

*Type of study: Original study*

# **Association of the Depth of Invasion with Lymph Node Metastasis in Oral Squamous Cell Carcinoma Patients - A Retrospective Study**

**Aklesha Behera<sup>1</sup>, Hannah.R<sup>2</sup>, Abilasha Ramasubramanian<sup>3</sup>, Pratibha Ramani<sup>4</sup>,**

<sup>1</sup>Research Associate, Dental Research Cell, <sup>2</sup>Senior Lecturer, Department of oral pathology, Saveetha Dental College and Hospitals, <sup>3</sup>Reader, Department of Oral Pathology, <sup>4</sup>Professor, Department of Oral Pathology, <sup>5</sup>Reader, Department of Oral Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

## **Abstract**

Oral squamous cell carcinoma is the most common oral malignancy representing upto 80 % to 90% of all malignancies of oral cavity. In Indian population, it ranks 3rd of all carcinomas. Dietary factors and external factors like tobacco, smoking and alcohol consumption are the major causes for progression of oral squamous cell carcinoma. Histopathologically, the tumor progression is assessed by TNM staging. It is the most common and widely practised histomorphological evaluation of tumor progression. Depth of invasion is also another tool for evaluating tumor progression in OSCC and is also used widely in every clinico histopathological slide evaluation and diagnosis. In this study, a correlation was made between depth of invasion and nodal metastasis. All the data was collected after checking 86,000 patient records. Details such as age, sex, pathological TNM staging, depth of invasion and cases with nodal metastasis were tabulated. Association was made using the IBM SPSS version 20.0. Pearson chi square test did not show any significant association between depth of invasion with nodal metastasis. Other factors like pattern of invasion, tumor differentiation, site of the lesion as well as the age of the patient has to be taken into consideration for future assessment.

**Keywords:** *Oral squamous cell carcinoma, depth of invasion, metastasis, Oral cancer, lymph node.*

## **Introduction**

Oral squamous cell carcinoma is the most common oral malignancy representing upto 80 to 90 % of all malignancies<sup>1</sup>. In India, oral cancer represents more than 50% of all cancer cases<sup>2</sup>. Population of India is mostly habituated with consumption of tobacco and tobacco related products, leading to higher prevalence and even higher incidence rates of cancer. According to a study

conducted, the global estimate of oral cancer accounts for 2% to 4% of all cancers<sup>3</sup>. Annually, incidence of oral cancer around the world is 275000 cases and 128000 deaths annually<sup>4</sup>. Etiological factors that lead to development of oral cancer are multifactorial but it is majority due to environmental and lifestyle factors. Consumption of tobacco in the form of smoking or chewing leads to oral cancer<sup>5</sup>. Tobacco is consumed in many forms. Along with habits, other etiological factors are virus infection, candida, syphilis<sup>5 6</sup>.

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### **Corresponding author**

**Hannah.R**

Senior Lecturer, Department of Oral Pathology,  
Saveetha Dental College and Hospitals,  
Saveetha Institute of Medical and technical Sciences ,  
Saveetha University, 162 , PH Road , Chennai 600077,  
TamilNadu , India  
Email Id:hannahr.sdc@saveetha.com

OSCC has unpredictable behaviour, due to which it's difficult to correctly measure the invasion of OSCC. One such method of assessing the prognosis is by TNM staging. TNM staging is used to estimate the clinical and survival outcome of the patient. Along with these conventional methods, newer methods are in vogue. Such methods are detection of OSCC using immunohistochemistry, serum and saliva metabolomics

7,8 9 10 11 11,12 13 14 15 6,16 Histopathologically, OSCC is graded based on the proportion of tumor resembling normal oral epithelium and the amount of keratin production<sup>17</sup>. The lesions are classified as well differentiated, moderately differentiated, and poorly differentiated<sup>18, 66,19,20,21,24</sup>

Recent studies hypothesize that histomorphological parameters like DOI (Depth of invasion) may be used as a prognostic factor in patients with OSCC. All the cases of OSCC should be neatly photographed and documented clinically and histologically for future reference<sup>21</sup>. The aim of the study is to associate the depth of invasion with lymph node metastasis and to find out which method is better for cancer prognosis.

