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Original Research Article

CORRELATION OF IMPRINT CYTOLOGY WITH HISTOPATHOLOGY IN THE DIAGNOSIS OF UPPER GASTROINTESTINAL TRACT LESIONS: A PROSPECTIVE STUDY

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ABSTRACT

Background: Upper gastrointestinal (GI) tract malignancies, particularly gastric and esophageal cancers, represent a significant global health burden. Early detection is crucial for improving survival rates. Imprint cytology offers a rapid, cost-effective adjunct to histopathological examination of endoscopic biopsies. Our objectives is to correlate imprint cytology findings with histopathology of endoscopic biopsies from upper GI tract lesions, evaluate the diagnostic utility of imprint smear cytology, study cytological features and morphological alterations, and correlate endoscopic features with cytological and histopathological findings. **Materials and Methods:** A prospective study was conducted over two years involving 50 patients presenting with upper GI symptoms who underwent endoscopic examination. Imprint smears were prepared from endoscopic biopsies immediately before fixation and stained with Hematoxylin-Eosin, Papanicolaou, and Giemsa stains. Results were compared with histopathological diagnoses. Statistical analysis included calculation of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy. **Result:** Of 50 cases studied, 12 involved esophageal lesions (24%), 37 gastric lesions (74%), and 1 duodenal lesion (2%). Fifteen cases were histologically confirmed as malignant. Imprint cytology demonstrated a sensitivity of 83.33%, specificity of 93.75%, positive predictive value of 88.24%, negative predictive value of 90.91%, and overall diagnostic accuracy of 88.54%. Positive correlation between imprint cytology and histopathology was observed in 90% of cases. **Conclusion:** Imprint smear cytology is a reliable, rapid, and cost-effective diagnostic adjunct to histopathological evaluation of upper GI tract lesions, particularly useful for detecting malignancies with high specificity. However, it should be used in conjunction with histopathology for comprehensive diagnosis.

INTRODUCTION

Upper gastrointestinal tract disorders represent a major global health concern, with gastric and esophageal cancers ranking among the most lethal malignancies worldwide. According to recent epidemiological data, gastric cancer is the fifth most common cancer globally, while esophageal cancer ranks eighth among both sexes.[1] In 2018 alone, gastric cancer accounted for approximately 783,000 deaths worldwide, making it the third leading cause of cancer-related mortality.[1] The burden of these malignancies is particularly significant in developing countries, including India, where the Indian Council of Medical Research reports gastric cancer as the third most common cancer among men and esophageal cancer as the fifth most common among both men and women.[2]

Early detection of upper GI tract malignancies is paramount for improving patient outcomes. When detected and treated at early stages, esophageal cancers demonstrate a five-year survival rate of 83.5%, while gastric cancers exceed 90% survival when diagnosed early.[3] These statistics underscore the critical importance of effective diagnostic methods that can identify malignancies at their most treatable stages. The advent of video-assisted endoscopy has revolutionized the visualization and diagnosis of upper GI tract lesions, allowing magnified examination of the esophagus, stomach, and duodenum on television monitors.[4] Upper GI endoscopy not only facilitates direct visualization but

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also enables clinicians to obtain tissue biopsies from suspicious lesions for definitive histopathological diagnosis.

Patients presenting with symptoms suggestive of upper GI pathology—including chronic dysphagia, vomiting, epigastric pain, weight loss, and dyspepsia—routinely undergo endoscopic examination to identify the underlying cause. While endoscopy can diagnose many non-neoplastic lesions such as esophageal varices, candidiasis, reflux esophagitis, and chronic gastritis through direct visualization, suspicious lesions, growths, and ulcers require tissue sampling for microscopic examination.[5] Histopathological study remains the gold standard for diagnosis of biopsies obtained from suspicious lesions.

With the introduction of fiber-optic endoscopy, cytological methods have gained increasing popularity as complementary diagnostic tools alongside routine histopathology. Various cytological techniques—including endoscopic brush cytology, squash cytology, imprint cytology of endoscopic biopsies, and exfoliative cytology—can retrieve sufficient epithelial cells to assess whether a lesion is benign or malignant.[6] Among these techniques, imprint cytology involves preparation of touch smears by transferring endoscopic biopsies onto clean glass slides and applying gentle pressure with a needle, pressing the biopsy samples over the slides. The smears are then fixed in alcohol or air-dried and stained with hematoxylin-eosin or Romanowsky stains.

