. Furthermore, several research have been conducted in order to determine the role of USG, with one study reporting a sensitivity of 95.24 percent and a specificity of 100 percent for USG in detecting lymph node cancer. In a metaanalysis published in 2012, researchers discovered that ultrasound had a sensitivity of 66 percent and a specificity of 78 percent for diagnosing lymph node cancer. Suresh et al., discovered 85.4 percent sensitivity, 90 percent specificity, 81.8 percent positive predictive value, and 87.50 percent negative predictive value.<sup>8-11</sup>

There is no consistency in the aforementioned data supplied in the form of sensitivity and specificity, since sensitivity is reported as low as 66 percent and as high as 95.34 percent, while specificity is also reported as 78 percent, 10 percent, and 100 percent.<sup>9,10</sup> So we designed this study to find the diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients taking histopathology as gold standard. As no local study is, reported yet and global studies gave variable diagnostic accuracy. The study was necessary to be done to establish evidence regarding diagnosis of cervical lymph node as its malignancy can delay the prognosis of the disease. Histopathology delays the diagnosis USG being non-invasive is quick and readily available.

Thus the aim of this study is to determine the diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients, taking histopathology as gold standard.

## Methods

Study Design: Descriptive, Case Series study.

**Setting:** Department of Radiology, Jinnah Hospital, Lahore.

Duration of Study: 28<sup>th</sup> September 2018 to 27<sup>th</sup>

#### March 2019.

**Sample Size:** Sample size of 168 cases has been calculated with 95% confidence level, and taking expected prevalence of malignant lymph nodes as 18.65%8 and 11% margin of error for sensitivity of USG as 85.7%<sup>III</sup> and 5% margin of error for specificity of 90%.<sup>III</sup>

**Sample Technique:** Non-probability, consecutive sampling.

### Sample Selection:

**Inclusion Criteria:** Newly diagnosed cases of age 20-80 years, either gender, having head and neck carcinoma. Head and neck carcinoma was found in oral, nasal cavity, Paranasal sinuses, thyroid, larynx, pharynx, and salivary glands that take different Histopathological tumours including adenocarcinoma, paraganglioma, adenocystic carcinoma, squamous cell carcinoma, mucoepidermoid carcinoma, and rhabdomyosarcomas. In this study all cases with such findings on biopsy were taken.

**Exclusion Criteria:** Patients with history of previous neck surgery, on chemotherapy or any other oncology treatment before USG assessment, recurrent cases of any tumour were excluded from the study.

Data Collection Procedure: After permission from local ethical review committee, total number of 168 patients referred by clinician to the radiology department fulfilling the inclusion criteria were selected. After taking informed consent, ultrasonography of neck was performed. Each USG findings were interpreted by one consultant radiologist (at least 5 years of experience) and were looked for malignant lymph nodes. Malignant lymph nodes on ultrasonography were labeled when there was presence of contour irregularity, hypo echogenicity, size >10 mm, absence of calcification, round shape and abnormal vascular pattern on grey scale ultrasonography, high resolution pulsed and color Doppler ultrasonography. Benign features were considered to be the opposite of these findings. Ultrasound findings were compared with histopathology findings. Malignant lymph nodes on histopathology were confirmed by using light microscopy the histological examination was done. Using H & E paraffin embedded tissue was cut in 4mm thin slides. When metastatic cells from any primary site were known it was labeled as malignancy of lymph node. All this data including the demographic data (age, gender) was recorded on a specially designed proforma.

**Data Analysis:** Collected data was analyzed through computer software SPSS 20.0. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography for diagnosis of

malignancy of lymph node in newly diagnosed head and neck carcinomas patients.

