

## Original Article

## Diagnostic Yield of Brush Cytology for Biliary Strictures During ERCP

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## Abstract

**Objective:** The aim of this study was to assess the yield of brush cytology in patients with biliary strictures detected at ERCP when a systematic approach is used and when a dedicated pathologist performs the cytological analysis.

**Methods:** A retrospective study was conducted to assess the accuracy of diagnostic brush cytology during ERCP for biliary stenosis. The study included patients with biliary strictures identified during ERCP who experienced biliary brushing cytology. We reviewed all ERCPs carried out from January, 2021 to June, 2024 in the department of Gastroenterology at Arif Memorial Teaching Hospital Lahore and Fatima Memorial Hospital Lahore. During a standard ERCP, a brush specimen was collected, and the cytology sample was promptly transferred to a glass slide by the nursing staff, who smeared the cellular material directly from brush onto the slide. The slides were then immersed in a fixative (alcohol). Subsequently, a dedicated pathologist performed the cytological analysis and categorized the samples in 3 categories: positive for malignancy, negative for malignancy, or invalid.

**Results:** A total of 126 patients underwent brushing for cytology in strictures seen at ERCP. There were 44 females and 82 males; 33.3% of the patients were between 45 and 65 years of age and 66.7% were older than 65 years. Overall sensitivity was 62.0% (78.0% in males and 53.0% in females).

**Conclusion:** Study concluded that brushing the biliary strictures for cytology is a sensitive method for the diagnosis of biliary malignancies. Using a rapid fixing technique and single dedicated pathologist reviewing the slides appears to be the reason for this high yield.

**Keywords:** Biliary strictures, ERCP, brush cytology, diagnostic yield, dedicated pathologist.

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## Introduction

Biliary duct narrowing is one of the most common problems that is observed during endoscopic retrograde cholangiopancreatography (ERCP) procedures, especially in patients with obstructive jaundice.<sup>1</sup> These strictures may originate from a group of causes, like cancerous neoplasms, benign inflammatory conditions, iatrogenic injuries, and primary sclerosing cholangitis.<sup>2</sup> A precise and timely diagnosis of these strictures is must for the purpose of fashioning a suitable intervention. While this approach will contribute to maximizing patient outcomes, it will also ensure the avoidance of needless, invasive procedures.<sup>3</sup>

The technique of brushing cytology was introduced to ease up the tissue getting during pathological evaluation by having less load on the technician's procedures, the safety conferred on the technician, and the fact that

the material is easily available to the technician. During the course of the ERCP, the brush is introduced into the biliary ductal system through the endoscope channel, which has a working channel that in turn permits the collection of the cellular material from within the stricture. This method provides several benefits that alternative techniques, for instance, intraductal bile aspiration cytology, endobiliary forceps biopsy, and fine needle aspiration (FNA), don't have, like a less complex and safer operation as well as a larger area of the stenosis that is being sampled.<sup>4</sup>

Although cytology of brushing is a widely used diagnostic method, debate arises about the sensitivity of cytology of brushing to detect cancer within biliary strictures. Sensitivity, as reported in studies, has broadly oscillated around 40% of the measured values. This is likely due to a variety of factors, for instance, patients'

demographic differentiation, sampling as well as specimen management, and variability in pathologists' experience and its interpretation.<sup>5</sup>

Since giving the diagnosis at an early stage in the right way, thereby directing the therapeutic manner, is meanwhile believed to be very important, optimizing the amount of positive results by brush cytology is the focus of this retrospective study. Witnessing improvements in the sensitivity of methodology systems may bring in centralized pathologist reviews and standardized protocols on sampling, which promise the diagnosis of BR malignancies during ERCPs.<sup>6</sup>

In this manner, this study hopes to investigate the diagnostic role, brushed cytology plays in ERCP patients diagnosed with biliary strictures by means of systematic evaluation and centralized pathologist assessment. Our main purpose is to conduct the analysis of the results from a dedicated period to determine whether the brush cytology diagnostic sensitivity is increased through the optimized test conditions we are applying, with the final goal of producing more accurate diagnostics and care for those patients who have to be diagnosed with biliary malignancy.

