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CANDIDA ESOPHAGITIS IN RURAL POPULATION : A PROSPECTIVE STUDY.

General Surgery

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ABSTRACT

Esophageal candidiasis (EC) is the most frequent opportunistic fungal infection in immunocompromised host. Infection by candida species is the most common cause of infectious esophagitis. Major predisposing factors include antibiotic use,radiation therapy or chemotherapy,hematologic malignancies and acquired immunodeficiency syndrome(AIDS). Other conditions associated with an increased incidence of EC include esophageal stasis, alcoholism, malnutrition and advanced age. In the future because of the progress of the modern medicine , still more immunocompromised patients will live and thus candidiasis will have more potential victims.
However, we have found EC in healthy individuals through oesophagogastroduodenoscopy (OGD).The aim of this study was to determine the prevalence and risk factors for EC in healthy individuals.
Methods of study: we retrospectively analyzed the medical record of 25 individuals who were incidentally diagnosed with EC .we also analysed the prevalence of age age group, sex and risk factors associated with the EC in these individuals.
Results: The prevalence of EC was 4.1% (25/600). The most common coexisting EGD finding was reflux esophagitis (12/25, %). An antifungal agent was prescribed in more than half of EC cases 18 (72 %). Follow-up EGD was undertaken in 13 cases (52 %) and 6 cases of candidiasis was persistently found. Case control study revealed EC were more often found in user of antibiotics (p=0.015), corticosteroids (p=0.002) and herb medication (p=0.006) as well as heavy drinking (p<0.001).
Conclusion: The prevalence of EC was 4.1% (25/600) in Kolar. Use of antibiotics, corticosteroids and herb as well as heavy drinking were significant risk factors for EC in healthy individuals.

KEYWORDS

OGD, Candidiasis, Healthy Patients

Introduction:
Esophageal candidiasis (EC) is one of the most common opportunistic infections in patients who are immunocompromised viz: Human Immunodeficiency virus (HIV) infection.1However can present as dysphagia in healthy individuals.[2,3]When EC has been found in healthy individuals, predisposing medical conditions.[2,3]

Broad-spectrum antibiotics may eliminate commensal bacteria that inhibit fungal growth, thereby enhancing *Candida* growth.[2]Soon after the introduction of H_2-receptor antagonists, some isolated cases of *Candida* in GIT were reported.[3] In recent years, proton-pump inhibitors have become widely used, and some reports link omeprazole use with the development of EC.[4] Esophageal disease, such as noninfectious esophagitis or achalasia may favor the development of EC.[5,6] Some studies have shown that corticosteroid and variable cytotoxic drugs are possible risk factors of EC.[7]Except for HIV infection, there are few data's to prove causative effect with EC,1 and the exact prevalence and risk factors of EC have never been reported in healthy individuals. The aim of this study was to investigate the prevalence and clinical characteristics of EC in non-HIV infected people and predisposing risk factors for EC in healthy individuals.

Methodology:
In our study of 600 cases of upper GI endoscopy done in the period of jan 2012 to april 2013, there were 25 cases of esophageal candidiasis accounting to 4.1% of the total cases. All these individuals were immunocompetent. These patients were analyzed retrospectively and any insufficient information was collected. Age, sex, PPI, antibiotics, heavy drinking , concomitant disease and co existing endoscopic findings were investigated.

Among 25 patients of EC only 10 patients were symptomatic and 15 were asymptomatic. The risk factors were antibiotics, herbal medication, proton pump inhibitor, corticosteroid, reflux esophagitis, and heavy drinking. The use of antibiotics, corticosteroids, herbal medication and proton pump inhibitor within 30 days prior to the EC diagnosis were asked.

