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Bridging Endoscopic Appearance and Histopathological Diagnosis in Esophageal Lesions

Gundlapalli Sravani[1], Rajarikam Nagarjuna Chary[2], Naval Kishore Bajaj[3]

Abstract: ***Background: Esophageal carcinoma (EC) is an aggressive malignancy associated with substantial morbidity and mortality, largely due to delayed diagnosis and advanced stage presentation. Understanding regional clinicopathological characteristics and associated risk factors is essential for improving early detection and patient outcomes. Aim: To evaluate the epidemiological, clinical, endoscopic, and histopathological characteristics of esophageal lesions and assess clinicopathological correlations in patients with suspected esophageal carcinoma. Methods: This cross-sectional observational study included 96 patients with endoscopically suspected esophageal carcinoma who underwent upper gastrointestinal endoscopy and biopsy at a tertiary care centre in South India. Demographic, clinical, endoscopic, and histopathological parameters were analysed, and clinicopathological correlations were assessed using the Chi-square test. Results: The mean age of the study population was 55.29 ± 14.31 years, with the highest frequency observed in the 61–70-year age group. Males constituted 53.1% of cases, and 58.3% were from rural areas. Dysphagia was the predominant presenting symptom (99.0%), followed by weight loss (72.9%) and loss of appetite (71.9%). Exposure to potential risk factors was common, including hot beverage consumption (97.9%), spicy food intake (59.4%), obesity (51.0%), smoking (38.5%), alcohol consumption (37.5%), gutka use (31.3%), and paan chewing (25.0%). The lower esophagus was the most frequently involved site (37.5%). Endoscopically, altered mucosa (55.2%) and ulcerated mucosa (22.9%) were the most common findings, while luminal narrowing was observed in 81.3% of cases. Histopathological examination revealed malignant lesions in 70.8% of cases, predominantly squamous cell carcinoma (60.4%) and adenocarcinoma (10.4%), with proliferative endoscopic growth patterns showing a significant association with malignancy ($p < 0.001$). Conclusions: Squamous cell carcinoma was the predominant malignancy, with dysphagia and luminal narrowing representing the most frequent clinical and endoscopic manifestations. The significant association between proliferative endoscopic growth patterns and malignant histology highlights the importance of endoscopic evaluation and histopathological confirmation for early diagnosis and optimal patient management.***

Keywords: Esophageal lesions; Esophageal carcinoma; Esophageal Squamous cell carcinoma; Esophageal Adenocarcinoma; Upper gastrointestinal endoscopy; Endoscopic growth patterns; Histopathological diagnosis; Dysphagia; Clinicopathological correlation.

1. Introduction

Esophageal carcinoma (EC) remains a major global health challenge owing to its high incidence and mortality. According to GLOBOCAN 2020, approximately 604,100 new cases were diagnosed worldwide, corresponding to an age standardised incidence rate of 6.3 per 100,000 population. Squamous cell carcinoma (SCC) accounted for nearly 85% of cases and remains the predominant histological subtype globally followed by Adenocarcinoma of esophagus. Recent estimates indicate that esophageal cancer accounted for approximately 576,000 new cases and 538,000 deaths globally in 2021. [1]

In high-incidence regions, particularly parts of China and South Asia, areca nut chewing has emerged as a potential risk factor for esophageal squamous cell carcinoma (ESCC). Epidemiological studies have reported a positive association between areca nut consumption and ESCC risk, although the underlying biological mechanisms remain incompletely elucidated. Furthermore, chronic thermal injury resulting from the habitual consumption of very hot beverages and foods has been implicated in esophageal carcinogenesis through repeated mucosal damage and inflammation.[2]. Non modifiable factors such as older age, male sex, and hereditary predisposition also play a significant role. The rising incidence of adenocarcinoma is closely linked to increasing rates of obesity and GERD [3].

Common clinical presentation of EC includes progressive dysphagia, odynophagia, weight loss, and chest pain. BE, a precursor to Esophageal adenocarcinoma (EAC), usually manifests as chronic heartburn and dysphagia. The elasticity of esophagus and the aggressive biology of these tumours often result in late stage presentation, with many patients remaining asymptomatic until the disease is advanced [4,5].