### Materials and Methods

A retrospective study was conducted in the department of oral pathology. A total of 36 OSCC patient details were retrieved after assessing 86,000 patient details. On receiving approval from the scientific review board of Saveetha Dental College, the data of OSCC patients were collected. Cross verification of the cases were done by correlating reports and photographs. Both internal and external validity were applicable. Data collection was done between march 2019 till march 2020 and tabulated in the excel sheet. Demographic data was collected along with the clinical details of the tumor. Variables like clinical details, depth of invasion, TNM staging of OSCC, age of the patient, sex, site of the lesion, histopathological evaluation, depth of invasion and lymphnode metastasis were considered. The confidential details of OSCC patients were masked. After procuring the patient details, data was tabulated in excel sheets. The data was then exported to SPSS and the appropriate statistic was done. Chi square test was used to associate the depth of invasion with lymph node metastasis.

### Results and Discussion

The results of the study show that the predominant number of oral squamous cell carcinoma cases belong to 40 -60 years of age (Figure1). Males were most commonly affected than females (Figure 2). The most common habit that was observed was pan chewing. Histopathological slides showed that most of the cases showed 6-10mm depth of invasion (Figure 3). On associating the depth of invasion with gender, 6-10mm depth of invasion was seen in the majority of male and female population. But > 10mm depth of invasion was

more common in males than in females. (Figure 4). On assessing the lymph node involvement, 55.5% of the cases showed lymph node metastasis and 44.44% did not show any metastasis(Figure 5). On associating the lymph node involvement with depth of invasion, it was found that 60% of the cases with lymph node involvement had 6-10mm DOI. On the other hand only 20% of the cases with DOI <6mm had lymph node involvement. On the contrary 43.75% of the cases with 6-10mm DOI did not show lymph node involvement. Chi square analysis also did not show any statistical significance with  $p = 0.608$  ( $p$  value > 0.05) (Figure 6).

Head and neck cancers constitute for approximately 5% of all malignant tumors in the body. According to the present study, males are affected more than females (80.5%, 19.5%). In the majority of prevalent studies relating to OSCC, almost most of the authors have found similar results. OSCC is seen to affect males six times more than the females<sup>1</sup>.

The results of the previous studies are in accordance with the present study. The reason for higher male predilection could be due to external factors like the tobacco consumption habit, smoking and alcoholism. Males have a higher probability of consumption of tobacco, mostly in the South east Asian population where tobacco in any and all forms is easily available. Even though tobacco related products are easily available and a person doesn't need any document to procure such products, consumption of tobacco products and alcohol are comparatively lesser amongst the female population. It could be due to social stigma attached against females. Patients had a habit of tobacco consumption. Studies have proven that tobacco consumption is directly related to OSCC. Fabio et al found that young patients who did not have tobacco consumption habits suffered from OSCC<sup>22</sup>.

The prognosis for OSCC can be predicted by various histomorphological parameters. TNM staging is determined by DOI, nodal involvement and distant metastasis. It is the most common and frequently applied parameter for assessing tumor progression. Other histomorphological parameters like depth of invasion is an independent prognostic factor in early detection of OSCC. In previous studies, authors have found the DOI of 4 mm to be common, but in the present study, 6 -10 mm was the commonest depth of invasion. In a study conducted by Inne J denn Toom et al, DOI having < 3.4 mm were having distant metastasis<sup>23</sup>. Meta-

analysis studies have found that DOI > 4mm leads to nodal metastasis<sup>18</sup>. The cut off value in Inne et al study was found to be 3.4 mm<sup>23</sup>. In the present study, an association was made between depth of invasion and involved and not involved lymph nodes, there was no possible significance found. Association was made between depth of invasion among males and females ( *p* value = 0.608). A Chi square test was performed between the two variables. No significant association was seen ( *p* value = 0.851)

In the current study, a correlation between DOI being > 4mm would lead to nodal involvement was not quantified. Presence of cases with DOI > 10 mm with no nodal metastasis is observed, whereas in cases

where DOI is < 6mm with nodal metastasis is observed as well. In the present study, we have only considered DOI and pTNM to study the tumor invasiveness. In a previous study conducted by Kailiu Wu<sup>24</sup> along with depth of invasion > 4mm, he included other variables like neurovascular invasion, trabes pattern, poor differentiation and old age for lymph node relapse and poor prognosis. Hence it would be safe to conclude that just depth of invasion isn't sufficient enough to rule out the possibility of lymph node metastasis. Other factors like type of invasion, extent of neurovascular invasion, type of epithelial or tumor differentiation, site of the lesion as well as the age of the patient has to be taken into consideration.

