

# Original Research Article

## **A study of Clinical and microbiological profile of esophageal candidiasis in a tertiary care center: Observational study**

### **Abstract**

**BACK GROUND:** Candida, a yeast organism, is a normal resident of the human alimentary canal and urogenital system in healthy individuals, forming part of the natural flora. However, when the local or systemic immune system is compromised, candida overgrowth can occur, leading to candida infections. Among these, esophageal candidiasis stands out as a significant infection, with a high incidence in immunocompromised individuals. The clinical spectrum, predisposing factors and microbiological profile of esophageal candidiasis has not been evaluated previously in our hospital.

**AIM:** To analyze the clinical and microbiological profile of patients with esophageal candidiasis.

**METHODS:** The study is a single center cross sectional study involving 100 patients with candida esophagitis, meeting inclusion criteria conducted at Madras medical college Chennai during the period 2021-2022. EC had been diagnosed when characteristic candidal plaques were endoscopically identified, biopsied using standard biopsy forceps and pathological confirmation of yeast forms typical for candida was found invading the esophageal mucosa (with hematoxylin-eosin [H-E] and periodic acid-Schiff stains [PAS]) in association with an active esophagitis. Clinical symptoms at the time of presentation, comorbidities, precipitating factors, indication for endoscopy, findings during endoscopy, grading of candidiasis, KOH mount, fungal culture & drug sensitivity noted. Candida esophagitis was diagnosed when characteristic candidal plaques were endoscopically identified and pathological confirmation of yeast forms typical for candida was found in association with an active esophagitis.

**RESULTS:** During the study period, around 16,000 upper endoscopies were performed in our endoscopy unit. One hundred patients were diagnosed with candida esophagitis on the basis of endoscopic and histopathologic criteria. The main findings of our study was that the prevalence of EC was less observed (0.62%, 100/16000). One fourth (26%) of our cases were presented with dysphagia followed by nausea (15%), dyspepsia (15%), asymptomatic (11%), regurgitation (9%), chest discomfort (8%), vomiting (6%), odynophagia (5%) and hiccups (5%). No comorbidities in one fifth of cases (20%) followed by liver disease (17%), malignancy (13%), diabetes (10%), COPD (9%) and HIV (8%). No precipitating factor in 42% cases of EC followed by PPI/H2RA (23%), antibiotics (13%), immune suppressants (13%), and inhaled steroids (9%). More than half (59%) of cases during endoscopy were grade 1 esophageal candidiasis followed by grade 2 EC (32%), grade 3 EC (8%) & oropharyngeal candidiasis observed in (1%). More than one third (39%) of cases candida lesions observed in distal esophagus followed by entire esophagus in (27%), mid esophagus in (24%) and upper esophagus in (10%). KOH mount positive in 56% cases and more than 2/3rd (67%) of EC were due to candida albicans species & one fifth (20%) showed resistance to fluconazole.

**CONCLUSION:** In conclusion, Candida esophagitis may be more common than previously suspected. Neither the presenting symptoms nor the endoscopy findings are always classic for this disease. Large-size prospective studies are needed to further identify the clinical & microbiological profile of esophageal candidiasis.

Keywords: Esophageal candidiasis, Dysphagia, Fluconazole

## Introduction

Candida, a yeast organism, is a normal resident of the human alimentary canal and urogenital system in healthy individuals, forming part of the natural flora. However, when the local or systemic immune system is compromised, candida overgrowth can occur, leading to candida infections [1]. There are over 15 distinct candida species that can cause diseases, with the most prevalent being *C. albicans*, *C. glabrata*, and *C. tropicalis*.

Commonly, mucosal candida infections affect areas such as the oropharynx, esophagus, and vagina, particularly in the general population. Among these, esophageal candidiasis stands out as a significant infection, with a high incidence in immunocompromised individuals. Additionally, patients who have undergone treatments involving broad-spectrum antibiotics, steroids, and immunosuppressants are susceptible due to the disruption of the body's natural microflora and immune responses [2]. The clinical spectrum, predisposing factors and microbiological profile of esophageal candidiasis has not been evaluated previously in our hospital. In this study we aim to analyze the clinical and microbiological profile of patients with esophageal candidiasis, identification of common species of candida causing candidiasis and their sensitivity patterns may help us predict response to treatment and tailor our treatment accordingly.