Diagnosis relies primarily on endoscopic biopsy of the esophageal mucosa, with pathological confirmation. Endoscopic assessment allows a rather accurate estimation of the invasion depth of early EC. But to determine the final treatment modality, the final histological staging obtained by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is crucial [6]. Endoscopic ultrasound (EUS), aids in local staging and assessment of tumor extent, while computed tomography (CT) is critical for evaluating lymph node involvement and distant metastases [7]. Even with evolving management strategies and improved diagnostic tools, most cases are detected at an advanced stage, making early detection and identification of at risk populations crucial for improving outcomes [8].

2. Materials and Methods

Study Design

This cross-sectional observational study was conducted in the Department of Pathology at a tertiary care referral center, Hyderabad between January 2024 and March 2026. The study was carried out over a period of two years, following approval from the Institutional Ethics Committee. The study population comprised patients with endoscopically suspected esophageal carcinoma and relevant clinical history. During the study period, a total of 218 upper gastrointestinal endoscopic biopsies were received. Of these, 96 patients who fulfilled the predefined inclusion criteria were enrolled in the study and subjected to further analysis.

Inclusion Criteria
- Provided informed consent to participate in the study.
- Presented with clinical symptoms including dysphagia, weight loss, regurgitation, and/or chronic heartburn.
- Had endoscopic findings suspicious for esophageal carcinoma.

Exclusion Criteria
- Had a history of acid or alkali ingestion.
- Diagnosed with non-specific esophagitis.

3. Methodology

Patients with clinical and endoscopic suspicion of esophageal carcinoma who underwent upper gastrointestinal endoscopy, and biopsy specimens were obtained from suspicious lesions. Endoscopic findings, including the location, morphology, and extent of the lesion, were documented. Biopsy specimens were immediately fixed in 10% neutral buffered formalin and processed using standard histopathological techniques and paraffin embedded, following which thin sections measuring 4–5 µm were prepared.

Histopathological Examination
Tissue sections were stained using hematoxylin and eosin (H&E). All stained slides were examined under light microscopy, and histopathological evaluation was performed to confirm the diagnosis and determine the tumor type according to the World Health Organization (WHO) classification of esophageal tumors. Tumors were further graded based on the degree of differentiation as well differentiated, moderately differentiated, or poorly differentiated where applicable.

Statistical Analysis
Data were entered into Microsoft Excel (Version 2021) and analyzed using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. Statistical significance was defined as a two-tailed p-value <0.05.

4. Observation and Results

The clinical details, endoscopic findings, and histopathological features were analysed to assess the distribution of esophageal malignancies and their clinicopathological correlations. The biopsy specimens were processed and examined microscopically to determine the histopathological type of the lesion.

A total of 96 patients with esophageal lesions were included in the study. Histopathological examination revealed malignant lesions in 68 cases (70.8%), benign lesions in 21 cases (21.9%), and non-neoplastic lesions in 7 cases (7.3%) (Table 1).

Among the malignant lesions, squamous cell carcinoma (SCC) was the predominant histological subtype, accounting for 58 cases (85.3% of malignancies; 60.4% of the total cohort), while adenocarcinoma was identified in 10 cases (14.7% of malignancies; 10.4% of the total cohort). Tumor differentiation was assessed in all malignant epithelial neoplasms. Among SCC cases, well-differentiated tumors constituted the majority (39/58, 67.2%), followed by moderately differentiated (15/58, 25.9%) and poorly differentiated tumors (2/58, 3.4%). Among adenocarcinomas, five cases (50.0%) were well differentiated, four (40.0%) were moderately differentiated, and one (10.0%) was poorly differentiated.

Within the benign category, low-grade squamous dysplasia was the most frequent diagnosis, comprising 12 cases (12.5%), followed by high-grade squamous dysplasia in 7 cases (7.3%). Barrett's esophagus with low-grade dysplasia and benign squamous papilloma were identified in one case each (1.0%).

Non-neoplastic lesions constituted a small proportion of the cohort and included post-chemoradiotherapy stricture and esophageal melanosis (2 cases each, 2.1%), along with eosinophilic esophagitis, reflux esophagitis, and esophageal web (1 case each, 1.0%).

Age distribution differed markedly between benign and malignant lesions. Benign lesions were predominantly observed in younger individuals, with 75.0% occurring in patients aged ≤30 years. In contrast, malignant lesions were more frequently encountered in older age groups, with the highest proportions observed in patients aged 61–70 years (82.6%), 51–60 years (80.9%), and >70 years (73.3%). The frequency of malignant lesions progressively increased with advancing age.