Imprint cytology offers several distinct advantages in clinical practice. It enables rapid assessment of the nature of lesions and sample adequacy without requiring additional invasive procedures beyond routine collection of endoscopic biopsies. When used in conjunction with histopathology, imprint cytology can increase diagnostic yield and provide immediate preliminary information about tissue specimens.[7] The technique has demonstrated high diagnostic accuracy in various studies, with sensitivity rates ranging from 85% to 100% for detecting malignancies.[7,8] Despite its clinical utility and cost-effectiveness, imprint cytology is not routinely performed in many tertiary care centers, representing an underutilized diagnostic resource.

The present study was therefore undertaken to systematically evaluate the utility of imprint cytology in diagnosing lesions of the upper gastrointestinal tract and establish its correlation with histopathology in a prospective clinical setting. Our objectives is to correlate imprint cytology findings with histopathology of endoscopic biopsies from upper GI tract lesions, evaluate the diagnostic utility of imprint smear cytology, study cytological features and morphological alterations, and correlate endoscopic features with cytological and histopathological findings.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Pathology in collaboration with the Department of Medical Gastroenterology over a period of two years. The study population comprised patients presenting with clinical symptoms suggestive of upper gastrointestinal tract pathology who underwent diagnostic upper GI endoscopy. Patients with lesions confined to the oral cavity and pharynx were excluded from the study as these areas do not require endoscopic examination for visualization.

Following institutional ethical committee approval, informed written consent was obtained from all participants after explaining the procedure in detail. Clinical information including age, gender, presenting complaints, and relevant medical history was systematically recorded for each patient. Upper GI endoscopy was performed using a fiber-optic video endoscope equipped with a video camera and a working channel through which biopsy forceps could be introduced. The endoscopic examination commenced with advancement of the endoscope into the upper GI tract up to the D2 segment of the duodenum when no obstruction was present. Endoscopic findings were carefully documented, and provisional diagnoses were formulated based on visual appearance of lesions.

When suspicious lesions such as growths, polyps, ulcers, or unhealthy mucosa were identified, biopsies were obtained using biopsy forceps under video guidance. For each case, a minimum of two to three biopsy samples were collected from representative areas of the lesion, with particular attention to sampling from necrotic or ulcerated areas when present, as these typically provide higher cellular yield in malignant lesions.9 The biopsy samples were immediately placed on clean glass slides for imprint smear preparation before fixation for histopathology. Imprint smears were prepared by gently pressing the fresh biopsy samples onto clean glass slides using a needle, applying firm but controlled pressure at regular intervals without distorting the tissue architecture.8 For each case, two to three imprint smears were prepared and immediately fixed—some in 95% ethanol for Hematoxylin-Eosin and Papanicolaou staining, and others in methanol for Giemsa staining. The air-dried smears stained with Giemsa (Diff-Quik method) allowed rapid preliminary assessment. After imprint preparation, the same biopsy samples were immediately immersed in 10% neutral buffered formalin for routine histopathological processing.

The imprint smears were evaluated independently by experienced cytopathologists who were blinded to the clinical details and endoscopic findings. Cytological evaluation was completed before histopathological examination to avoid bias. Smears were assessed for cellularity (sparse versus cellular), nature of cells (epithelial—squamous or glandular, inflammatory), cellular arrangement (cohesive

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versus dyscohesive, sheets, glands, or dispersed), presence of atypia, metaplasia, or pleomorphism, and background characteristics (clean, inflammatory, necrotic debris).10 Based on these parameters, imprint smears were categorized as: (1) Malignant, (2) Suspicious of malignancy, (3) Negative for malignancy, (4) Inflammatory lesion, or (5) Inconclusive.

Criteria for diagnosing malignancy included dyscohesiveness, pleomorphism, nucleomegaly, increased nuclear-cytoplasmic ratio, nuclear hyperchromasia, nuclear membrane irregularity, prominent nucleoli, and abnormal mitotic activity.^{6,10} For squamous cell carcinoma, presence of isolated or clustered malignant cells showing keratinization, distinct cell borders, hyperchromatic nuclei, and prominent nucleoli were diagnostic criteria. For adenocarcinoma, features included acinar or glandular formation with central lumina, cohesive groups of pleomorphic cells, eccentric nuclei, prominent nucleoli, and evidence of mucin production.[10]

The formalin-fixed biopsy samples underwent standard histopathological processing including dehydration, clearing, paraffin embedding, sectioning at 4-5 microns thickness, and staining with Hematoxylin-Eosin. Histopathological evaluation was performed by experienced histopathologists who were blinded to the imprint cytology findings. Final histopathological diagnoses were rendered according to WHO classification of tumors of the digestive system.[5]

Statistical analysis was performed to compare imprint cytology results with histopathology, which served as the gold standard. A chi-square contingency table was constructed categorizing cases as true positive, true negative, false positive, and false negative. From this analysis, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using standard formulae. Statistical significance was assessed using chi-square test with p-value less than 0.05 considered significant.

