

# Incidence and Diagnosis of Ampullary Carcinoma in Dhulikhel Hospital, Kathmandu University Hospital

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## ABSTRACT

### Background

Endoscopy from a suspected ampulla of vator may establish an early preoperative diagnosis of ampullary carcinoma. However, information regarding the diagnostic accuracy of this procedure is limited and variable.

### Objective

To study the preoperative diagnostic accuracy of Endoscopic/ERCP appearance of ampullary tumors with that of endoscopic biopsy.

### Method

Among patients who were performed endoscopy during a one year period; a suspicious ampulla of vator was seen in 44 cases. Endoscopic biopsy specimens were classified into four groups based on the degree of epithelial atypia: group 1 (no evidence of malignancy), group 2 (presence of dysplasia), group 3 (suspicious of malignancy) and group 4 (positive for malignancy). In each case comparison was made between the pre-endoscopic biopsy clinical diagnosis and endoscopic appearance.

### Result

Endoscopic biopsy diagnosis of malignancy (group 4) were seen in 22 cases, Suspicious of malignancy (group 3) in 3 cases, dysplasia (group 2) in 9 cases and no evidence of malignancy (group 1) in 10 cases. Pre-endoscopic diagnostic accuracy of endoscopy/ ERCP was 50% compared to the diagnosis by biopsy.

### Conclusion

Diagnostic accuracy of endoscopy/ERCP was 50% compared to the diagnosis by biopsy. A diagnosis of non malignancy in the forceps biopsy material does not rule out the presence of cancerous foci in ampullary neoplasms.

## KEY WORDS

*Ampulla of Vator, Ampullary carcinoma, Diagnostic accuracy, Dysplasia, Endoscopic biopsy, ERCP*

## INTRODUCTION

Ampullary carcinoma is the term employed for any malignant epithelial tumor centered in the ampulla of Vater. Its origin is from the intestinal-type mucosa of the ampullary region, often on the preexisting villous adenoma or villoglandular polyp.<sup>1</sup> The incidence of ampullary tumors has recently increased because of the widespread use of endoscopy for health surveillance. A wide variety of lesions like adenocarcinomas, adenoma, neuroendocrine tumors as well as inflammatory tumors, lipoma, fibroma arise at the ampulla of Vater.<sup>2</sup> Endoscopy is the most valuable method of identifying ampullary carcinomas. Ampullary cancers account for 0.2% of gastrointestinal cancers and approximately 7% of all periampullary cancers.<sup>3</sup>

The ampulla of Vater consists of papilla, common channel, distal common bile duct and the distal main pancreatic duct. Most ampullary carcinomas are adenocarcinomas.<sup>4</sup> Clinically, most individuals are over the age of 60, and there is a slight male predominance.<sup>5</sup>

Dhulikhel hospital is one of the tertiary centers for endoscopic biopsy and ERCP and the number of endoscopic biopsy and suspicious ampullary carcinoma cases are frequently seen. The purpose of this study was to study the preoperative diagnostic accuracy of Endoscopic/ERCP appearance with that of endoscopic biopsy in all cases with suspicion of tumor at ampullary region.

## METHODS

The files of the Departments of Pathology at Dhulikhel Hospital, Kathmandu university Hospital were searched for cases of Endoscopic biopsy taken in a year (1 August 2017 to 30 July 2018). Suspicious biopsies taken from ampulla was analyzed. The slides were reviewed.

Endoscopic biopsy specimens were classified into three groups based on the degree of epithelial atypia: group 1 (no evidence of malignancy), group 2 (presence of dysplasia), group 3 (suspicious of malignancy) and group 4 (positive for malignancy). In these cases comparison were made between the clinical diagnosis and endoscopic biopsy appearance.

The defining features of malignancy were nuclear atypia with enlarged, hyperchromatic nuclei that lose their basal orientation and no longer maintained nuclear polarity. There were usually prominent nucleoli as well as mitotic figures in the neoplastic epithelium with basement membrane invasion. Dysplasia is defined as loss in uniformity and architectural orientation characterized by pleomorphism, nuclear hyperchromasia, mitosis and loss of polarity without invasion of basement membrane. Suspicious of malignancy were the cases that show dysplasia with suspected areas of invasion.

Due to the lack of Whipple's operation performed in this institution the study is unable to include the definitive histological diagnosis.

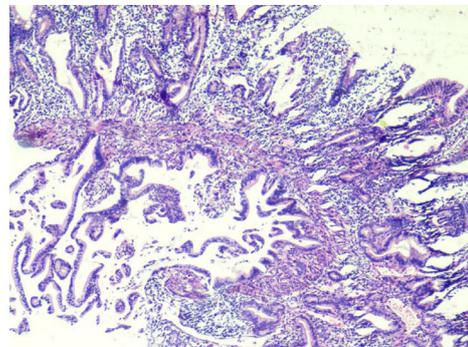
## RESULTS

Among patients referred to the institute for endoscopy/ERCP, a suspicious carcinoma of ampulla of vator was seen in 44 cases. Endoscopic biopsy diagnosis of malignancy (group 4) was seen in 22 cases, Suspicious of malignancy (group 3) in 3 cases, dysplasia (group 2) in 9 cases and no evidence of malignancy (group 1) in 10 cases. Diagnostic accuracy of endoscopy/ERCP was 50% compared to the diagnosis by biopsy.