Among malignant neoplasms, SCC demonstrated a peak incidence in the sixth and seventh decades of life, accounting for 29.3% of cases in patients aged 61-70 years and 25.9% in those aged 51-60 years. Adenocarcinoma showed a relatively younger age distribution, with 40.0% of cases occurring in the 31- 40 year age group, followed by 20.0% each in the 51- 60 and 61-70 year age groups.

The gender distribution of the study population, 51 (53.1%) were males and 45 (46.9%) were females, yielding a male-to-female ratio of 1.13:1. The findings indicate a slight male predominance in the study cohort. Analysis of sex distribution among malignant tumors revealed a male predominance in both major histological subtypes. SCC occurred in 32 males and 26 females, whereas adenocarcinoma was identified in 7 males and 3 females.

56 patients (58.3%) were from rural areas, while 40 (41.7%) were from urban areas. This suggests a higher representation of rural patients, possibly reflecting referral patterns or higher exposure to risk factors in rural populations.

Obesity was present in 49 patients (51.0%), while 47 (49.0%) were non-obese. The nearly equal distribution suggests that obesity may play a contributory role in esophageal pathology in this population. Hot beverage consumption was reported in 94 patients (97.9%), making it the most common habit. Spicy food consumption was noted in 59.4%, smoking in 38.5%,

alcohol in 37.5%, gutka in 31.3%, and paan in 25.0%. These findings suggest high exposure to potential mucosal irritants and known carcinogenic risk factors.

Dysphagia was the predominant presenting symptom, reported by 95 patients (99.0%). Other common symptoms included weight loss in 70 patients (72.9%) and loss of appetite in 69 patients (71.9%). Regurgitation and odynophagia were observed in 42 (43.8%) and 38 (39.6%) patients, respectively.

The lower third of the esophagus was the most frequently involved site, accounting for 36 cases (37.5%), followed by the middle third in 31 cases (32.3%). Cervical esophageal involvement was noted in 19 cases (19.8%), whereas the upper esophagus was involved in only 9 cases (9.4%). Stratification by histopathological category revealed that the lower third of the esophagus was the most common site for both benign (38.1%) and malignant lesions (35.3%). Among malignant neoplasms, SCC showed a broad anatomical distribution, occurring most frequently in the middle third (36.2%), followed by the cervical (27.6%), lower (24.1%), and upper thirds (12.1%). In contrast, all adenocarcinomas were located in the lower third of the esophagus. A significant association was observed between tumor location and histological subtype ($p < 0.05$) (Table 2).

On endoscopic examination, altered mucosa was the most common finding, observed in 53 patients (55.2%), followed by ulcerated mucosa in 22 patients (22.9%). Other mucosal abnormalities were less frequent. Luminal narrowing was present in 78 patients (81.3%), while circumferential involvement was seen in 31 patients (32.3%) (Table 3, Graph 1).

With respect to macroscopic growth pattern, ulcero proliferative growth (UPG) was the most common morphology, seen in 30 cases (31.3%), followed by proliferative growth in 21 cases (21.9%). No obvious growth was identified in 37 cases (38.5%), while the remaining cases demonstrated other less common growth patterns (Table 4).

A significant association was observed between endoscopic growth pattern and histopathological diagnosis (χ^2 test, $p < 0.001$). Malignant lesions were predominantly associated with proliferative and ulceroproliferative growth patterns, whereas benign and non-neoplastic lesions were more frequently encountered in cases without discernible growth (Graph 2).

Luminal narrowing demonstrated a significant association with malignant histopathology, being identified in 62 of 68 malignant lesions (91.2%). In contrast, neither altered mucosa ($p = 0.250$) nor ulcerated mucosa ($p = 0.103$) showed a statistically significant association with histopathological category.

