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Original Research Article

A Study of Risk Factors of Esophageal Candidiasis in Non-HIV Infected Immunocompromised Patients

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Abstract: Esophageal Candidiasis is one of the most common opportunistic infections in patients with impaired immunity and the most common cause of esophageal disease in patients with Acquired Immune Deficiency Syndrome (AIDS). It can also occur in debilitated patients who have received broad-spectrum antibiotics, steroids and immunosuppressant drugs. This study was designed to determine risk factors of esophageal candidiasis in non-Human Immune Deficiency Virus (HIV) infected patients attending a tertiary care, teaching hospital. Clinical records of all patients of Esophageal Candidiasis diagnosed by esophagogastroduodenoscopy (EGD) and histopathology over a period of eighteen months were studied. Eighteen patients (10 males, 8 females), aged 21-77 years old (mean age 52.9 years) fulfilled the criteria (0.6% of the EGD). The common predisposing factors were carcinoma and diabetes mellitus. The frequent clinical symptoms were retrosternal discomfort, dysphagia and epigastric abdominal pain with endoscopic appearance of scattered mucosal plaques. The common predisposing factors were carcinoma and diabetes mellitus; other risk factors being corticosteroid and antibiotic therapy. All patients responded to treatment with fluconazole.
Keywords: Candidiasis, Esophageal, Immunocompromised, Esophagogastroduodenoscopy

INTRODUCTION

Esophageal Candidiasis is one of the most common opportunistic infections in patients with impaired immunity and the most common cause of esophageal disease in patients with Acquired Immune Deficiency Syndrome (AIDS) [1]. It can also occur in debilitated patients who have received broad-spectrum antibiotics, steroids and immune-suppressants. With the advent of organ transplantation and AIDS, esophageal infection is now a common medical problem [2]. The common infections involving immunocompromised Non-Human Immunodeficiency Virus (HIV) infected patients include *candida* and viral diseases such as *cytomegalovirus* (*CMV*) and *herpes simplex virus* (*HSV*) [3]. Immunocompromised patients who develop esophageal symptoms need to undergo endoscopy to rule out Esophageal Candidiasis. The purpose of the present study was to assess the risk factors associated with Esophageal Candidiasis in the immunocompromised Non- HIV infected patients.

AIM

This study was conducted with aim to study the risk factors associated with esophageal candidiasis in non- HIV infected patients attending a tertiary care teaching hospital in Rural Western India.

MATERIALS AND METHODS

Patients

The study was conducted at a tertiary care teaching hospital in Rural Western India. The patient data for a period of one year and a half, from January 2015 to June 2016 was retrospectively analysed in July 2016. Medical records of all the patients who underwent esophagogastro-duodenoscopy (EGD) at the hospital were analysed. All patients who were diagnosed as having esophageal candidiasis based on EGD and histopathology (HPE) findings were included in the study. Past/present history of oral and/or esophageal candidiasis, symptoms, physical findings, drug treatment including dosage and duration were noted. Investigations including but not limiting to Complete

Blood Count, Blood Glucose estimation, biochemical profile and HBV, HCV and HIV status were also recorded. Case patients were labeled as group A and the control group as group B which consisted of those patients without a diagnosis of Esophageal Candidiasis and in whom an endoscopic examination was performed immediately before and after every case patient was examined endoscopically.

Endoscopy

All endoscopic examinations were performed by using an Olympus video scope GIF x Q 140 (Figure 1 and 2). The severity of Esophageal Candidiasis both in HIV [4, 5] and in non-HIV populations was classified using a grading scale described by Kodsi *et al*. [6] or a modification thereof.7 Esophageal Candidiasis was graded as the following:

Grade 1 as scattered mucosal plaques involving less than 50% of the esophageal mucosa,

Grade 2 as mucosal plaques involving more than 50% esophageal mucosa,

Grade 3 as confluent plaque material circumferentially coating at least 50% of the esophageal mucosa but without luminal impingement,

Grade 4 as circumferential plaque mat coating at least 50% of the esophageal mucosa with luminal impingement despite air insufflations.

Histopathology

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). A lesion was considered Esophageal Candidiasis only when it was found endoscopically and confirmed on histopathology [7] (Figure 3).

