Candida Esophagitis: A Retrospective Study of Upper Gastrointestinal Endoscopic Grading and the Characteristic Profile

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ABSTRACT

Background: *Candida esophagitis is a common abnormality found on esophagogastroduodenoscopy (EGD) procedure in patients with recognizable risk factors. However, the finding is frequently incidental as most of them are asymptomatic. There has been no study on the characteristics of Candida esophagitis in Indonesia. The aim of this study was to describe the degree of Candida esophagitis and its characteristics in patients who underwent EGD procedure at Cipto Mangunkusumo Hospital.*

Method: *A retrospective study was conducted on all EGD procedures at the Gastroenterology Procedure Room, Internal Medicine Department, Cipto Mangunkusumo Hospital, between January 2007 and December 2009 with a total of 2,311 samples. The study was carried out by visually examining all endoscopic procedures and grading them according to the Kodsi severity grading (1976), and evaluating medical records. Data analysis was performed using Microsoft Excel 2007.*

Results: *During the study period, Candida esophagitis was found in 2.6% patients with predominant male (68.9%) and the average age was 49.8 ± 15 years. The chief complaints found were dyspepsia (34.4%), melena (21.3%) and dysphagia (4.9%) and 32.8% patients were asymptomatic. The most frequent risk factors were age ≥ 60 years old (28.3%), proton pump inhibitor or H_2 receptor antagonist user (26.4%), and antibiotics (17.0%). Grade II Kodsi candidiasis was the most prevalent degree in this study (44.3%).*

Conclusion: *Candida esophagitis was one frequent finding in endoscopy based on the complaint of dyspepsia in patients with certain risk factors. However, the results of this study still need further validation in prospective studies.*

Keywords: *Candida esophagitis, esophagogastroduodenoscopy, risk factors, grading*

ABSTRAK

Latar belakang: *Esofagitis kandida merupakan salah satu kelainan yang sering ditemukan pada pasien dengan faktor risiko tertentu pada pemeriksaan esofagogastroduodenoskopi (EGD). Temuan ini seringkali insidental karena pada kebanyakan kasus tidak bergejala, namun hingga saat ini belum ada penelitian mengenai karakteristik esofagitis kandida di Indonesia. Tujuan dari penelitian ini adalah untuk mendeskripsikan derajat esofagitis kandida dan karakteristiknya pada pasien yang menjalani pemeriksaan EGD di Rumah Sakit Cipto Mangunkusumo (RSCM).*

Metode: *Penelitian ini merupakan studi retrospektif yang dilakukan pada semua pasien yang menjalani pemeriksaan EGD di ruang prosedur endoskopi saluran cerna RSCM antara Januari 2007 hingga Desember*

2009 dengan melibatkan 2.311 sampel. Semua hasil prosedur endoskopi diperiksa secara visual untuk kemudian dikatagorikan berdasarkan derajat keparahan Kodsi (1976). Analisis data dilakukan dengan menggunakan program Microsoft Excel 2007.

***Hasil:** Selama periode penelitian, esofagitis kandida ditemukan pada 2.6% dari keseluruhan sampel dengan proporsi terbanyak pada laki-laki (68.9%) dengan rerata usia 49.8 ± 15 tahun. Keluhan terbanyak pasien adalah dispepsia (34.4%), melena (21.3%), dan disfagia (4.9%). Sebanyak 32.8% pasien dilaporkan tidak bergejala. Faktor risiko utama yang ditemukan adalah usia ≥ 60 tahun (25.8%), pengguna penghambat pompa proton atau antagonis reseptor H_2 (24.1%) dan antibiotik (15.5%). Derajat esofagitis kandida terbanyak pada penelitian ini adalah derajat II Kodsi (44.3%).*

***Kesimpulan:** Esofagitis kandida merupakan salah satu kelainan yang sering ditemukan pada endoskopi berdasarkan keluhan dispepsia pada pasien dengan faktor risiko tertentu. Hasil penelitian ini masih membutuhkan validasi lebih lanjut menggunakan studi prospektif.*

***Kata kunci:** esofagitis kandida, endoskopi gastroduodenal, faktor risiko, derajat keparahan*

INTRODUCTION

Candida esophagitis is one of the most frequent abnormalities found on esophagogastroduodenoscopy (EGD) as *Candida*, especially *Candida albicans*, is normally found in the throat.[1] It is a common disease with a broad spectrum of severity, ranging from asymptomatic to severe symptoms, which may cause inability to eat and dehydration.[2,3] These findings are frequently incidental in nature, because a lot of patients with *Candida* esophagitis present without any symptoms. The prevalence cited from a series of study shows that 20% of normal healthy adults and up to 40% of immunocompromised patients were reported asymptomatic. Constitutional findings, including fever occur occasionally.[4] As the infection become more severe, clinical features like odynophagia may develop, as well as other symptoms such as dysphagia, chest pain, epigastric pain and hemorrhage.[1-4]