Table 1: Distribution of Study Subjects according to the Histology (N = 96)

Histology	No.	Percent
Non-Neoplastic		
Post CT RT Stricture	2	2.1
Oesophageal Melanosis	2	2.1
Eosinophilic Esophagitis	1	1.0
Reflux Esophagitis	1	1.0
Oesophageal Web	1	1.0
Total	**7**	**7.3**
Benign		
Barrett's low grade dysplasia	1	1.0
Benign Squamous Papilloma	1	1.0
High Grade Squamous Dysplasia	7	7.3
Low Grade Squamous Dysplasia	12	12.5
Total	**21**	**21.9**
Malignant		
SCC	58	60.4
Adeno Carcinoma	10	10.4
Total	**68**	**70.8**

Table 2: Site and Histology (N = 96)

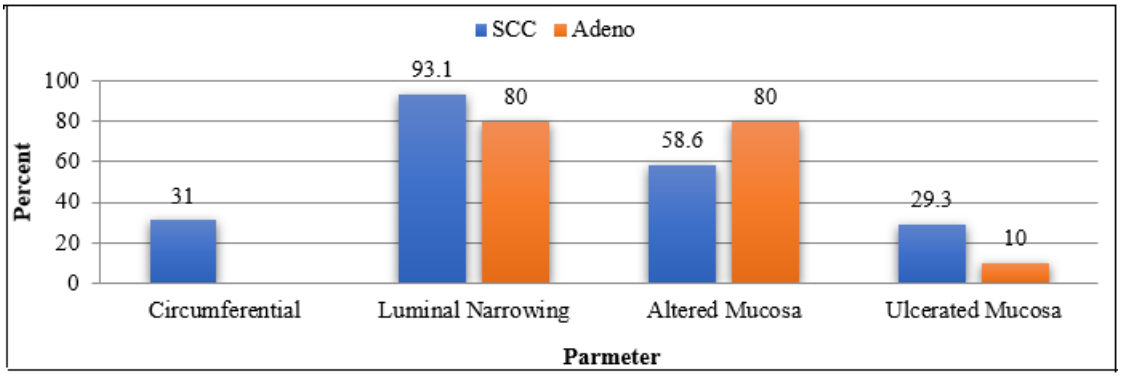
Histology	No.	Site				
		Cervical (n=16) n (%)	Low (n=36) n (%)	Mid (n=31) n (%)	Mid and Low (n=1) n (%)	Upper (n=9) n (%)
Non-Neoplastic						
Post CT RT Stricture	2		1	1		
Oesophageal Melanosis	2		1		1	
Eosinophilic Esophagitis	1		1			
Reflux Esophagitis	1		1			
Eesophageal Web	1	1				
Total	**7**	**1**	**4**	**1**	**1**	**-**
Benign						
Barrett's dysplasia	1		1			
Benign Squamous Papilloma	1					1
High Grade Squamous Dysplasia	7		1	5		1
Low Grade Dysplasia	12	2	6	4		
Total	**21**	**2**	**8**	**9**	**-**	**2**
%		**9.5**	**38.1**	**29.0**		**9.5**
Malignant						
SCC	58	16 (27.6)	14 (24.1)	21 (36.2)		7 (12.1)
Adeno Carcinoma	10		10 (100.0)			
Total	**68**	**16**	**24**	**21**	**-**	**7**
%		**23.5**	**35.3**	**30.9**	**-**	**10.3**

Table 3: Distribution according to the Endoscopy Mucosa (N=96)