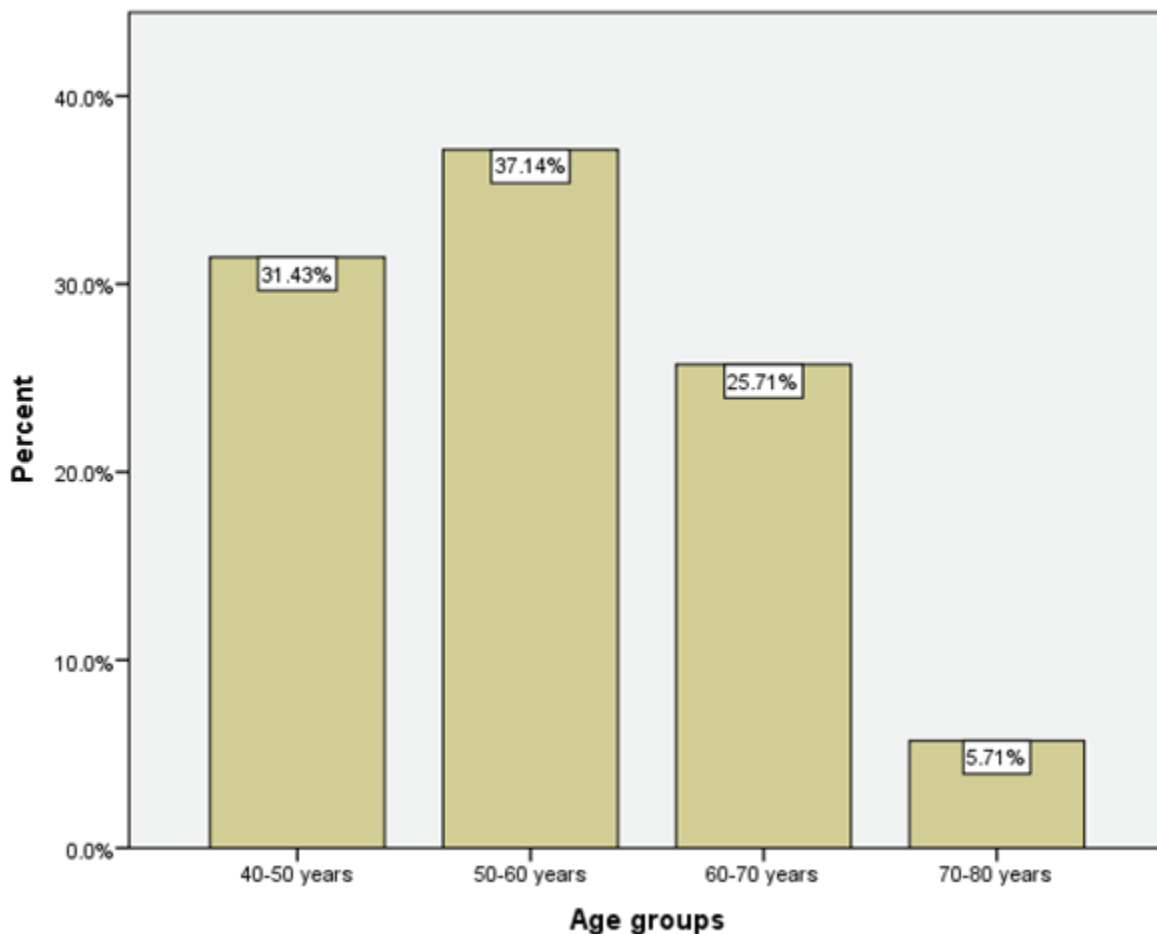


Figure 1: Bar graph depicts the age distribution of oral squamous cell carcinoma patients. X axis depicts the age groups and Y axis depicts the percent of cases. 37.14% of the cases belong to 50-60 years of age, 31.43% 40-50 years, 25.71% 60-70 years and 5.71% 70-80 years of age.