Although the cases might often be found incidentally, patients with *Candida* esophagitis usually have several recognizable risk factors. With the increased usage of immunosuppressive agent for chronic inflammatory diseases and chemotherapy along with the acquired immune deficiency syndrome (AIDS) epidemic and other immunocompromised conditions such as diabetes mellitus, esophageal infections with *Candida* species have become relatively common.[1] In addition, some studies have discovered several risk factors in developing *Candida* esophagitis, including carcinoma, proton pump inhibitor or H2 blocker usage, age above 65 years old, prior use of antibiotics, uncontrolled diabetes mellitus, and long term corticosteroid therapy, chronic renal failure, and inhaled corticosteroid.[5,6] Although rare, infectious esophagitis also occurs among the non-immunocompromised, with *Candida albicans* being the most common pathogen.[1]

The severity of *Candida* esophagitis was described by Kodsi through his study involving 27 cases in 1976.[7] Despite of the variety of clinical presentations and its severity, until now, there was no study available on the characteristics of patients with *Candida* esophagitis in Indonesia as well as the severity of the disease. The aim of this study was to describe the degree of severity of *Candida* esophagitis, along with its characteristics in patients who underwent EGD procedures at Cipto Mangunkusumo Hospital.

METHOD

A retrospective analysis of all patients who underwent EGD procedure at the Gastroenterology Procedure Room in Internal Medicine Department, Cipto Mangunkusumo Hospital was carried out by visually examining all endoscopic procedures between January 2007 and December 2009. Patients with incomplete medical status and could not be traced were excluded. There were a total of 2,311 samples obtained during the study period according to inclusion and exclusion criteria. Medical records of patients with *Candida* esophagitis were reviewed to identify potential risk factors for the infections as well as the clinical symptoms at time of presentation, diagnosis and the severity grading.

Candida esophagitis was endoscopically diagnosed when typical candidal plaques were identified. To describe the severity of *Candida* esophagitis, a grading scale described by Kodsi was used. According to endoscopic appearance, Kodsi classified *Candida* esophagitis into four categories. Type I cases refer to a few whitish or beige plaques up to 2 mm in diameter without ulceration. Type II plaques are greater than 2 mm in diameter and more numerous. In milder grades, plaques may be

hyperemic or edematous, but there is no ulceration. Type III plaques may be confluent, linear, nodular, and elevated with hyperemia and frank ulceration, and type IV plaques are Type III plaques which additionally have increased friability of the mucosa and narrowing of the lumen.[4,8] Statistical analysis of the compiled data from visual examination and medical records was performed by using Microsoft Excel 2007.

RESULTS

Throughout the study period, a total number of patients who underwent EGD procedures were 2,311 patients. Based on the visual examination during endoscopy, *Candida* esophagitis was found in 61 cases (2.6%), with the majority of male patients (68.9%).

Table 1. The characteristics of patient with *Candida* esophagitis

Variable	n (%)
Age (years)	
Mean ± SD	49.8 ± 15.2
Range	22-79
Sex	
Male	42 (68.9)
Female	19 (31.1)
Underlying disease	
CKD	25 (50.0)
Liver cirrhosis	15 (30.0)
DM	6 (12.0)
SLE	2 (4.0)
Tuberculosis	1 (2.0)
Solid tumor	1 (2.0)
Risk factors	
Age > 60 years	15 (28.3)
PPI/H_2RA	14 (26.4)
Prior antibiotic use	9 (17.0)
CKD	6 (11.3)
Chronic steroid usage	3 (5.7)
Solid tumor	2 (3.8)
DM	2 (3.8)
Steroid inhalation	1 (1.9)
Cytostatics	1 (1.9)
Kodsi grading	
Grade I	12 (19.7)
Grade II	27 (44.3)
Grade III	15 (24.6)
Grade IV	7 (11.5)

CKD: chronic kidney disease; DM: diabetes mellitus; SLE: systemic lupus erythematous; PPI/ H2RA: proton pump inhibitor/H2 receptor antagonist

The patients in this study ranged in age between 22 and 79 years with 28.3% patients at over 60 years of age. When the underlying disease was taken into account, chronic kidney disease was found to be the largest proportion among the patients with *Candida* esophagitis (50%). Based on the Kodsi endoscopic grading, this study revealed that Grade II was the most prevalent severity. The summary of patient characteristics can be seen in Table 1.

Table 2 showed the noted patients' clinical complaints when the EGD procedures were carried out. There were 32.8% patients who did not have any complaints. The main clinical manifestation was dyspepsia, which was found in 21 patients, followed by melena and dysphagia.