## MATERIALS AND METHODS:

The study is a single center cross sectional study involving 100 patients with candida esophagitis, meeting inclusion criteria conducted at Madras medical college/Rajiv Gandhi government general hospital, Chennai during the period 2021-2022. EC had been diagnosed when characteristic candidal plaques were endoscopically (esophago-gastro-duodenoscopy) identified, biopsied using standard biopsy forceps by the senior faculty and pathological confirmation of yeast forms typical for candida was found invading the esophageal mucosa (with hematoxylin-eosin [H-E] and periodic acid-Schiff stains [PAS]) in association with an active esophagitis.

Clinical symptoms at the time of presentation, comorbidities, precipitating factors, indication for endoscopy, findings during endoscopy, grading of candidiasis as per Kodsí grading for endoscopic severity, site & extent, associated oropharyngeal candidiasis, complete blood count, neutrophil lymphocyte ratio, random blood sugar, ECOG performance status, KOH mount, fungal culture & drug sensitivity noted. All endoscopic examinations were performed by faculty of our hospital's gastroenterology section, using an Olympus videoscope GIF x Q 170. Candida esophagitis was diagnosed when characteristic candidal plaques were endoscopically identified and pathological confirmation of yeast forms typical for candida was found in association with an active esophagitis.

To describe the severity of candida esophagitis, a grading scale was described by Kodsí et al has been used. Candida esophagitis was graded as the following: Grade 1 as few raised lesions (<2mm) without surrounding edema or laceration, grade 2 as multiple raised lesions (>2mm) without surrounding edema or laceration, grade 3 as linear, nodular and confluent lesions, grade 4 same as grade 3 with narrowing of lumen and friability of mucosa, grade 5 as thick white plaque covering the lumen in circumferential manner causing narrowing of lumen, grade 6 as endoscopy can detect oropharyngeal candidiasis. At the time of endoscopy, routine biopsies were performed on all endoscopic abnormalities. At least 2 biopsies were performed on each esophageal lesion with standard biopsy forceps. All tissue specimens were submitted for routine histopathology, and stained with hematoxylin-eosin (H-E) and periodic acid-Schiff stains (PAS).

Data entry was accomplished using Microsoft Excel, and subsequent analysis was conducted using SPSS program version 22. The findings were presented within the text, detailing mean and standard deviation (SD) for quantitative variables, while percentages were provided for qualitative variables. To compare the mean and SD of quantitative variables across different groups, an unpaired Student's t-test

was employed. For proportions or percentages among groups, the chi-square test was applied. Employing the stepwise selection method, multivariate logistic regression was employed, with a focus on variables from univariate analysis demonstrating significance at a threshold of  $P < 0.01$ .

**RESULTS:** During the study period, around 16,000 upper endoscopies were performed in our endoscopy unit. One hundred patients were diagnosed with candida esophagitis on the basis of endoscopic and histopathologic criteria. The age and gender distribution of esophageal candidiasis cases given in table 1.

**TABLE1: age and gender distribution of esophageal candidiasis cases.**

		Frequency	Percentage
Age group	<50	42	42.0%
	>51	58	58.0%
Gender	F	36	36.0%
	M	64	64.0%

The clinical symptoms were dysphagia 26(26%), odynophagia 5(5%), dyspepsia 15(15%), regurgitation 9(9%), nausea 15(15%), Vomiting 6(6%), chest discomfort 8(8%), hiccups 5(5%), asymptomatic 11(11%). The comorbidities & precipitating factors for esophageal candidiasis were described in table 2. **Table 2: Clinical symptoms, comorbidities and precipitating factors of esophageal candidiasis.**

		Frequency	Percentage
Symptoms	Dysphagia	26	26.0%
	Odynophagia	5	5.0%
	Dyspepsia	15	15.0%
	Regurgitation	9	9.0%
	Nausea	15	15.0%
	Vomiting	6	6.0%
	Chest discomfort	8	8.0%
	Hiccups	5	5.0%
Asymptomatic	11	11.0%	
Comorbidities	No comorbidities	20	20.0%
	Diabetes	10	10.0%
	Stroke	3	3.0%
	COPD	9	9.0%
	Malignancy	13	13.0%
	Liver disease	17	17.0%
	HIV	8	8.0%
	Others	20	20.0%
Precipitating factors	No precipitating factors	42	42.0%
	Inhaled steroids	9	9.0%
	Immuno suppressants	13	13.0%
	Antibiotics	13	13.0%
	PPI/H2RA	23	23.0%

The various indications for endoscopy in EC cases were described in table 3.