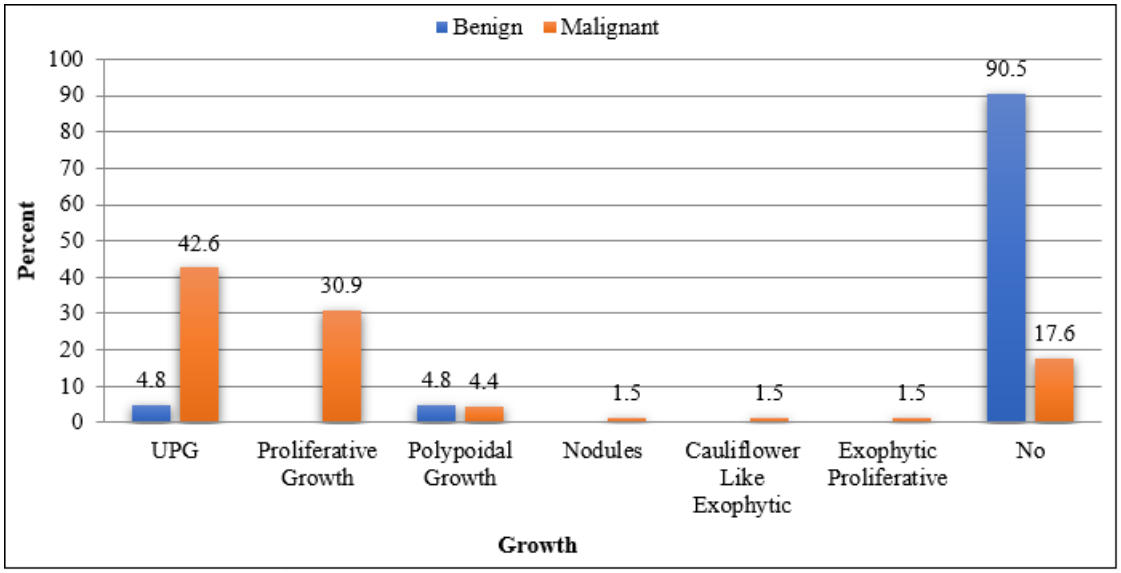
Mucosa	No.	Percent
Altered Mucosa	53	55.2
Ulcerated Mucosa	22	22.9
Blackish Linear	1	1.0
Erythematous	1	1.0
Erythematous And Brown	1	1.0
Erythematous Mucosa	1	1.0
Erythematous Nodular Mucosa	1	1.0
Erythematous Ulceration	1	1.0
Multiple Ulcers	1	1.0
Necrosis	1	1.0
Necrotic Mucosa	1	1.0
Nodular Mucosa	1	1.0
Nodular Ulcerated Mucosa	1	1.0
Nodularity	1	1.0
Normal	1	1.0
Pallor	1	1.0
Pallor, Ulceration	1	1.0
Papery Mucosa	1	1.0
Salmon Coloured Mucosa	1	1.0
Ulcerated and Friable	2	2.1
Altered and Friable	1	1.0
Altered Friable Mucosa	1	1.0

Table 4: Distribution of Growth pattern and lesion (N = 96)

Lesion	No.	Growth						
		Cauliflower (n=1) n (%)	Exophytic Proliferative (n=1) n (%)	Nodules (n=2) n (%)	Polypoidal (n=4) n (%)	Proliferative (n=21) n (%)	UPG (n=30) n (%)	None (n=37) n (%)
Non-Neoplastic								
Post CT RT Stricture	2							2
Esophageal Melanosis	2			1				1
Eosinophilic Esophagitis	1							1
Reflux Esophagitis	1							1
Oesophageal Web	1							1
Total	**7**			**1**				**6**
Benign								
Barrett's dysplasia	1							1
Benign Squamous Papilloma	1				1			
High Grade Dysplasia	7						1	6
Low Grade Dysplasia	12							12
Total	**21**				**1**		**1**	**19**
%					**4.8**		**4.8**	**90.5**
Malignant								
SCC	58	1 (1.7)	1 (1.7)	1 (1.7)		19 (32.8)	24 (41.4)	12 (20.7)
Adeno Carcinoma	10				3 (30.0)	2 (20.0)	5 (50.0)	
Total	**68**	**1**	**1**	**1**	**3**	**21**	**29**	**12**
%		**1.5**	**1.5**	**1.5**	**4.4**	**30.9**	**42.6**	**17.6**



Graph 1: Endoscopic Characteristics According to Histological Type



Graph 2: Histology and Growth

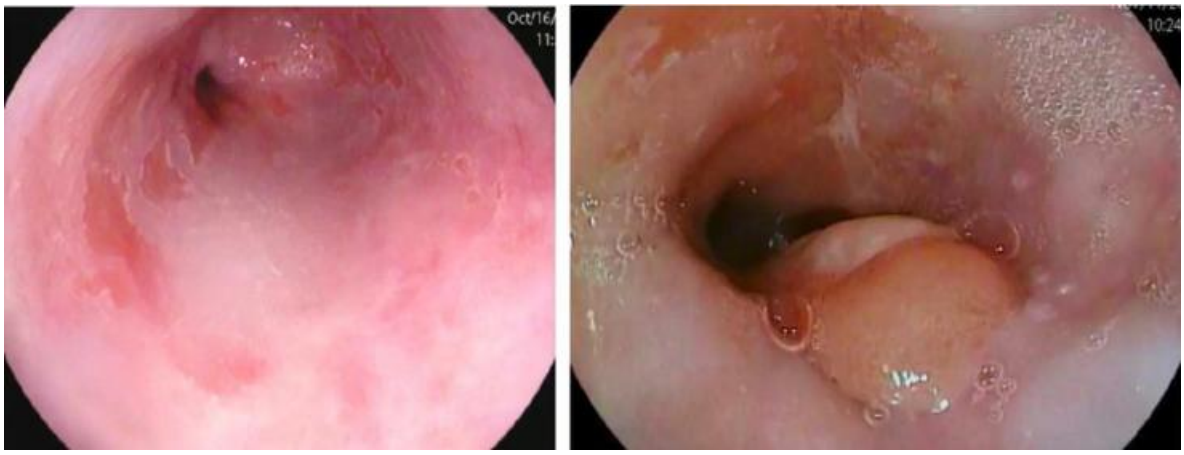


Figure: Upper endoscopy showing the salmon colour patches in the distal esophagus and proliferative lesion which showed adenocarcinoma on histopathology