## Results

Age range in this study was from 20-80 years with mean age of  $50.33\pm11.98$  years. Majority of the patients 92 (54.76%) were between 20-50 years of age. Out of these 168 patients, 98 (58.33%) were males and 70 (41.67%) were females with ratio of 1.4:1 (Figure III). Mean duration of disease was  $6.93\pm1.74$  months. The most common site was oral cancer (32.7%), followed by thyroid cancer (20.8%), larynx & pharynx cancer (17.9%), salivary gland cancer (14.9%) and nose and paranasal sinuses (13.7%). Table 1

All the patients were subjected to USG and found that 83 were True Positive and 08 were False Positive. Among 77, USG negative patients, 07 (False Negative) had malignant lymph nodes on histopathology whereas 70 (True Negative) had benign lymph nodes on histopathology (p=0.0001) as shown in Table IV. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients was 92.22%, 89.74%, 91.21%, 90.91% and 91.07% respectively. Table 2

#### Table 1: Demographics of Patients

	No. of Patients	%age
Total cases	168	100%
Age (years)	$50.33 \pm 11.98$	
20-50	92	54.76
51-80	76	45.24
Gender		
Male	98	58.3%
Female	70	41.7%
Duration of disease	$6.93 \pm 1.74$	
(months)		
<b>≤6</b> months	68	40.48
>6 months	100	59.52
Site of cancer		
Oral	55	32.74
Nose and paranasal sinuses	23	13.69
Salivary glands	25	14.88
Larynx and pharynx	30	17.86
Thyroid	35	20.83

**Table 2:** Diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients, taking histopathology as gold standard.

	Positive result on Histopathology	Negative result on Histopathology
Positive result on USG	83	08
Negative result on USG	07	70

Sensitivity: 92.22%

Specificity: 89.74%

**Positive Predictive Value (PPV):** 91.21% **Negative Predictive Value (NPV):** 90.91%

Diagnostic Accuracy: 91.07%

### Discussion

In patients with head and neck carcinomas, determining nodal status is critical since it predicts prognosis and aids in treatment selection. The presence of a unilateral metastatic node reduces the 5-year survival rate by 50% in patients with established head and neck carcinomas, but the presence of bilateral metastatic nodes reduces the 5-year survival rate to 25%. The annual incidence of HNCC varies by region, ranging from 0.03 to 3.5 cases per 100,000 persons. Patients who reside near the equator are more likely to present at a younger age than those who live farther away.

The highest rate of HNCC has been observed in Australia, where nonmelanoma skin cancer occurrences as high as 1.17 per 100 have been reported, a rate 5 times higher than all other malignancies combined. The high prevalence is most likely attributable to the vast number of light-skinned persons who have spent a lot of time in the sun in this area.<sup>12-16</sup>

In head and neck carcinomas, metastatic cervical lymph nodes are frequently site specific in relation to the initial tumor's location. As a result, examining the distribution of metastatic nodes in individuals with an unknown underlying tumour may provide insight on the primary tumor's location. Furthermore, the presence of metastatic nodes in an unusual location suggests that the underlying tumour is physiologically more aggressive.<sup>17</sup>

Apart from metastases, lymphoma is a frequent malignancy with a high rate of head and neck involvement. Lymphoma of the cervical lymph nodes is difficult to distinguish clinically from other types of lymphadenopathy, such as metastatic nodes. Because treatment choices differ, it's critical to determine the nature of the disorders. Cervical lymph node evaluation is a crucial procedure for patients with head and neck malignancies since the results influence prognosis and treatment options.<sup>18</sup>

Ultrasonography can be performed to determine the location, number, size, internal features, and vascularity of the cervical lymph nodes in these patients. The ultrasonography criteria for metastatic lymph nodes, on the other hand, remain debatable. Ultrasound has a wellestablished role in the diagnosis of cervical lymphadenopathy. Particularly, it is more sensitive than clinical examination (96.8% vs. 73.3%, respectively) in cases of HNCC with post-radiation neck-fibrosis.<sup>19-22</sup>

We have conducted this study to determine the diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients, taking histopathology as gold standard. Age range in this study was from 20-80 years with mean age of  $50.33 \pm 11.98$  years. Majority of the patients 92 (54.76%) were between 20-50 years of age. Out of these 168 patients, 98 (58.33%) were males and 70 (41.67%) were females with ratio of 1.4:1. All the patients were subjected to USG and found that 83 were True Positive and 08 were False Positive. Among 77, USG negative patients, 07 (False Negative) had malignant lymph nodes on histopathology whereas 70 (True Negative) had benign lymph nodes on histopathology (p=0.0001). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography for diagnosis of malignancy of lymph node in newly diagnosed head and neck carcinomas patients was 92.22%, 89.74%, 91.21%, 90.91% and 91.07% respectively. In patients with head and neck tumours the prevalence of lymph node is reported as 18.65%.

