

Risk Factors for Esophageal Candidiasis in Non-HIV Patients: A Systematic Review

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ABSTRACT

Esophageal candidiasis is commonly associated with HIV infection but also occurs in patients without HIV. This systematic review aimed to summarize risk factors for esophageal candidiasis in non-HIV patients. PubMed, the Cochrane Library, and ScienceDirect were searched for studies evaluating risk factors in non-HIV populations or reporting non-HIV subgroups separately, and the findings were synthesized qualitatively. Four studies met the inclusion criteria, comprising retrospective case-control and prospective observational studies in endoscopy-based settings. Reported prevalence among non-HIV patients ranged from 0.34% to 8.99%, depending on the population and case ascertainment. Corticosteroid use was the most consistently reported risk factor (odds ratios 2.05 to 6.67), and one study found a higher risk with higher doses. Proton pump inhibitor use (odds ratio 1.66), broad-spectrum antibiotic exposure (4.55), diabetes mellitus (7.34), malignancy (8.05), and increasing age (1.02 per year) were also reported, but proton pump inhibitor use and diabetes mellitus were significant in one study and not in another. Dysphagia and odynophagia predicted esophageal candidiasis in one prospective study, whereas a retrospective study found no correlation between symptoms and endoscopic severity. Corticosteroid exposure is the most consistent risk factor for esophageal candidiasis in non-HIV patients. Prospective multicenter studies with standardized definitions are needed to clarify the other associations.

Keywords : corticosteroids, esophageal candidiasis, non-HIV, proton pump inhibitors, risk factors

INTRODUCTION

Candida species are the most common cause of infectious esophagitis. Affected individuals typically present with odynophagia, dysphagia, and chest discomfort, and persistent infection may lead to hemorrhage, perforation, or stricture formation. Fluconazole remains the standard therapy, and the diagnosis is confirmed by endoscopy combined with cytology or histopathology.¹ The condition is frequently associated with HIV infection, with reported prevalence among people living with HIV ranging from 9.8% to 12.0%.² Clinical symptoms alone do not reliably identify affected patients; in a United States cohort, dysphagia accounted for 16.94% of reported symptoms, and 3.58% of cases were asymptomatic.¹ Because endoscopy is costly and invasive in unselected populations, clinicians must focus on identifying individuals at elevated risk.³

A large Japanese endoscopy study included 80,219 patients who underwent endoscopy between 2002 and 2014. During this period, prevalence among HIV-infected patients decreased from 13.6% to 9.0% (not statistically significant), whereas prevalence among non-HIV patients increased from 0.6% to 2.5%. The



The authors attributed this increase to an aging population, a higher burden of comorbidities, and wider use of immunosuppressive agents.³ Reported prevalence in non-HIV patients varies by clinical setting, and earlier studies estimated it at 0.32% to 5.2%.¹ A United States multicenter study reported a prevalence of 8.99% among patients who underwent esophageal biopsy.¹ An Iranian study identified a prevalence of 3.5% among 455 HIV-negative adults with upper gastrointestinal symptoms who underwent endoscopy.⁴

Esophageal candidiasis also occurs in immunocompetent people, and the literature lacks consensus on predisposing conditions. Potential risk factors include immunosuppression (particularly corticosteroid use and prior organ transplantation), older age, diabetes mellitus, malignancy, antibiotic use, and denture use.^{1,3-5} The association with proton pump inhibitors (PPIs) remains controversial, with inconsistent findings across studies.^{1,6}

Earlier studies frequently lacked case-control designs, included small samples, or enrolled only immunocompromised patients. A recent systematic review of mucosal candidiasis in people living with HIV included 15 studies, of which 13 addressed oral candidiasis, one addressed oropharyngeal candidiasis, and only one addressed esophageal candidiasis.² To date, no systematic review has synthesized risk factors for esophageal candidiasis in non-HIV patients. Such evidence is needed by prescribers of PPIs, corticosteroids, and antibiotics to identify patients who may benefit from early diagnosis and treatment.¹ This systematic review therefore aimed to evaluate risk factors for esophageal candidiasis in non-HIV patients.

METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.⁷ Studies were eligible if they were original observational studies (cohort, case-control, or cross-sectional) that enrolled patients without HIV infection, or that enrolled both HIV-positive and HIV-negative patients and reported the non-HIV subgroup separately through a stratified analysis or subgroup comparison. Esophageal candidiasis had to be diagnosed by upper gastrointestinal endoscopy, with or without histopathological, cytological, or culture confirmation, and at least one potential risk factor had to be compared between patients with and without esophageal candidiasis, with an effect estimate or data from which the association could be assessed. Case reports, case series, reviews, editorials, conference abstracts, burden-of-disease or cost analyses, studies of treatment or diagnostic tests, and studies restricted to HIV-positive patients were excluded.

PubMed, the Cochrane Library, and ScienceDirect were searched from inception to 9 October 2026, the date of the last search. The same Boolean string, “(esophageal candidiasis) AND (non-HIV)”, was used in each database with database-specific settings. In PubMed, the string was entered in the default search field, which searches all fields with automatic term mapping. In the Cochrane Library, it was applied to the Title, Abstract and Keyword fields across all Cochrane products, including the Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Trials. In ScienceDirect, it was applied to the Title, abstract and keywords field. No filters for publication date, language, or article type were applied.

All retrieved records were combined, and duplicates were removed by matching title, authors, and source. Titles and abstracts were screened against the eligibility criteria, and the full texts of potentially eligible reports were then assessed, with the reason for each full-text exclusion recorded. The numbers of records identified, screened, excluded, and included at each stage are presented in a PRISMA 2020 flow diagram. Two reports derived from the same patient cohort were both retained because they analyzed different exposures, but they were treated as one population when the consistency of associations across studies was judged.

The first author and year, country, study design and setting, study period, population and sample size, method of diagnosing esophageal candidiasis, exposures assessed, comparison group, effect estimates (odds ratios with 95% confidence intervals and P values), and whether the estimates were adjusted were extracted from each included report into a predefined table. Methodological quality was assessed with the Newcastle-

Ottawa Scale (NOS).⁸ The case-control version, with a maximum of nine stars across selection, comparability, and exposure, was used for case-control analyses, and the version adapted for cross-sectional studies, with a maximum of ten stars across selection, comparability, and outcome, was used for cross-sectional analyses.⁹ The findings were synthesized narratively by grouping exposures into pharmacological factors, host factors, and symptoms, and the consistency of each association was judged from the direction and statistical significance of the estimates across studies.

RESULTS

The searches retrieved 28 records, comprising 14 from PubMed, 14 from ScienceDirect, and none from the Cochrane Library. After two duplicates were removed, 26 records were screened by title and abstract, and 20 were excluded because they concerned HIV-positive populations only ($n = 8$), were burden-of-disease or cost analyses ($n = 4$), case reports ($n = 3$), or treatment or diagnostic studies ($n = 3$), or were conference abstracts ($n = 2$). Six reports were assessed in full text, and one was excluded because HIV-positive and HIV-negative patients were analyzed together without a separate risk factor analysis for the non-HIV group.¹⁰ Five reports met the inclusion criteria (see Figure 1).^{1,3,5,11,12}