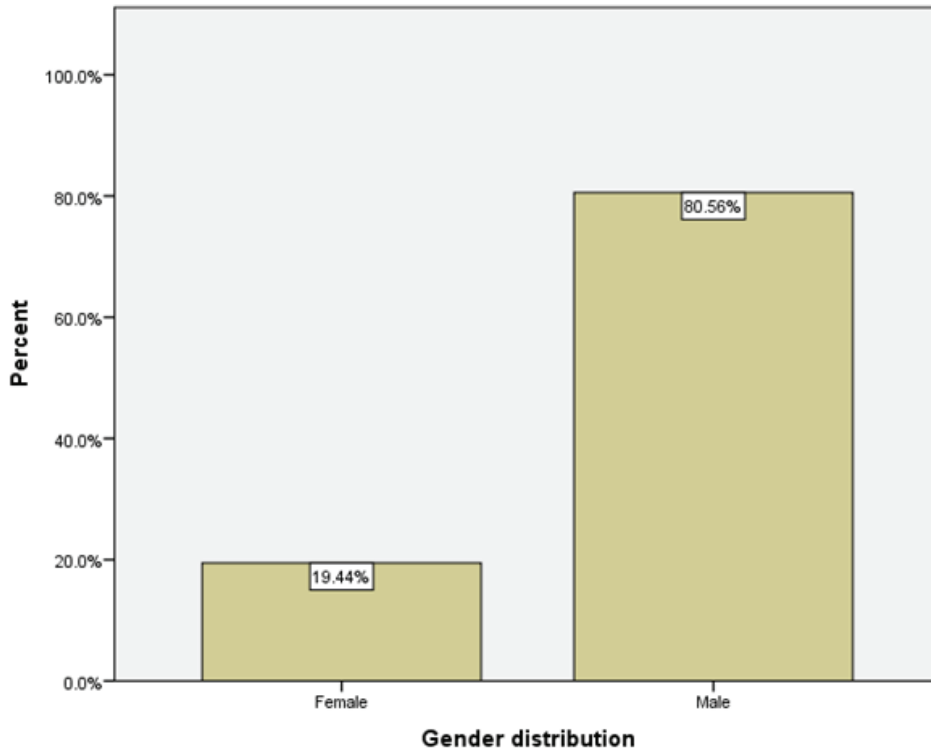


Figure 2: Bar graph depicts the gender distribution of oral squamous cell carcinoma patients. X axis depicts the distribution of males and females and Y axis depicts the percentage. 18.56% of the population are males and 19.44% are females.

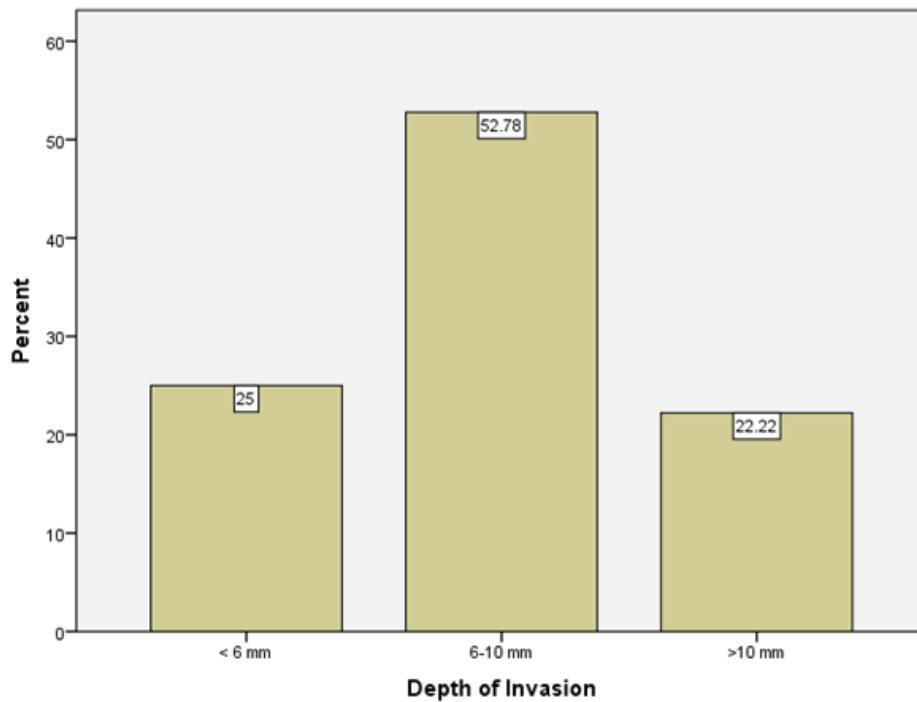


Figure 3: Graph depicting the depth of invasion in oral squamous cell carcinoma patients. X axis depicts the depth of invasion and Y axis depicts the percentage of cases. 52.78% of cases have DOI of 6-10mm, 25% have <6mm and 22.22% have > 10 mm.