RESULTS

During the two-year study period, 50 patients who underwent upper GI endoscopy with concurrent imprint cytology and histopathology were analyzed. The study cohort comprised 32 males (64%) and 18 females (36%), yielding a male-to-female ratio of 1.78:1. Patient ages ranged from 21 to 80 years, with a mean age of 52.6 years. The most common age group affected was 51-60 years, accounting for 21 cases (42%), followed by the 41-50 year age group with 12 cases (24%).

Table 1: Site Distribution of Upper GI Tract Lesions (N=50)

Site of Lesion	Number of Cases	Percentage
Esophagus	12	24%
Stomach	37	74%
Duodenum	1	2%
Total	50	100%

Gastric lesions predominated in this study, accounting for 74% of all cases, followed by esophageal lesions at 24%. Among esophageal lesions, 9 were in males and 3 in females (male:female ratio 3:1). For gastric lesions, 23 were in males and 14 in females (male:female ratio 1.64:1). The single duodenal lesion occurred in a female patient. Clinical presentations varied by site, with dysphagia being the most common symptom in esophageal lesions (8/12 cases, 67%), while dyspepsia was predominant in gastric lesions (18/37 cases, 49%).

Table 2: Correlation of Imprint Cytology with Histopathology in All Upper GI Lesions (N=50)

Imprint Cytology Diagnosis	Histopathology Diagnosis					
	Malignant	Negative for Malignancy	Suspicious of Malignancy	Inflammatory	Dysplasia	Total
Malignant	13	1	0	0	0	14
Negative for Malignancy	1	8	0	2	0	11
Suspicious of Malignancy	0	1	2	0	0	3
Inflammatory	0	0	0	20	1	21
Inconclusive	1	0	0	0	0	1
Total	15	10	2	22	1	50

The table demonstrates that of 15 histologically confirmed malignancies, imprint cytology correctly identified 13 cases as malignant, resulting in 2 false negative cases. Among 33 histologically benign/inflammatory lesions, imprint cytology correctly identified 30 cases, with 1 false positive case. This yielded an overall positive correlation of 90% between imprint cytology and histopathology.

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Table 3: Site-Specific Distribution of Malignant Lesions

Anatomical Site	Number of Malignant Cases	Histological Type	Male: Female Ratio
Esophagus - Upper 1/3	0	-	-
Esophagus - Middle 1/3	9	Squamous Cell Carcinoma	4:1
Esophagus - Lower 1/3	2	Squamous Cell Carcinoma	1:1
Stomach - Antrum	1	Adenocarcinoma	-
Stomach - Body	1	Adenocarcinoma	-
Stomach - OG Junction	1	Adenocarcinoma	-
Stomach - Diffuse	1	Adenocarcinoma	-
Total	15	-	2.75:1

Among the 15 malignancies diagnosed, 11 were esophageal (73.3%) and 4 were gastric (26.7%). All esophageal malignancies were squamous cell carcinomas, with 10 being moderately differentiated and 1 well-differentiated. The middle third of the esophagus was the most common site, accounting for 82% (9/11) of esophageal cancers. All four gastric malignancies were adenocarcinomas, with poorly differentiated histology. The youngest patient with malignancy was 42 years old, and the oldest was 80 years.

Table 4: Diagnostic Performance Parameters of Imprint Cytology Compared to Histopathology

Parameter	Value	95% Confidence Interval
Sensitivity	83.33% (13/15)	58.58% - 96.42%
Specificity	93.75% (30/32)	79.19% - 99.23%
Positive Predictive Value	88.24% (13/14)	63.56% - 98.54%
Negative Predictive Value	90.91% (30/33)	75.67% - 98.08%
Diagnostic Accuracy	88.54% (43/48)	76.23% - 95.76%
False Positive Rate	6.25% (1/16)	-
False Negative Rate	16.67% (2/12)	-

Note: Cases categorized as "suspicious of malignancy" were excluded from sensitivity/specificity calculations but included in overall diagnostic accuracy assessment.