## Methods

This retrospective study assessed the diagnostic accuracy of brush cytology in ERCP patients who were diagnosed with biliary stricture. The research was conducted in the Department of Gastroenterology, Arif Memorial Teaching Hospital Lahore and Fatima Memorial Hospital Lahore, from January, 2021 to June, 2024. Being enrolled in the study, patients met the following criteria: (1) they received ERCP at Arif Memorial Teaching Hospital between 01/2021 and 06/2024; (2) they were found to have biliary strictures; and (3) they were brushed to be sampled from the stricture site in the same ERCP. Only records with none or a little missing data and patients with no follow-up data or records were left out of the analysis. The records and individual reports of compatible patients were examined retrospectively to assemble pertinent demographic and clinical data, which comprised age, gender, explanation of ERCP, outcomes of ERCP, cytology of brushes, and, if accessible, histological diagnoses. Data collection was carried out by personnel who had been trained and who guaranteed the accuracy and uniformity of this process. The cytology sampling was done during ERCP if biliary strictures were clearly visualized. A cytology brush was sneaked through the working channel of the duodenoscope and then carefully manoeuvred to the location of the stricture with the use of fluoroscopy. The brush was guided to designate the form and angles of sampling by brushing through the structure's surface. Care was undertaken to cover all possible areas of the stenosis. Immediately

after brush cytology, the nursing staff members transferred the cells obtained onto glass slides. The slides were dipped into the fixation solution (alcohol) to fix the cellular structure and ease diagnostic trails later. The slides prepared in the cytology lab were submitted to the pathology department, and each one was evaluated by a fortified pathologist who dealt only with gastrointestinal pathology. The pathologist performed the most comprehensive cytological analysis of the specimen, checking the arrangement of the cellular morphology, nuclear structures, and patterns. The cytological findings were classified in 3 categories: positive (malignancy), negative (benign), or invalid (due to an insufficiency of cellular material or technical artefacts). Descriptive statistics were applied to summarize the demographic and clinical parameters of the study population. The accuracy of the surface cytobrush in detecting malignancies in biliary strictures was computed with 95% confidence intervals. Subgroups of specific individuals were studied to analyze and get a clearer picture of the extent of interaction between gender and age groups. Statistical analysis was performed with SPSS 25.0, and a p-value <0.05 was considered statistically significant.

## Results

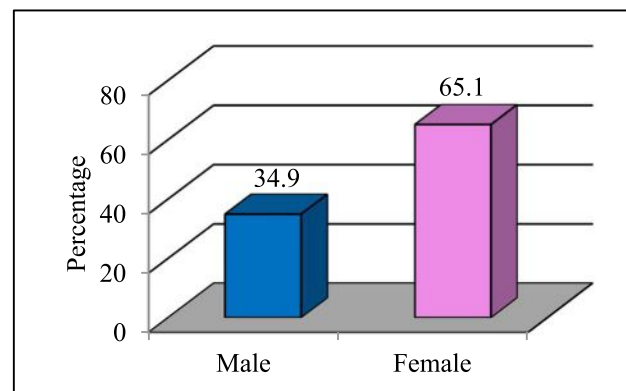
A total of 126 patients who underwent emergency endoscopic retrograde cholangiopancreatography (ERCP) with brush cytology for biliary strictures were included in the study. Among these patients, 44 (34.9%) were males and 82 (65.1%) were females. The age bracket encompassed patients from 45 to over 65 years, with 42(33.3%) between the ages of 45 and 65 years while 84(66.7%) above the age of 65 years.

**Table 1:** Frequency of allergies in a sample of 300 medical students in Lahore, Pakistan, in 2014

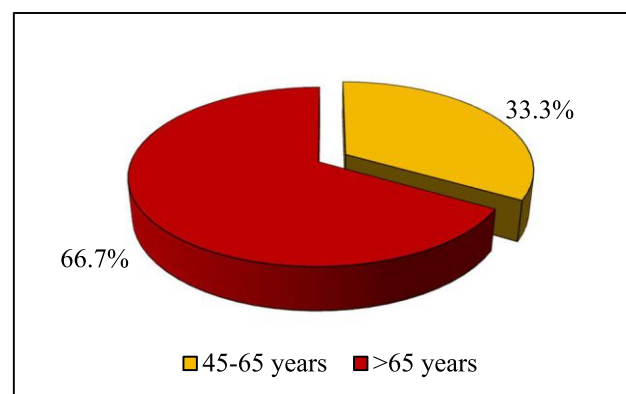
	Frequency	Percentage
<b>Gender</b>		
Male	44	34.9
Female	82	65.1
Total	126	100.0
<b>Age</b>		
45-65 years	42	33.3
>65 years	84	66.7
Total	126	100.0

The karyological picture of the cytology of the brush biopsy fragments varied. The dedicated pathologist classified the samples into three categories: positive for malignancy, negative for malignancy, or invalid. Out of 126 patients, 77 (61.1%) samples were diagnosed as malignant. Considering this, the brush cytology sensitivity was 62.0% with a 95% confidence interval of

44–80%.