Statistical analysis

Results were expressed as mean ± standard deviation, median range for all continuous variables (*e.g*., age) and number (percentage) for categorical data (*e.g*., gender, diabetes mellitus, steroids, etc) were provided. Univariate analysis was performed using the independent sample *t*-test, Pearson Chi-square test and Fisher exact test whenever appropriate. A *P* value < 0.05 was considered as statistically significant.

RESULTS

Patients

During the study period, 3000 upper endoscopies were performed in the hospital. Eighteen patients were diagnosed with esophageal candidiasis on the basis of endoscopic findings and histopathologic criteria. The age, sex and percentage of the patients are given in Table 1.

Clinical Features

The clinical details are given in Table-2. The clinical symptoms in group A were retrosternal discomfort in 38.9% (7/18) patients, of these 2/7were associated with dysphagia and 1/7 with epigastric pain. Dysphagia was present in 27.8% (5/18) and epigastric symptoms in 33.3% (6/18) with only (3/6) describing it as an epigastric pain. In control group B, retrosternal discomfort was described in 30.5% (11/36), dysphagia in 19.4% (7/36) and epigastric symptoms in 50% (18/36)

Endoscopy Findings

The endoscopic appearance of plaques varied in color from yellow to white. With increasing severity, scattered mucosal plaques coalesced circumferentially coating the mucosal surface and impinged into the esophageal lumen. In group A, 3 patients had grade 1 esophageal candidiasis, 7 patients had grade 2, 3 patients had grade 3, and 5 patients had grade 4 esophageal candidiasis. In 16.8% (3/18) of group 'A' patients, associated endoscopic findings included 5.6% (1/18) with antral gastritis, 5.6% (1/18) with gastric ulcer, 5.6% (1/18) with duodenitis. In control group 'B', esophageal disease was found in 33.3% (12/36) cases, gastric disease in 38.9% (14/36) cases, and duodenal pathology was seen in 27.8% (10/36) cases. No patient in control group had evidence of esophageal candidiasis.

Correlation of clinical symptoms and endoscopic feature

There was no correlation between clinical symptoms and endoscopic findings.

Table-1: Demographic Details of Patients and Controls

	Cases	**Control**
	***n*=18**	***n* = 36**
Sex		
Male	10 (53)	21 (58)
Female	8 (47)	15 (42)
Age in years		
Range:	21-77	19-74
Mean ± SD	52.9 ± 14.6	50.08 ± 12.64
No: % of In-patients	12 (64)	19 (54)

Table-2: Risk factors for *Esophageal Candidiasis*

Risk Factor	Cases	Controls
Steroid therapy	6(33.3%)	2 (5.6%)
Diabetes mellitus type 1 and 2	8 (44.4%)	2 (5.6%)
Carcinoma (*e.g*. breast, gastric, esophagus)	4 (22.3%)	1 (2.8%)
Broad spectrum antibiotics	-	1 (2.8%)
Chronic liver disease	-	2 (5.6%)
Ischemic heart disease	-	9 (25%)
Peptic ulcer disease	-	10(27.8%)
Chronic anemia	-	9 (25%)

Table-3: Clinical Features of the patients of Esophageal Candidiasis

Symptom	Patients	Controls
Retrosternal discomfort	7 (38.9%)	11 (30.5%)
Dysphagia	5 (27.8%)	7(19.4%)
Epigastric symptoms	6 (33.3%)	18 (50%)

Table-4: Endoscopic Grading of Esophageal Lesions

Endoscopic Grading of the Lesions	Number of Patients
Grade 1	3
Grade 2	7
Grade 3	3
Grade 4	5

Table-5: Results of Univariate Analysis of Potential Risk Factors for acquisition of Esophageal Candidiasis

Risk Factor	No. of cases (%)	No. of control (%)	Odd ratio (95%CI)	*P* value
Diabetes mellitus	8 (44.4%)	2 (5.6%)	13.6 (2.47-74.62)	0.0027
Steroids use	6 (33.3%)	2 (5.6%)	8.5 (1.50-47.96)	0.0153
Carcinoma	4 (22.3%)	1 (2.8%)	10.0 (1.02-97.50)	0.0475

Histopathology

Histopathology revealed varying degrees of hyperplastic squamous mucosa with varying degree of acute-chronic inflammation in the surface epithelium. Mucosal surface was covered with desquamated epithelium and inflammatory necrotic slough. Superficial colonies of *candida* organism showed non-branching hyphae. In cases of ulcerative esophagitis, intact and focally ulcerated mucosa revealed moderate-severe inflammation, basal cell hyperplasia with non-septate fungal hyphae.