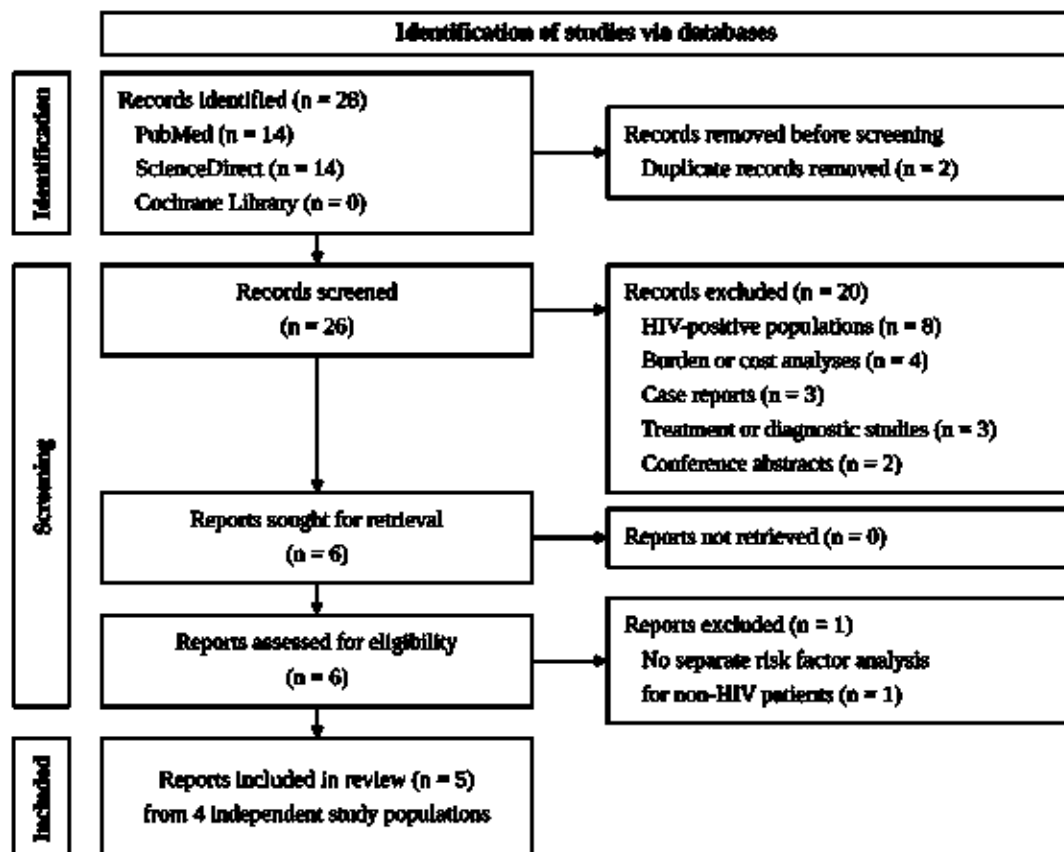


Figure 1. PRISMA 2020 flow diagram of study selection

The five reports came from four independent study populations in the United States, Japan, Pakistan, and Taiwan, because the two reports by Takahashi et al. analyzed risk factors and symptoms in the same Japanese subcohort of 6,011 patients recruited between September 2009 and April 2014.^{3,12} Three analyses used a case-control design, namely those of Kimchy et al., Yakoob et al., and the risk factor analysis of Takahashi et al., and two were cross-sectional analyses of patients undergoing upper gastrointestinal

endoscopy, namely the symptom analysis of Takahashi et al. and the study by Ou et al.^{1,3,5,11,12} Reported prevalence among non-HIV patients ranged from 0.34% to 8.99% (see Table 1).^{1,5}

Table 1. Characteristics and main findings of the included reports

Author (year)	Study design	Population	Exposure	Comparison	Outcome
Kimchy et al. (2023)¹	Multicenter retrospective case-control study, United States; cases confirmed by esophageal biopsy	1,969 adults with esophageal biopsies at five hospitals (2015-2020); 177 non-HIV patients with EC (8.99%)	Clinical risk factors, including prior organ transplantation, PPI use, and corticosteroid use	Non-HIV patients with EC vs. matched controls without histopathological evidence of <i>Candida</i> infection	Independent risk factors: PPI use (OR 1.66, P = 0.030); corticosteroid use (OR 2.05, P = 0.007); prior organ transplantation (OR 5.81, P = 0.009)
Takahashi et al. (2015)³	Observational study, Japan, comprising a long-term prevalence trend analysis and a case-control risk factor analysis	80,219 patients undergoing upper GI endoscopy (2002-2014); 1,595 HIV-positive and 78,624 non-HIV; risk factors analyzed in a subcohort of 6,011 (2009-2014)	HIV infection and immune status (CD4 count, HAART), systemic corticosteroid use and dose, age, lifestyle factors, comorbidities, and medications	Patients with <i>Candida</i> esophagitis vs. endoscopy controls without it, with analyses stratified by HIV status	Non-HIV: increasing age (OR 1.02, P = 0.008); systemic corticosteroid use (OR 5.80, 95% CI 3.90-8.63, P < 0.001); PPI use not associated (OR 1.16, P = 0.388). All patients: HIV infection (OR 4.92, P < 0.001); corticosteroid dose $\geq$ 20 mg/day prednisone equivalent (OR 3.09, P = 0.019)
Takahashi et al. (2015)¹²	Prospective, endoscopy-based cross-sectional study at a single referral center, Japan	6,011 adults undergoing upper GI endoscopy (Sep 2009-Apr 2014): 430 HIV-positive and 5,581 non-HIV; <i>Candida</i> esophagitis in 11.2% (HIV) vs. 2.9% (non-HIV)	Nine upper GI symptoms (e.g., dysphagia, odynophagia, heartburn, acid regurgitation, nausea) measured with the modified GSRS	Patients with <i>Candida</i> esophagitis vs. patients without organic GI disease, stratified by HIV status and adjusted for age, sex, and PPI use	Non-HIV, <i>Candida</i> esophagitis: dysphagia (OR 1.20, 95% CI 1.05-1.38); odynophagia (OR 1.22, 95% CI 1.01-1.48). Non-HIV, erosive esophagitis: heartburn (OR 1.33, 95% CI 1.24-1.42); acid regurgitation (OR 1.40, 95% CI 1.31-1.49)
Ou et al. (2014)¹¹	Retrospective single-center study of all patients undergoing upper GI endoscopy, Taiwan; EC diagnosed by endoscopy (n = 156) or biopsy (n = 12)	43,217 non-HIV patients undergoing endoscopy (2009-2012); 168 with EC (0.39%); 3,017 with liver cirrhosis	Liver cirrhosis, malignancy, diabetes mellitus, antibiotics, corticosteroids, PPIs, and previous gastric surgery	Patients with EC vs. patients without EC	Adjusted: malignancy (OR 8.43, 95% CI 5.74-12.39); PPI use (OR 8.86, 95% CI 5.61-13.97); previous gastric surgery (OR 6.81, 95% CI 3.36-13.79); corticosteroids (OR 2.26, 95% CI 1.1-4.68); liver cirrhosis (OR 1.74, 95% CI 1.06-2.87); diabetes mellitus (OR 0.78) and antibiotics (OR 0.91) not significant