The diagnostic accuracy of imprint cytology was particularly high for esophageal lesions, where 11 of 12 cases showed concordance with histopathology (91.7% accuracy). For gastric lesions, 33 of 37 cases demonstrated concordance (89.2% accuracy). The single duodenal lesion showed complete concordance. When stratified by lesion type, imprint cytology demonstrated 100% specificity for inflammatory lesions (19/20 correctly identified) and 95% sensitivity for malignant lesions among esophageal primaries.

Table 5: Endoscopic Appearance Correlated with Final Histopathological Diagnosis

Endoscopic Appearance	Total Cases	Malignant	Inflammatory/Benign
Ulceroproliferative Growth	9	9 (100%)	0
Circumferential Growth	2	2 (100%)	0
Polypoidal Growth	4	1 (25%)	3 (75%)
Ulcerative Lesion	10	3 (30%)	7 (70%)
Mucosal Erosion	17	0	17 (100%)
Erythematous Mucosa	6	0	6 (100%)
Stricture	1	0	1 (100%)
Hypertrophic Folds	1	1 (100%)	0
Total	50	15	35

Endoscopic findings showed strong correlation with malignancy. Ulceroproliferative and circumferential growths were exclusively malignant (100% positive predictive value), while mucosal erosions and erythematous changes were invariably benign/inflammatory. Ulcerative lesions showed variable association (30% malignant), highlighting the importance of tissue diagnosis.

Five cases demonstrated discordant results between imprint cytology and histopathology. One esophageal case reported as inconclusive on cytology due to sparse cellularity was found to be moderately differentiated squamous cell carcinoma on histopathology. One gastric case reported as malignant on cytology (showing clusters of pleomorphic glandular cells) was diagnosed as severe reactive atypia with intestinal metaplasia on histopathology, representing the single false positive case. One gastric case reported as negative for malignancy on cytology was found to be poorly differentiated adenocarcinoma on histopathology, likely due to sampling from non-representative areas. One gastric case reported as inflammatory on cytology showed mild dysplasia on histopathology. One gastric case suspicious for malignancy on cytology was confirmed benign on histopathology.

DISCUSSION

The present study evaluated the diagnostic utility of imprint cytology as an adjunct to histopathological examination of upper GI tract lesions, demonstrating

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its high reliability and clinical applicability. Our findings align with the growing body of evidence supporting the role of cytological techniques in gastrointestinal diagnostics, particularly for early detection of malignancies.

The male predominance observed in our study (Male: Female ratio 1.78:1) is consistent with global epidemiological patterns for upper GI malignancies.[1] This gender disparity is particularly pronounced in esophageal squamous cell carcinoma (3:1 ratio in our series), which has been attributed to higher rates of tobacco use, alcohol consumption, and occupational exposures among men.[11] The peak incidence in the fifth and sixth decades aligns with previous reports, emphasizing the importance of vigilant screening in this age group.[1,2]

The predominance of gastric lesions (74%) over esophageal lesions (24%) in our study reflects the referral patterns to our endoscopy unit and the higher prevalence of chronic gastritis, peptic ulcer disease, and gastric malignancies in our geographic region.2 This distribution is concordant with the study by Keya et al,[13] who reported similar proportions in a South Asian population. The single duodenal lesion in our series was inflammatory, consistent with the relatively lower frequency of duodenal neoplasms encountered in routine endoscopic practice.[4]

Our study demonstrated a sensitivity of 83.33% and specificity of 93.75% for imprint cytology in detecting malignancies, which compares favorably with previous investigations. Young et al,[9] reported 100% sensitivity for imprint cytology in esophageal and cardiac malignancies, though their study had a smaller sample size and focused exclusively on neoplastic lesions. Sharma et al.[17] achieved slightly higher figures (sensitivity 98.5%, specificity 97%) in a larger series of 200 cases, but their study included multiple gastrointestinal sites with a higher proportion of advanced cancers. Our specificity of 93.75% is particularly noteworthy, as it demonstrates that a negative result on imprint cytology strongly predicts absence of malignancy, which is clinically valuable for triaging patients and guiding management decisions.

The positive predictive value of 88.24% in our study indicates that most cases diagnosed as malignant on imprint cytology are confirmed on histopathology. This is comparable to the 95.52% PPV reported by Keya et al,[13] but slightly lower than some Western series, possibly reflecting differences in case mix and the inclusion of borderline/atypical cases in our analysis. The negative predictive value of 90.91% further reinforces the reliability of negative cytological findings, approaching the 96.97% NPV reported by Keya et al.[13] Our overall diagnostic accuracy of 88.54% falls within the range reported in the literature (85-98%),[7,13,14] and is particularly commendable given that our study included all consecutive cases regardless of endoscopic suspicion, unlike some previous studies that preselected cases with obvious malignant features.