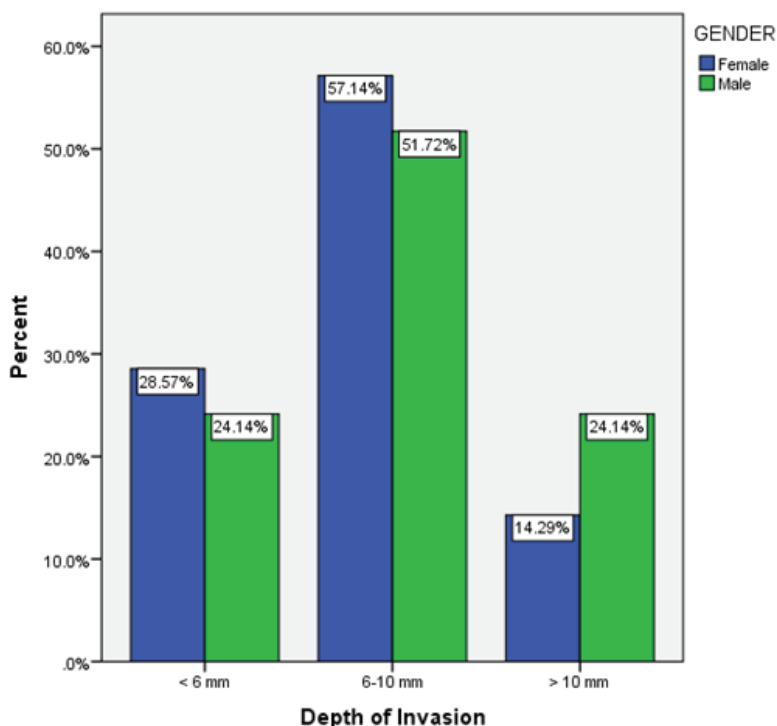


Figure 4: The graph depicts an association between gender and depth of invasion in oral squamous cell carcinoma patients. X axis depth of invasion and Y axis depicts the percentage of cases based on gender. 6-10 mm depth of invasion was seen in the majority of male and female population. But > 10mm depth of invasion was more common in males than in females. However chi square test did not show any statistical significance with  $p = 0.851$  ( $p > 0.05$ ).