Fig-1: All endoscopic examinations were performed by using an Olympus Videoscope GIF x Q 140.

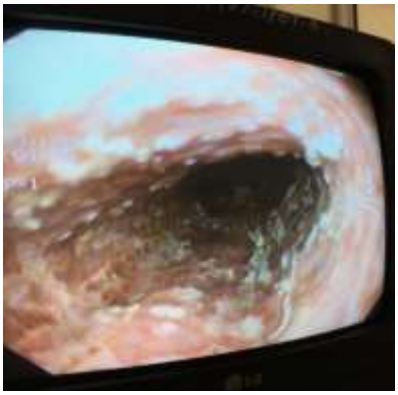

Fig-2: Characteristic C*andida* Plaques

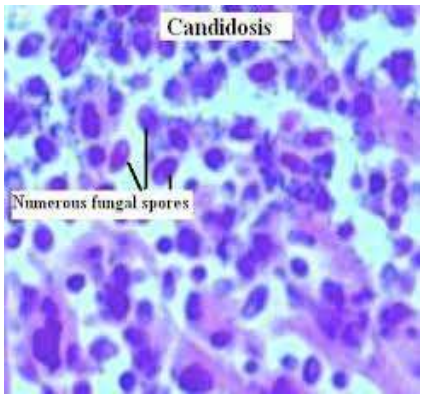

Fig-3: HPE showing Candida spores

DISCUSSION

The current study was conducted to evaluate the risk factors for esophageal candidiasis in non-HIV immunocompromised patients. Diabetes Mellitus, prior use of steroids and malignancy are the important risk factors for esophageal candidiasis. None of the patients diagnosed with esophageal candidiasis had an oral thrush, indicating thereby that esophageal candidiasis is not necessarily associated with or is extension of oropharyngeal candidiasis. This finding is similar to a study by Bonacini et al. [8]. In our study, the patients had received oral, intravenous and nebulized steroid treatment in varying durations and doses of therapy. Diabetic patients complicated with esophageal candidiasis had uncontrolled diabetes at the time of presentation, irrespective of its type. Malignancies beside other mechanisms are also associated with esophageal stasis due to mechanical obstruction that predisposes to esophageal candidiasis [9]. However, esophageal obstruction was not a feature in our cases of candida esophagitis associated with malignancies.

Epigastric pain has been known to be associated with *candida* infection [10]. In our study, no correlation was found between the symptoms and the endoscopy grade score. This finding is similar to the study conducted by Rodríguez et al. [11]. The presence of classic whitish exudates or plaques on endoscopy, should predict candidiasis in at least 90% of cases. Occasionally, viral infection might cause a similar appearance.

These esophageal candidiasis patients were treated with fluconazole 150 mg a day by mouth for 5 days. All patients responded to this treatment. The limitation of our study small sample size and retrospective design, nevertheless, the study brings out an important fact that esophageal candidiasis is associated with chronic diseases and prolonged corticosteroids use. The Patients on these medications need to be monitored and reviewed frequently. Esophageal candidiasis should be considered early in patients who have been on steroids or suffering from chronic illness/s and present with upper gastro-intestinal symptoms. Oral candidiasis does not necessarily accompany esophageal candidiasis. Our study also showed that candida esophagitis by itself is an easily managed complication.

CONCLUSION

This study was conducted to study the risk factors for esophageal candidiasis in non- HIV immunocompromised patients. Most common risk factors were diabetes mellitus, malignancies and prior steroid use. There was no correlation between symptoms, clinical findings and severity of esophageal candidiasis. None of the patients had oropharyngeal candidiasis.

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