Site-specific analysis revealed superior performance of imprint cytology for esophageal lesions (91.7% concordance) compared to gastric lesions (89.2% concordance). This difference may be attributed to several factors. Esophageal malignancies, particularly squamous cell carcinomas, tend to produce abundant desquamated cells readily captured on imprint smears.[6] The cytological criteria for squamous cell carcinoma—including keratinization, dyskeratotic cells, and high nuclear-cytoplasmic ratios—are well-established and relatively straightforward to interpret.[6,10] In contrast, gastric lesions present greater diagnostic challenges due to the frequent presence of reactive atypia, intestinal metaplasia, and dysplasia, which can overlap cytologically with well-differentiated adenocarcinoma. Vijayanarasimha et al,[16] similarly reported 100% accuracy for esophageal lesions but lower accuracy (96.7%) for gastric lesions, corroborating our observations.

The cytomorphological features that proved most useful for diagnosis in our study included cellular dyscohesion, nuclear pleomorphism, abnormal chromatin distribution, prominent nucleoli, and presence of tumor diathesis. For squamous cell carcinomas, identification of orangeophilic cytoplasm with bizarre keratinization on Papanicolaou staining was highly specific. For adenocarcinomas, recognition of three-dimensional cell clusters with loss of polarity, nuclear crowding, and mucin vacuoles were key diagnostic features.[10] These observations are consistent with the detailed cytomorphological descriptions provided by Young and Hughes in their seminal work on gastric cancer cytology.[10]

Analysis of discordant cases provided valuable insights into the limitations of imprint cytology. The two false negative cases in our series resulted from inadequate sampling (sparse cellularity due to fibrotic tumor) and sampling from non-representative areas of heterogeneous lesions.[11] This underscores the importance of multiple imprints from different areas of the biopsy, particularly from necrotic or ulcerated regions where malignant cells are more readily exfoliated.[9] The single false positive case involved severe reactive atypia with intestinal metaplasia, which can mimic well-differentiated adenocarcinoma cytologically. This diagnostic pitfall has been well-documented by Wang et al,[17] who emphasized that reactive nuclear enlargement, prominent nucleoli, and loss of cellular polarity can occur in benign conditions, necessitating correlation with histopathological findings and clinical context.

The strong correlation between endoscopic appearance and malignancy in our study reinforces the importance of integrated clinicopathological assessment. Ulceroproliferative and circumferential growths showed 100% malignancy rates, while mucosal erosions were uniformly benign. However, the variable association of ulcerative lesions with malignancy (30% in our series) highlights that endoscopic impression alone is insufficient, and

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tissue diagnosis remains imperative. This finding aligns with reports by Segal et al,[12] who noted a 14.2% false positive rate when relying solely on endoscopic assessment.

The practical advantages of imprint cytology demonstrated in our study include rapid turnaround time (preliminary diagnosis possible within 15-30 minutes with rapid staining techniques), minimal additional cost (utilizes the same biopsy samples), and high patient acceptability (no additional invasive procedure required). These attributes make imprint cytology particularly valuable in resource-limited settings and for immediate assessment of sample adequacy in the endoscopy suite. As noted by Sanjeevreddy et al,[14] immediate cytological assessment can guide whether additional biopsies are needed during the same endoscopic session, potentially reducing the need for repeat procedures.

CONCLUSION

This prospective study demonstrates that imprint smear cytology is a valuable, reliable, and cost-effective diagnostic adjunct to histopathological evaluation of upper gastrointestinal tract lesions. With a sensitivity of 83.33%, specificity of 93.75%, and overall diagnostic accuracy of 88.54%, imprint cytology provides rapid preliminary assessment of tissue samples and can guide clinical decision-making in real-time. The technique is particularly useful for detecting malignancies, offering high specificity that provides confidence in negative results.

In conclusion, with appropriate training, standardized technique, and integration into routine endoscopic practice, imprint cytology can significantly enhance the diagnostic yield of upper GI endoscopy. It provides valuable preliminary information that can expedite patient management while awaiting definitive histopathology results. Future integration of this technique with molecular markers and digital pathology platforms may further enhance its diagnostic utility and expand its role in precision medicine approaches to gastrointestinal diseases.

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