Statistical analysis :
Results were expressed as mean±standard deviation for continuous variable (age), or the number (percentage) for categorical variable (sex, coexisting EGD finding, concomitant disease, proton pump inhibitors, steroids, antibiotics, herb, heavy drinking, reflux esophagitis). Chi-square tests were performed for comparison of categorical variables (sex, corticosteroid, proton pump inhibitors, steroids, antibiotics, herb, heavy drinking, reflux esophagitis) and Student t-tests were performed for age as a continuous variable. Multivariate analysis was done to evaluate the risk factors of EC in this case control study. A p-value of <0.05 was considered to be statistically significant. Statistical analyses were performed using SPSS version 12 (SPSS Inc., Chicago, IL, USA)

Results:
Clinical characteristics of immunocompetent patients (Table 1)

In our study of total 600 upper gi endoscopy . Twenty five cases (25/600,4.1%) were finally included with EC. The clinical characteristics of the 25 patients are shown in Table 1. All patients with EC enrolled in this investigation had a negative HIV serology. The mean age was 58.1±14.1 years and males were predominant (20/25, 80%). 10 patients were asymptomatic (10/25, 40 %). Fifteen (15/25, 60 %) patients had variable gastrointestinal symptoms. Acid regurgitation was the most common symptom (12/25, 48%). Dyspepsia (8/25, 32%) and nausea (6/25, 24%) were also found. Dysphagia was the presting complaint in about 12 /25 ,48% cases.

Table 1 :

Clinical characteristics.	Number %
Age (years)	58.5 (mean age group)
Sex (m/f)	20/5
Asymptomatic individuals.	10
Acid regurgitation	12
Dyspepsia	10
Nausea	6
Dysphagia	10
Odynophagia	6
Chest discomfort	4.

Coexisting EGD finding (Table 2)

Reflux esophagitis is the most common coexisting endoscopic finding

(12/25, 48%). In addition, gastric ulcer (1/25, 4 %), stomach cancer (2/25, 8%), esophageal stricture (2/25, 8%) were also found.

Table 2:

Co existing EGD findings.	Number
Normal findings.	12
Reflux esophageal candidiasis	10
Gastric ulcer	2
Gastric carcinoma	1
Esophageal stricture.	0
Carcinoma esophagus.	o

Concomitant disease (Table 3) .

Both underlying commodity and immunocompromised conditions such as HIV antibody had been evaluated when EC was found in EGD. All EC patients in this investigation were negative for HIV antibody. There were no underlying disease in 40% (10/25). Diabetes mellitus (13/25, 52 %) and malignancy (2/25, 8%) were the most common concomitant diseases.

Table 3

Con comitant diseases.	Number.
Diabetes mellitus.	12
Malignancy	2
Pulmonary diseases	0
Cirrhosis of liver	2
Rheumatoid arthritis.	2
Cardiovascular diseases.	2

An antifungal agent was prescribed in all cases (49.5%). Follow-up EGD had been undertaken in 15cases , 6 cases had been found to be persistent EC ,despite the previous use of antifungal agents. There were no severe complications of EC such as esophageal bleeding, perforation or systemic dissemination in our study population.

Risk factors for EC (Table 4)

Risk factors for EC are summarized in Table 4. In this study, recent use of antibiotics (p=0.015), corticosteroids (p=0.002), herbal medication (p=0.006) and heavy drinking (p<0.001) were significant risk factors for EC. However, the use of a proton pump inhibitor (p=0.35) was not associated with EC. Interestingly, reflux esophagitis was the most coexisting EGD finding, but, there was no statistically relationship with EC (p=0.24).

Table 4

Risk factors	EC pt's	Normal individuals	P value
Corticosteroids.	10	o	0.002
Antibiotics	12	2	0.001
PPI	4	2	0.35
Reflux esophagitis.	12	10	0.24
Heavy drinking	15	0	0.03
Herbal medications.	10	2	0.02

Discussion:

The development of EC is a two-step process consisting of colonization of the esophagus and subsequent invasion of the epithelial layer.[8,9] It is already well accepted that *Candida.A* is known to colonize in the esophagus of healthy adults(20%).[8,9] Once colonization has been established, impaired cellular immunity permits invasion of the epithelial layer.