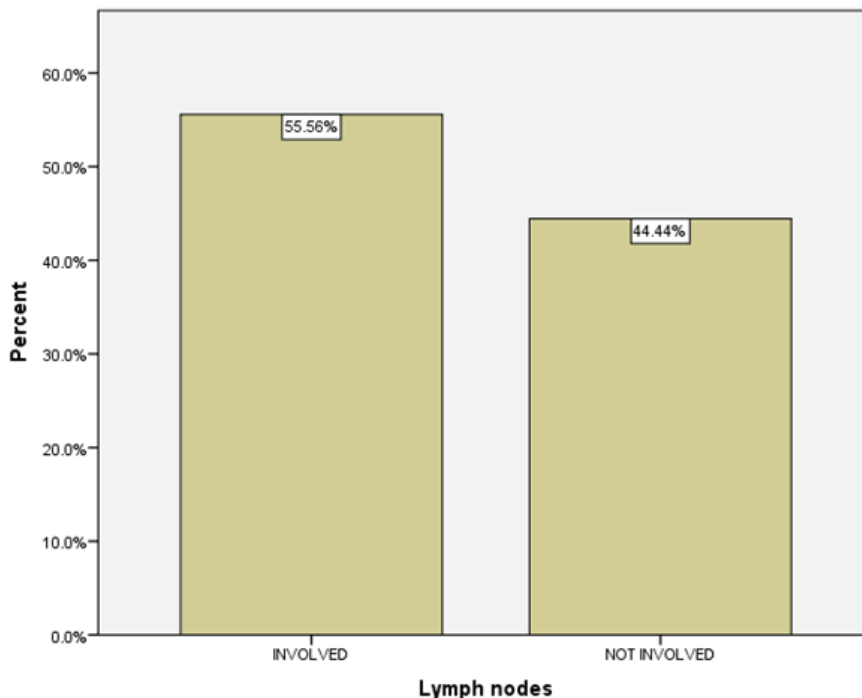
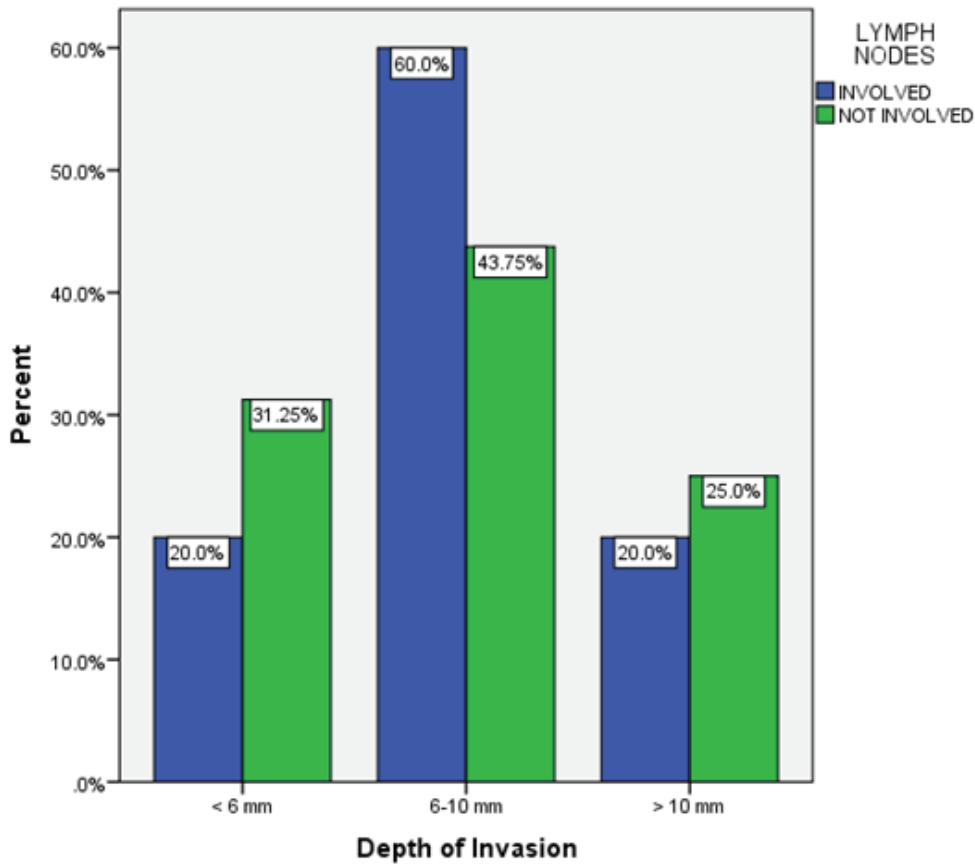


Figure 5: Bar graph depicts the frequency distribution of involved and not involved lymph nodes in oral squamous cell carcinoma patients. X axis depicts the lymph node involvement and Y axis depicts the percentage. 55.56% of the cases show lymph node involvement, whereas 44.44% do not show any involvement of lymph nodes.



**Figure 6:** Bar graph depicts the association between depth of invasion and lymph node involvement. X axis depicts the depth of invasion and Y axis the percentage of lymph node involvement. Blue depicts the involved lymph nodes and green depicts the uninvolved lymph nodes. 60% of the cases with lymph node involvement had 6-10mm DOI. However, Chi square analysis did not show any statistical significance with  $p = 0.608$  ( $p$  value  $> 0.05$ ).

### Conclusion

It was concluded from this study that depth of invasion is a fine histomorphological tool for assessing tumor invasiveness, but it is not enough to correlate with the nodal metastasis. Some cases with depth of invasion  $>10$  mm had no nodal metastasis and some cases had nodal metastasis even though the depth of invasion was less than  $< 6$ mm. Other factors like pattern of invasion, tumor differentiation, site of the lesion as well as the age of the patient has to be taken into consideration for future assessment.

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**Ethical Clearance:** It is taken from “Saveetha Institute Human Ethical Committee” (Ethical Approval Number- SDC/SIHEC/2020/DIASDATA/0619-0320)

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