**Table 3: Various indications for endoscopy in EC cases.**

		Frequency	Percentage
Indication for endoscopy	Abdomen pain	5	5.0%
	Achalasia	1	1.0%
	Anemia	3	3.0%
	Atypical chest pain	5	5.0%
	Ca Pancreas	1	1.0%
	Ca stomach	3	3.0%
	Chronic pancreatitis	1	1.0%
	Diarrhoea	2	2.0%
	Dyspepsia	16	16.0%
	Dysphagia	22	22.0%
	GERD	13	13.0%
	Globus pharyngeus	1	1.0%
	GOO	1	1.0%
	Hiccups	3	3.0%
	Odynophagia	4	4.0%
	UGI bleed	15	15.0%
Vomitings	4	4.0%	

In cases of candida esophagitis, the severity was assessed using the Kodsi grading scale. The distribution among different grades is as follows:56(56%) cases were categorized as Grade 1,32(32%) cases were categorized as Grade 2,8(8%) cases were categorized as Grade 3, 2 (2%)cases were categorized as Grade 4, 1(1%) case was categorized as Grade 5 and 1(1%) case was categorized as Grade 6.The site and extent of candidiasis during endoscopy in cases were upper esophagus 10 (10%),mid esophagus 24(24%),distal esophagus 39 (39%), and pan esophagus 27(27%) described in table 4.

**Table 4: severity grading and extent of candidiasis**

		Frequency	Percentage
Grade of candidiasis	1	56	56.0%
	2	32	32.0%
	3	8	8.0%
	4	2	2.0%
	5	1	1.0%
	6	1	1.0%
Site & extent	Upper esophagus	10	10.0%
	Mid esophagus	24	24.0%
	Distal esophagus	39	39.0%
	Pan esophagus	27	27.0%

Anemia (Hb < 11 gm%) observed in 26 (26%) cases, remaining 74 (74%) cases Hb level was more than 11 gm%. RBS less than 125 seen in 47 (47%) cases and more than 125 seen in 53 (53%) cases. NLR (less than 2) seen in 44 (44%) cases and more than 2 seen in 56 (56%) cases described in table 6.

**Table 5: Hb ,NLR and RBS Values of EC cases.**

		Frequency	Percentage
Hb	<11	26	26.0%
	>11	74	74.0%
RBS	<125	47	47.0%
	>125	53	53.0%
NLR	<2	44	44.0%
	>2	56	56.0%

Fungal culture shows candida albicans in 67 (67%) cases, candida nonalbicans in 33 (33%) cases and sensitive to fluconazole in 80 (80%) cases, resistance to fluconazole in 20 (20%) cases as described in table 6.

**Table 6: ECOG performance, KOH mount status, fungal culture and fluconazole sensitivity of EC cases**

		Frequency	Percentage
ECOG performance	0	81	81.0%
	1	19	19.0%
	2	0	0.0%
	3	0	0.0%
KOH mount	Negative	44	44.0%
	Positive	56	56.0%
Fungal culture	Candida albicans	67	67.0%
	Candida non albicans	33	33.0%
Sensitive	Flu, Vor, itr, AmpB	80	80.0%
	Vor, Itr, AmpB	20	20.0%
Resistance for fluconazole	Yes	20	20.0%
	No	80	80.0%

## DISCUSSION:

The emergence of esophageal candidiasis (EC) involves a sequential process encompassing esophageal colonization and subsequent penetration of the epithelial layer. This phenomenon is recognized as the initiation of Candida colonization in approximately 20% of healthy adults. Once this colonization is established, compromised immune responses, such as those seen in HIV infections, facilitate the invasion of the epithelial layer [3]. Certain factors contribute to the susceptibility of EC includes use of proton pump inhibitors, H2-receptor antagonists, and prior vagotomy is linked to an elevated EC risk due to their impact on gastric pH. This modification influences the colonization patterns of microorganisms, including Candida, within the esophagus. The disturbance of the normal microbial balance by antibiotics

can lead to overgrowth and the colonization of *Candida* species [4]. Even individuals with functional immune systems can be rendered vulnerable to fungal infections. Corticosteroid administration hampers lymphocyte and granulocyte function, reducing the body's ability to combat infections, including fungal ones. EC may manifest in cases of esophageal obstruction, where stagnation promotes excessive *Candida* proliferation. However, while these factors contribute to EC development, the exact mechanisms underlying epithelial layer invasion in otherwise healthy individuals remain incompletely understood. In essence, the progression of EC is a multifaceted process, influenced by host-related factors, interactions among microorganisms, and immune responses [5]. Grasping these intricacies is pivotal in devising effective strategies to manage and treat EC in individuals at risk or afflicted by this condition.