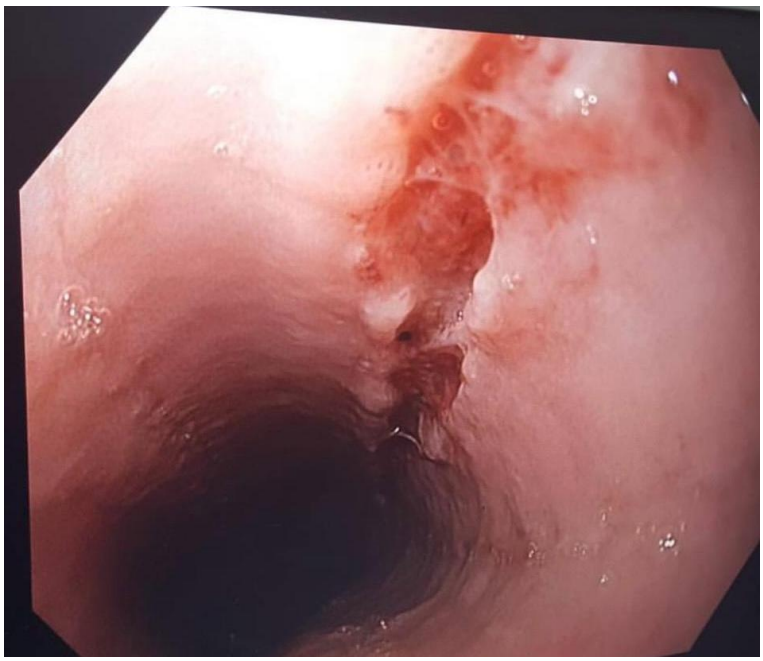


Figure: Ulcerated lesion with raised edges which showed SCC on histopathology

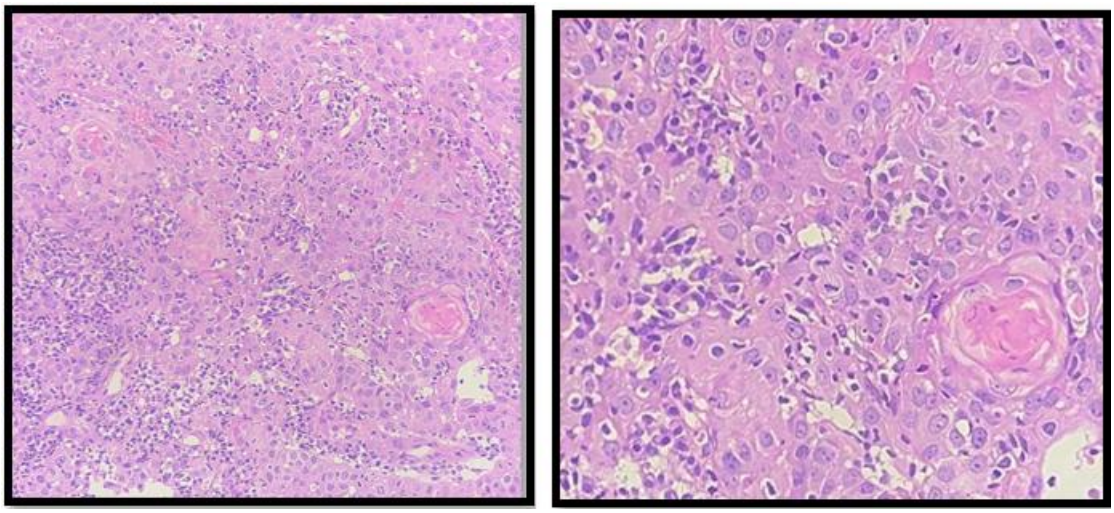


Figure: High power and low power view of Well differentiated SCC

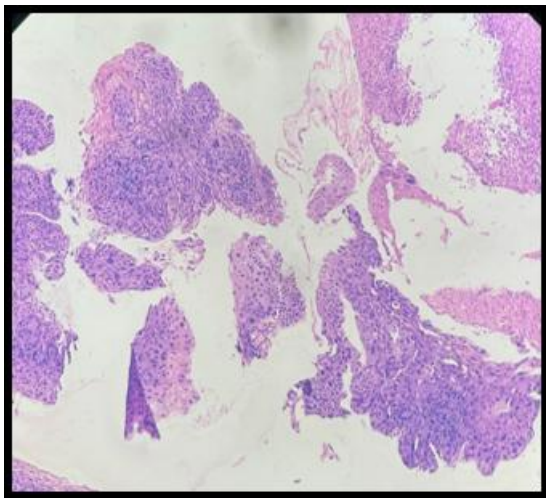


Figure: Low power view of Moderately differentiated SCC

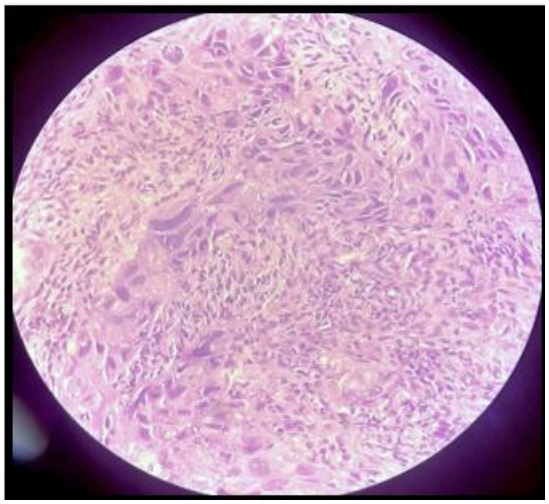


Figure: High power view of Poorly differentiated SCC

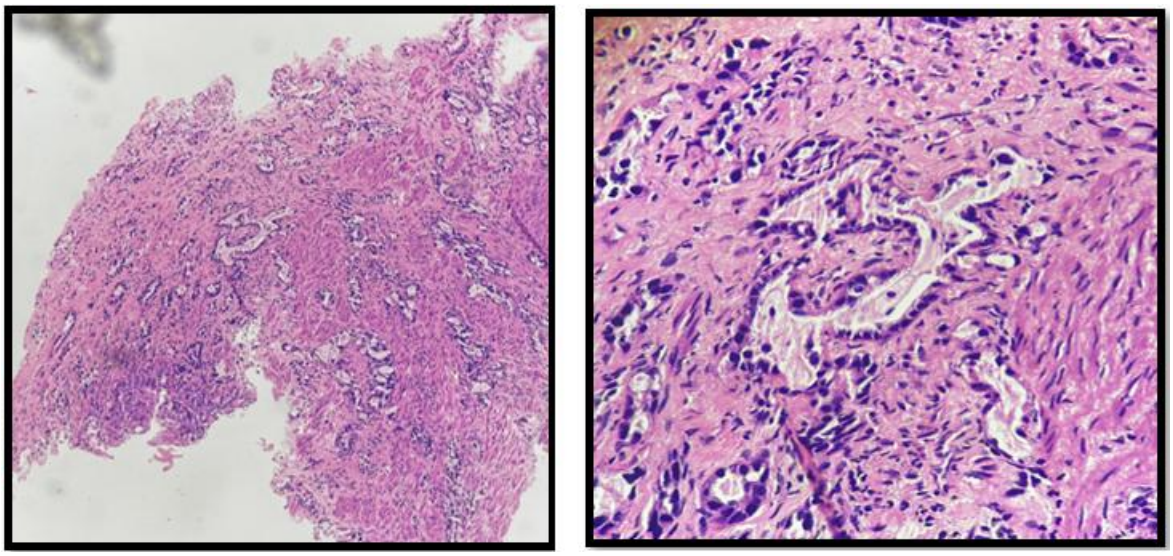


Figure: Low and high- power view of Adeno carcinoma

5. Discussion

Esophageal cancer remains a globally significant malignancy characterised by high mortality, aggressive behaviour, and profound geographical and histological variation. Worldwide, more than 604,100 new cases are diagnosed annually, with poor survival largely reflecting advanced stage presentation and limited curative options. The two principal histologic subtypes ESC and EAC differ fundamentally in epidemiology, etiologic drivers, molecular evolution, and anatomic distribution [1].