Furthermore, several research have been conducted in order to determine the role of USG, with one study reporting a sensitivity of 95.24 percent and a specificity of 100 percent for USG in detecting lymph node cancer. In a meta-analysis published in 2012, researchers discovered that USG had a sensitivity of 66 percent and a specificity of 78 percent for diagnosing lymph node cancer. Suresh et al., discovered 85.4 percent sensitivity, 90 percent specificity, 81.8 percent positive predictive value, and 87.50 percent negative predictive value.<sup>8-11</sup>

The sensitivity of B-mode sonography was 98 percent (95 percent CI, 94-100 percent), the specificity was 59 percent (42-76 percent), and the accuracy was 84 percent (76-91 percent). Elastography had an accuracy of 89 percent (83-96 percent), sensitivity of 83 percent (73-93 percent), and specificity of 100 percent (100-100 percent). Sensitivity was 92 percent (85-100 percent), specificity was 94 percent (85-100 percent), and accuracy was 93 percent (88-98 percent) in the combined evaluation. Another study found that Diag-

nostic Accuracy 0.83 of B mode Ultrasonography vs Histopathology had a sensitivity of 78.57 percent (Confidence Interval 49.21 percent - 95.09 percent) and a specificity of 84.62 percent (Confidence Interval 65.11 percent - 95.55 percent) with a sensitivity of 78.57 percent (Confidence Interval 49.21 percent - 95.09 percent). Furthermore, ultrasonic elastography was shown to have a sensitivity of 71.43 percent (Confidence Interval 41.92 percent - 91.43 percent) and a specificity of 92.31 percent (Confidence Interval 74.83 percent -98.83 percent) when compared to Histopathology with a Diagnostic Accuracy of 0.85.23, 24

Haberal et al. found that 22 patients had positive lymph nodes after pathologic examination. Palpation accuracy, sensitivity, specificity, NPV, and PPV were 64, 85, 74, 78, and 75 percent, respectively. Sensitivity, specificity, NPV, PPV, and accuracy were 72, 96, 80, 94, and 85 percent for USG and 81, 96, 85, 90, and 87 percent for CT, respectively.<sup>25</sup> Anand et al., examined metastatic lymph nodes in 100 patients with various head and neck malignancies and compared the findings of clinical examination, USG, and CT, as well as HPE of the neck dissection tissue.<sup>26</sup>

Saafan et al. studied 100 patients with histologically confirmed noncutaneous HNSCC in a group setting. Every patient had their cervical lymph nodes clinically examined, as well as CT scans of the neck with intravenous contrast and grey scale ultrasound scanning of the neck. The sensitivity, specificity, and accuracy of clinical palpation for cervical lymph nodes were 71.43 percent, 75.86 percent, and 72.7 percent, respectively. Clinical palpation was found to be inferior to a CT scan. CT had a sensitivity of 82.9 percent, a specificity of 89.66 percent, and an accuracy of 84.85 percent. The best modality for assessing metastases in cervical lymph nodes was determined to be USG. The accuracy was 95.96 percent, with a sensitivity of 97.1 percent, a specificity of 93 percent, and a sensitivity of 97.1 percent. The PPV was 97.1 percent and the NPV was 97.1 percent.<sup>27</sup> The diagnostic power of the combined evaluation was higher than that of the individual evaluations based on accuracy and area under the ROC curve. This shows that when B-mode sonography, which has a high sensitivity, and elastography, which has a high specificity, are used together, the examination will be most effective. Sonography practitioners should, however, apply both approaches in real time in clinical practise.<sup>2</sup>

## Conclusion

This study concluded that the ultrasound is a highly sensitive and accurate non-invasive modality for detecting malignant lymph node in head and neck cancers, and has not only dramatically improved our ability of accurate detection of lymph node metastasis in head and neck cancers patients but also improved patient care by pre-operatively planning of the proper management of patients. So, we recommend that USG should be used routinely as a prime modality for accurate detection of cervical lymph node metastasis in head and neck cancers which will result in proper pre-operative planning for these particular patients.

Conflict of Interest:	None
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