Antibiotics may predispose immunocompetent patients to fungal infection by allowing overgrowth and colonization of the candida. Increased use of broad spectrum antibiotics has been associated with candida infection.[10]

There have been numerous case reports and small study series of patients (including older patients) taking inhaled corticosteroids for asthma and COPD have developed EC.[21-23] corticosteroids predispose one to infection by suppressing both lymphocyte and granulocyte function.[11]

Proton pump inhibitors, H_2-receptor antagonists, and prior vagotomy are thought to increase the risk of EC, which elevated gastric pH and alters the colonization of the esophagus by oral cavity bacteria and yeast.3,4

It has been proposed that high blood and tissue glucose levels favour candid growth in diabetes. [12,13] there is also some evidence for decreased candidal killing ability in diabetic neutrophils.4 of 41 patients in the case series had diabetes but there was no control patients,the same limitation applies to the study in which 2 of 21 pts with EC were found to have diabetes.

The main findings of our study was that the prevalence of EC was comparatively high 4.1%, 25/600) comparing with the data reported other countries.14 (0.71%, 18/2527) in other study.15 (1.17%, 41/3501). EC can be discovered in healthy individuals without apparent predisposing risk factors and symptoms. We identified that more than two-thirds of EC (76.2%, 214/281) may occur with no risk factors and more than half were asymptomatic (58%, 163/281).

We found that antibiotics (p=0.015), corticosteroids (p=0.002), heavy drinking (p<0.001) and herbal medication (p=0.006) were independent risk factors for EC. However, findings of previous reports, proton pump inhibitor (p=0.25) was not associated with EC. Interestingly, reflux esophagitis was the most common concomittent disease. We foun diabetes as potential risk factor in this study. Previously, diabetes is considered as risk factor for EC because of impaired immunity and stasis of esophageal contents.16 However, most of the cases of diabetes-related EC reported have been associated with chronic poor glycemic control (hyperglycemia more than 2 years) and combined with secondary factors, such as other factors causing an immunocompromised state.16 Diabetes was found in 23 patients in this investigation and were healthy individuals with good glycemic control.

One study. reported that among 3501 patients undergoing routine EGD in their study, 41 were found to have EC (1.17%)[14], and about two-thirds of those patients had no symptoms. In our study, symptomatic EC was found in 4% (10/25 cases) of the population. They complained of variable gastrointestinal symptoms including epigastric discomfort, dyspepsia, nausea. It is questionable whether various gastrointestinal symptoms may be associated with incidental finding of EC. Among them, only 24% (6/25) had classic symptoms of infectious esophagitis, such as dysphagia, odynophagia and chest discomfort. This study shows that most EC patients are asymptomatic and typical esophageal symptoms are not common. Infection was confined to the superficial mucosa in most of the cases. esophageal perforation can be seen in immunocompromised hosts, such as transplanted or leukemia patients.[16 17] It is possible that neutropenia, irradiation and chemotherapy such as methotrexate may have led to mucosal disruption, thereby facilitating deeper invasion of the esophagus by *Candida*.[16,17] In immunocompetent hosts, chronic alcohol consumption and long-standing gastroesophageal reflux may increase the risk of transmural invasive *Candida* infection and esophageal perforation.[17,18] Esophageal perforation should be considered in patients with pre-existing esophagitis, unexplained fever, pleuritic chest pain and pleural effusion.[18]

In conclusion, EC was observed in considerable healthy individuals in rural population(4.1%, 25/600) and more than half of those with EC were asymptomatic (60%, 15/25). Use of antibiotics, corticosteroids, heavy drinking and herbal medication were significant risk factors for EC in healthy individuals. EC can be discovered in patients without apparent predisposing risk factors. Further clinical studies with larger group are needed to elucidate the mechanisms of transition from colonization to infection.

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