**Figure 1:** Gender distribution of patients



**Figure-2:** Age distribution of patients

**Table 2: Karyological Findings in Cytology**

	Frequency	Percentage
Positive	77	61.1
Negative	39	31.0
Invalid	10	7.9
Total	126	100.0

**Table 3: Sensitivity calculation**

Metric	Value
Sensitivity	62.0%
95% Confidence Interval	44.0% - 80.0%

Subgroup analysis stratified by gender showed gender-specific effects on sensitivity. Male patients showed a sensitivity of 78% (95% CI, 60–96), while female patients showed a lower sensitivity of 53% (95% CI, 34–72).

**Table 4: Sensitivity by gender**

Gender	Sensitivity	95% Confidence Interval
Male	78.0%	60.0% - 96.0%
Female	53.0%	34.0% - 72.0%

**Discussion**

Biliary tract stenosis is a common finding in ERCP procedures performed on patients with obstructive jaundice. Accurate pathological diagnosis is crucial for guiding appropriate treatment and avoiding the need for more invasive diagnostic procedures. The current study was carried out to assess the diagnostic yield of brush cytology among patients with biliary strictures detected at ERCP. To acquire appropriate outcomes, a group of 126 patients was included in the study and found that most of the patients (65.1%) were females while 34.9% were males. But the findings of a similar study undertaken by Nur and coworkers (2022) exhibited different scenario that majority of the patients (58.0%) were males while 42.0% were females.<sup>7</sup>

The results of our study revealed that majority of the patients, accounting for 66.7%, were aged over 65 years while 33.3% were between 45 and 65 years old. Almost comparable results were reported by a study undertaken by Nawaz and associates (2013) that mainstream (56.0%) of the patients were more than 65 years old and 44.0% were between 45 and 65 years old.<sup>8</sup>

During the study, cytology results were evaluated and found that among patients, 61.1% samples were diagnosed as malignant (positive) and 31.0% as negative while only 7.9% as invalid. The findings of our study are almost comparable with a study conducted by Ding and collaborators (2021) who asserted that among 48 patients who underwent brush cytology during ERCP, 56.3% had positive results.<sup>9</sup> Another study conducted by Sethi and partners (2016) reported that among 162 patients who experienced brush cytology during ERCP, 35.8% patients had positive cytology.<sup>10</sup> However, a study performed by Nur and coworkers (2022) confirmed that 84.0% patients were diagnosed with malignancy through ERCP brush cytology.<sup>7</sup> Likewise, Sheikh and teammates (2014) found that 78% of cases in the brush group demonstrated malignancy.<sup>11</sup> A study done by Abbasi and fellows (2016) indicated that brush cytology was carried out in 88 patients and malignancy was detected in 25.0% patients.<sup>12</sup>

It was found during study that the brush cytology sensitivity was 62.0%. The findings of our study are comparable with a study conducted by Ödemis and comrades (2015) who asserted that sensitivity of the brush cytology in identifying malignancy was 62.4%.<sup>13</sup> However, other studies carried out by Nur et al. (2022)<sup>7</sup>, Archibugi et al. (2021)<sup>14</sup>, Keshari et al.<sup>15</sup>, Juvvala et al.<sup>16</sup> and Eiholm et al.<sup>17</sup> reported higher sensitivity of brush cytology than our study (ranging from 66% to 84%). While studies performed by Nawaz et al.<sup>8</sup>, Elzubier et al.<sup>18</sup>, Costa et al.<sup>19</sup>, Gorris et al.<sup>20</sup> and Navaneethan et al. (2015)<sup>21</sup> reported lower sensitivity for brush cytology compared to our study with sensitivity ranging from 45% to 59.4%.