In this cross-sectional analysis of 96 patients with esophageal lesions, we evaluated demographic, clinical, endoscopic, histopathologic, and lifestyle related variables. Our findings align with established risk paradigms and provide additional epidemiologic insight from a population with high exposure to dietary irritants and tobacco/alcohol use.

A slight male predominance was observed in the present cohort (51 males and 45 females), consistent with the recognised male predominance of esophageal carcinoma worldwide [9,10]. Recent studies by Lagergren et al. (2021) and Morgan et al. (2022) similarly demonstrated higher incidence rates among males across both ESCC and adenocarcinoma subtypes [11,12]. The relatively balanced sex distribution in our cohort (1.13:1) may reflect changing exposure patterns and the contribution of biological factors, including sex-related differences in hormonal regulation, immune response, and susceptibility to carcinogenesis [13]. The predominance of older patients likely reflects the cumulative effects of long-term exposure to carcinogenic factors and age-related molecular alterations that contribute to malignant transformation [14].

Squamous cell carcinoma (SCC) was the predominant histological subtype, accounting for 85.3% of all malignancies. This pattern remains characteristic of several Asian populations where exposure related SCC continues to predominate despite the global rise in adenocarcinoma.[15] The observed association between tobacco use, alcohol consumption, gutka/paan chewing, and SCC supports their established role in esophageal carcinogenesis [16,17]. In contrast, obesity demonstrated a stronger association with adenocarcinoma, consistent with the recognized reflux–Barrett's esophagus–adenocarcinoma pathway.[18]

The substantial burden of dysplastic lesions observed in this study further supports a stepwise progression from chronic mucosal injury to invasive malignancy. The coexistence of dysplasia and carcinoma within similar exposure profiles highlights the biological continuum of esophageal carcinogenesis and emphasises the importance of surveillance in high-risk individuals [19].

Clinically, dysphagia was the predominant presenting symptom and closely paralleled the high frequency of luminal narrowing observed on endoscopy. Together with the frequent occurrence of weight loss and anorexia, these findings suggest that a large proportion of patients presented with structurally advanced disease. Similar observations have been reported in previous studies, reflecting the tendency of esophageal carcinoma to remain clinically silent until significant luminal compromise occurs [20].

The lower esophagus was the most frequently involved anatomical site, followed by the mid esophagus. All adenocarcinomas were confined to the distal esophagus, supporting their established association with Barrett's metaplasia and chronic gastroesophageal reflux [21]. SCC demonstrated a broader distribution with predominance in the mid esophagus, consistent with classical exposure-related disease patterns.

The principal finding of the present study is the significant correlation between endoscopic morphology and histopathological diagnosis. Malignant lesions were more frequently associated with altered mucosa, ulcerative or proliferative growth patterns, luminal narrowing, and circumferential involvement, whereas dysplastic and non-neoplastic lesions generally exhibited less pronounced endoscopic abnormalities. Among these features, ulceroproliferative growth, luminal narrowing, and circumferential involvement demonstrated the strongest association with malignant histopathology. These observations suggest that specific endoscopic findings may

serve as useful predictors of underlying pathology and assist in risk stratification during initial evaluation.

These findings have important clinical implications for early diagnosis and patient management. Recognition of high-risk endoscopic features, particularly ulceroproliferative lesions, luminal narrowing, and circumferential involvement, may prompt early histological evaluation and expedite diagnosis. Given the substantial burden of both malignant and dysplastic lesions observed in this cohort, careful endoscopic assessment combined with prompt biopsy remains essential for the early detection and management of esophageal neoplasia.

6. Limitations

This was a single-centre study with a relatively small sample size, which may limit generalizability. Referral bias may have contributed to an overrepresentation of symptomatic and advanced lesions. Complete TNM staging data was unavailable for all patients, and molecular or immunohistochemical analyses were not performed.

7. Conclusion

Squamous cell carcinoma was the predominant esophageal malignancy in this cohort. Malignant lesions frequently exhibited luminal narrowing and ulceroproliferative or proliferative endoscopic growth patterns, which showed significant association with malignant histopathology. These findings emphasize the importance of careful endoscopic evaluation and targeted biopsy, while histopathological examination remains the gold standard for definitive diagnosis and optimal patient management.

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