Our study is the first attempt to evaluate clinical symptoms, comorbidities, precipitating factors, endoscopic manifestations of candida esophagitis, fungal culture and drug sensitivity in major southern india city Chennai. The main findings of our study was that the prevalence of EC was less observed (0.62%, 100/16000) comparing with the data reported other countries by Underwood, et al. (0.71%, 18/2527) and by Naito, et al.13 (1.17%, 41/3501). We found that one fourth (26%) of our cases were presented with dysphagia followed by nausea(15%),dyspepsia(15%),asymptomatic(11%),regurgitation(9%),chest discomfort (8%),vomiting (6%),odynophagia (5%) and hiccups (5%). We also found that no comorbidities in one fifth of cases (20%) followed by liver disease (17%), malignancy(13%), diabetes(10%), COPD(9%) and HIV(8%).We also found that no precipitating factor in 42% cases of EC followed by PPI/H2RA (23%),antibiotics (13%), immunosuppressants(13%), and inhaled steroids(9%).

In our study we found that more than half(59%) of cases during endoscopy were grade 1 esophageal candidiasis followed by grade 2 EC (32%),grade 3 EC (8%) & oropharyngeal candidiasis observed in (1%).More than one third(39%) of cases candida lesions observed in distal esophagus followed byentire esophagus in (27%),mid esophagus in (24%) and upper esophagus in (10%).

In our study we found that KOH mount positive in 56% cases,we also observed that more than 2/3rd(67%) of EC were due to candida albicans species & one fifth(20%) showed resistance to fluconazole.

The limitation of our study included a small number of patients.

## **Conclusion**

*Candida* esophagitis may be more common than previously suspected. Neither the presenting symptoms nor the endoscopy findings are always classic for this disease. Although the majority of patients included in our study did not have an underlying malignancy or known immunosuppression, multiple predisposing risk factors were noted. All patients were found to have at least one predisposing condition or history of medication use, acid-suppressive therapy being the most frequently noted. Large-size prospective studies are needed to further identify the clinical & microbiological profile of esophageal candidiasis.

## **REFERENCES:**

1. Weerasuriya N, Snape J. Oesophageal candidiasis in elderly patients: risk factors, prevention and management. *Drugs Aging* 2008;25:119-30.
2. Underwood JA, Williams JW, Keate RF. Clinical findings and risk factors for *Candida* esophagitis in outpatients. *Dis Esophagus* 2003;16:66-9 .

3. Laine L, Bonacini M. Esophageal disease in human immunodeficiency virus infection. *Arch Intern Med* 1994;154:1577-82.
4. Thapa BR, Kumar L. Candida esophagitis after antibiotic use. *Indian J Pediatr* 1989;56:296-9.
5. Kochhar R, Talwar P, Singh S, Mehta SK. Invasive candidiasis following cimetidine therapy. *Am J Gastroenterol* 1988;83:102-3.
6. Karmeli Y, Stalnikowitz R, Eliakim R, Rahav G. Conventional dose of omeprazole alters gastric flora. *Dig Dis Sci* 1995;40:2070-3.
7. Baehr PH, McDonald GB. Esophageal infections: risk factors, presentation, diagnosis, and treatment. *Gastroenterology* 1994; 106:509-32.
8. Simon MR, Houser WL, Smith KA, Long PM. Esophageal candidiasis as a complication of inhaled corticosteroids. *Ann Allergy Asthma Immunol* 1997;79:333-8.
9. Mathieson R, Dutta SK. Candida esophagitis. *Dig Dis Sci* 1983;28:365-70.
10. Hoshika K, Iida M, Mine H. Esophageal Candida infection and adherence mechanisms in the nonimmunocompromised rabbit. *J Gastroenterol* 1996;31:307-13.
11. Vermeersch B, Rysselaere M, Dekeyser K, Rasquin K, De Vos M, Elewaut A, et al. Fungal colonization of the esophagus. *Am J Gastroenterol* 1989;84:1079-83.
12. Phaosawasdi K, Rice P, Lee B. Primary and secondary Candida esophagitis. *IMJ Ill Med* 1986;169:361-5