Subgroup analysis of our study revealed significant gender-specific differences in sensitivity, with males showing a sensitivity of 78% compared to 53% in females. These differences could potentially be attributed to underlying biological variations between genders or to differences in sampling methods and techniques. Our study's findings are consistent with those of Nawaz and associates (2013), who also observed significant gender-specific differences in the sensitivity. In their study, males had a sensitivity of 64.3%, while females had a sensitivity of 56.1%.<sup>8</sup>

## Conclusion

Study concluded that brushing the biliary strictures for cytology is a sensitive method for the diagnosis of biliary malignancies. Using a rapid fixing technique and single dedicated pathologist reviewing the slides appears to be the reason for this high yield. Further studies are required to be conducted on large scale to assess the yield of brush cytology among patients with biliary strictures detected at ERCP.

**Limitations:** Whilst the study offers many valuable perspectives for those in power to consider, there are also several limitations that should be noted. First, a retrospective design of the study can introduce the biases such as selection bias or decreased accuracy of collected data, which is inherent to it. Moreover, small sample interferes with the ability of the authors to come out with general conclusions and to a certain degree can yield inconclusive results thereby reducing reliability. Furthermore, anthropological testing was performed additionally and unconfirmed for all cases. It's possible that misclassification biasing was introduced as brush cytology results were a reference, and we used them.

In addition, there is a possibility of using a different set of protocols to take these samples while the difference in the experience of pathologists too have influenced the result. Variability in the cycle of cancer, preoperative sample collection, specimens processing and methods, as well as cytological interpretation could have affected the diagnostic outcome of the brush cytology. Moreover, the study did not include interobserver variability among pathologists, thus tending to be an essential factor of the reliability of cytological diagnoses.

Similarly, there was a lack of emphasis regarding patient specific factors such as the active etiology and precise site of biliary strictures on the diagnostic performance of brush cytology. Inconsistency in factors such as biliary stricture, bile reaction in specimen, the mucosal surface issue, and the lack of inflammatory cell reaction could affect the brushing cytology method to diagnose carcinoma as well as other malignancies within the biliary strictures.

Other than this, the research did not assess brush cytology in terms of its cost efficiency in relation to alternative diagnostic modalities. Although brush cytology is widely accessible and less expensive than other diagnostic tools, the performance of the diagnostic test in question should be closely scrutinized against its cost and perception of the implications, which may lead to further tests or interventions needed.

**Future implications:** While these restrictions may present some issues, the results of this study are important for the practice of clinical care and for further research. Findings reiterate the importance of brush cytologist diagnostic process of biliary strictures. This makes ERCP techniques a valuable tool in the diagnosis of malignancy after removing bile duct blockages. Enhancement of sampling techniques perfection, standardized protocols and centralized assessment by reviewer pathologists may be additional measures to increase diagnostic yield of brush cytology.

The next step of research must tackle the following issues which are: to improve the diagnostic capacity of brush cytology it is essential to conduct a follow-up study. A future study should have a larger sample size and provide results from comparative analyses with alternative diagnoses for this study to be more valid. The analysis should be more robust and offer more solid evidence. Besides that attempt, a plan to standardize protocols for brush cytology sample collection and cytological interpretation can help to decrease the variations among these results.

Additionally, studies investigating whether the contribution of patient-based detail such as the cause and site of biliary strictures to the diagnostic value of brush cytology are also needed. Identifying these factors impacting the brush cytology sensitivity and specificity can be applied to individualize the diagnostic planning of a patient in an effort to improve their state of health.

On the other hand, cost-effectiveness analyses showcasing the pros and cons of brush cytology versus other diagnostic methods aid in guiding people to better judge resource allocation and other practices in clinical places. In the lay of the cost-effectiveness of different diagnostic approaches in determining likely diagnostic algorithms, healthcare resources could be maximized while minimizing diagnostic costs.

To bring this study to conclusion, it can be argued that the learning in this research is of great significance to the diagnosis of biliary strictures using brush cytology through procedure ERCP. However, this study has limitations and more research needs to be done to improve the efficiency of the diagnostic strategies in this clinical challenge. Earning a gap in these studies can be crucial for clinicians to develop a better diagnostic, have an early intervention and ultimately comprehend the patient's

outcome.

**Ethical Approval:** The IRB/EC approved this study via letter no.IRB/2024/188 dated 10-10-2024.

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**Authors' Contribution:**

**MR:** Conception

**SY, AR:** Design of the work

**SY, HMI, AA:** Data acquisition, analysis, or interpretation

**MR, SY, AK:** Draft the work

**AK, AA, AR:** Review critically for important intellectual content

**MR, SY, HMI, AK, AA, AR:** Approve the version to be published

**MR, SY, HMI, AK, AA, AR:** Agree to be accountable for all aspects of the work

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