DISCUSSION

The prevalence of *Candida* esophagitis in Cipto Mangunkusumo Hospital is 2.6%. This proportion varies when compared with the population of other countries. A study in Brazil by Klieman et al, described that the prevalence of *Candida* esophagitis was 0.8% (n = 163). Their data was obtained from 21,248 upper gastrointestinal endoscopies that were carried out in 18 months.[6] Through a 6-year-duration of retrospective study in Saudi Arabia, Al Mofleh et al demonstrated that the prevalence of *Candida* esophagitis was 1% (n = 59) as evaluated from 5,028 upper gastrointestinal endoscopies.[9]

In this study, we found that a large proportion of patients were asymptomatic (32.8%). A retrospective study in Saudi Arabia showed that the prevalence of asymptomatic candidiasis reached 70% of the population.[9] In candidiasis patients, alterations in cellular immunity may lead to candidal colonization and superficial infection; while humoral immunity prevents invasive disease and dissemination.[3] Therefore, despite the vast numbers of yeast involved in the infection, systemic dissemination rarely occurs in immunocompetent individual.[2]

Table 2. The degree of clinical severity and endoscopic grading

Clinical manifestation	n (%)	Kodsi endoscopic grading (n = 61)			
		Grade I	Grade II	Grade III	Grade IV
Without complaint	20 (32.8)	3	10	6	1
Dysphagia	3 (4.9)	0	0	1	2
Melena	13 (21.3)	3	6	2	2
Dyspepsia	21 (34.4)	5	9	6	1
GERD	1 (1.6)	1	0	0	0
Dysphagia and vomiting	1 (1.6)	0	1	0	0
Odynophagia and disphagia	1 (1.6)	0	0	0	1
Dyspepsia and GERD	1 (1.6)	0	1	0	0

GERD: gastroesophageal reflux disease

Candida esophagitis is a common opportunistic infection in patients with HIV since their level of immunity is a primary risk factor for the disease.[2,3] Approximately 10-15% patients with AIDS will suffer from this disease during their lifetime.[10] Among patients with HIV infection who have esophageal symptoms, *Candida* is the most common identifiable pathogen on endoscopy, which is affecting up to 50% of patients.[2] However, no patient in this study was infected by the pathogen. The most common underlying disease in this study was chronic kidney disease. Immune defects in end-stage renal diseases may be related to metabolic and nutritional abnormalities, which probably impair both cellular and humoral immunities. In chronic renal failure, dialysis patients have increased risk of fungal infection, with candidiasis (79%) as the dominant etiology of fungal infection in chronic dialysis patients.[11]

Old age (> 60 years) is the most common risk factor in this study. One of our literatures showed that age over 60 years may predispose to candidal infection through defective cellular immunity.[12] This study revealed that 8 patients (13.1%) did not have any risk factor for esophageal candidiasis. It has been described that esophageal candidiasis could occur in immunocompetent individual. The mechanism might be related to the *Candida* strain virulence. It is generally said that most strains causing the disease are commensal in the patient; however, there are regulatory events that may switch the organism from a benign commensal to an invasive state.[13] A case report showed that an immunocompetent pediatric patient may suffer from *Candida* esophageal perforation even without instrumentation or any surgical intervention, except from the chronic gastroesophageal reflux.[14] Moreover, some reports of immunocompetent adults with esophageal infection suggest that the possible mechanism includes injuries to the esophageal ephitelium.[14,15]

The most frequent complaint of patients with *Candida* esophagitis in this study was dyspepsia (34.4%). It was discovered in every grade of *Candida* esophagitis, with the greatest proportion of grade I. Similar result was also found in a study in Pakistan demonstrating that epigastric symptoms were present in 35.3% patients with *Candida* esophagitis.[5]

Based on that, a raised suspicion of esophageal candidiasis is appropriate for patients presenting symptoms of dyspepsia with risk factors, especially with visible oropharyngeal candidiasis. It is well stated that oropharyngeal candidiasis is commonly associated with esophageal candidiasis in immuno-compromised as well as non immunocompromised patients.[2,3]

It should be noted that, because of the restrospective nature in this study, some data may be missing, particularly regarding the patients' complaints. In addition, it is a study reporting a prevalence which does not show any corelation between symptoms and the severity grading. Furthermore, it did not examine the risk factors statistically using multivariate analysis. Moreover, the biological importance of this study is unknown. However, this study provides clinical importance by suggesting that *Candida* esophagitis should be considered in patients who had recognizable risk factors and underlying diseases, including patients who presented with dyspepsia and other upper gastrointestinal symptoms. Therefore, further evaluation and EGD procedures can be carried out in time among these patients. Prospective studies on the association of patient characteristics and the severity grading should be carried out to further validate the results.

CONCLUSION

Candida esophagitis is one of the most frequent findings in patients with certain risk factors and a complaint of dyspepsia who undergo endoscopic procedures. However, immunocompetent patients might show no typical symptom of esophagitis. The results of this study would still need further validation in prospective studies.

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