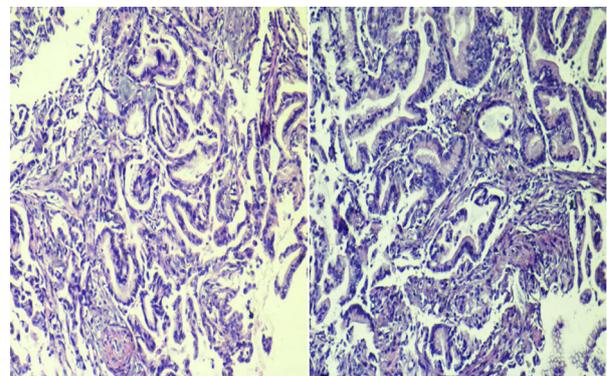


**Figure 1.** Endoscopic image of suspected Carcinoma of Ampulla

The average age in the malignancy group was 52.75 years (range, 31 to 76 y), and in the Dysplasia group was 58 years (range, 27 to 78 y). The male-to-female ratio was 0.69:1.



**Figure 2.** 200x ampullary adenocarcinoma with invasion



**Figure 3.** 400x magnification of adenocarcinoma in Ampulla

## DISCUSSION

Primary ampullary tumors are rare, with an incidence of approximately four to six cases per million population. They are responsible for 20 percent of all tumor-related obstructions of the common bile duct.<sup>6,7</sup>

This study demonstrated that the diagnostic accuracy of endoscopy was 50% for endoscopic imaging. Study by Lee et al. had accuracy of 67.3%.<sup>2</sup> Concordance of endoscopic and pathologic diagnoses according to the study by Elek et al. was 69 percent on average which increased to 83 percent after including repeated biopsies.<sup>8</sup> Accuracy of the study was less than other studies. The study by Lee et al. and other authors had compared the endoscopic imaging diagnosis and initial biopsy with that of surgically resected specimens.<sup>2,6</sup>

A well trained endoscopist might be able to determine the type of a papillary alteration by its macroscopic appearance and consistency when taking forceps biopsy. There are series with more accurate diagnoses by endoscopic appearance than by histology from the endoscopic biopsy.<sup>6,9</sup> Correlation of the pathologic features of biopsy specimens with endoscopic appearances may result in more accurate diagnoses.<sup>10</sup>

The most frequent debate between pathologist and endoscopist is whether the alteration is inflammation or adenoma. If the biopsy is too small the pathologist is prone to diagnose inflammation, because the dysplasia cannot be established with certainty and a concomitant inflammation is always present in adenomas. Diagnosis of adenomas is based on the typical morphological features, but may be difficult if the specimen is fragmentary because it makes impossible to verify the lobular structure of the alteration.<sup>6</sup>

The diagnosis of an ampullary carcinoma is established by a combination of endoscopic, radiologic, and histologic features. Ampullary carcinomas are thought to arise from ampullary adenomas, a premalignant precursor lesion displaying the adenoma-carcinoma sequence.<sup>11</sup>

The average age at diagnosis of sporadic ampullary carcinomas is 60 to 70 years old.<sup>12,13</sup> According to study by Agoff et al. the average age in the carcinoma group was 64 years.<sup>14</sup> Our study showed the mean age group of 52.75.

The male-to-female ratio in the study of Agoff et al. was 1.6:1.<sup>14</sup> The result was not similar to this study. Our study showed marked female dominance in incidence.

The most important factor during biopsy is the selection of accurate biopsy sites. Because ampullary cancer usually derives from the ampullary portion of the bile duct and pancreatic duct or the common channel, a forceps biopsy specimen should be obtained from the bile duct and pancreatic duct orifice.<sup>6</sup>

Endoscopic/ERCP obtained forceps biopsies from suspicious papillas can establish an early and immediate preoperative diagnosis. However in some cases it is very difficult even for experienced pathologists to distinguish invasive carcinomas from non-invasive lesion.<sup>15</sup>

This high rate of missed malignancy from endoscopic forceps biopsies (pitfalls) may be due to a forceps biopsy sample composed of the overlying benign mucosal lesions missing the deeper located carcinomas.<sup>16</sup> Other reasons for missed malignancy cases are due to inadequate sample because of the difficult biopsy technique in the second portion of the duodenum. Similarly Inability to diagnose the invasion may be another cause. Well differentiated carcinomas are sometimes difficult to differentiate with normal which might be missed. Similarly Inflammation may resemble reactive atypia.

Since this is a single center study limited number of patients and limited number of pathologist are involved in diagnosis and discussion of cases. Greater number of pathologist and multiple center study would have made this a better study. Due to the lack of Whipple's operation performed in this institution the study is unable to include the definitive histological diagnosis.

## CONCLUSION

Diagnostic accuracy of endoscopy/ERCP was 50% compared to the diagnosis by biopsy. A diagnosis of non malignancy in the forceps biopsy material does not rule out the presence of cancerous foci in ampullary neoplasms. The accuracy of clinical diagnosis and endoscopy is limited. This limitation must be considered when evaluating the optimal management of patients with suspected ampullary tumor.

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