Author (year)	Study design	Population	Exposure	Comparison	Outcome
Yakoob et al. (2003)⁵	Retrospective case-control study, Pakistan, based on medical record review over 5 years (1997-2001)	15,000 upper GI endoscopies reviewed; 51 non-HIV patients with <i>Candida</i> esophagitis (0.34%) and 102 controls (2 per case)	Predisposing conditions and treatments: carcinoma, diabetes mellitus, corticosteroid therapy, and broad-spectrum antibiotic use	Cases vs. patients without <i>Candida</i> esophagitis, endoscoped immediately before and after each case by the same endoscopy team	Unadjusted: carcinoma (OR 8.05, 95% CI 1.91-47.1, P = 0.001); diabetes mellitus (OR 7.34, 95% CI 2.26-27.5, P = 0.001); corticosteroid therapy (OR 6.67, 95% CI 2.20-22.3, P = 0.001); broad-spectrum antibiotics (OR 4.55, 95% CI 1.14-21.5, P = 0.02)

CI, confidence interval; EC, esophageal candidiasis; GI, gastrointestinal; GSRS, Gastrointestinal Symptom Rating Scale; HAART, highly active antiretroviral therapy; OR, odds ratio; PPI, proton pump inhibitor.

Methodological quality scores ranged from 5 to 7 of a possible 9 stars for the case-control analyses and from 6 to 7 of a possible 10 stars for the cross-sectional analyses, and no study achieved the maximum score (see Table 2). The most common deductions were the use of hospital-based controls, unreported non-response, and the absence of a sample size justification. The analysis by Yakoob et al. received no comparability stars because its odds ratios were derived from univariate comparisons without adjustment for potential confounders.⁵

Table 2. Methodological quality of the included reports assessed with the Newcastle-Ottawa Scale

Author (year)	NOS version	Selection	Comparability	Exposure or outcome	Total	Main limitations
Kimchy et al. (2023)¹	Case-control	3/4	2/2	2/3	7/9	Hospital-based controls; more coded cases than matched controls excluded for missing pathology or incomplete records
Takahashi et al. (2015)³	Case-control	2/4	2/2	2/3	6/9	Consecutive enrolment not stated and most eligible patients not interviewed; hospital-based controls; non-response not reported
Takahashi et al. (2015)¹²	Cross-sectional	2/5	2/2	3/3	7/10	No sample size justification; responders and non-responders not compared
Ou et al. (2014)¹¹	Cross-sectional	2/5	1/2	3/3	6/10	No sample size justification; completeness of records not reported; no adjustment for age or sex
Yakoob et al. (2003)⁵	Case-control	3/4	0/2	2/3	5/9	Hospital-based controls; univariate analysis only; non-response not reported

Case-control version, maximum of 4 stars for selection, 2 for comparability, and 3 for exposure (total 9). Cross-sectional version, maximum of 5 stars for selection, 2 for comparability, and 3 for outcome (total 10). NOS, Newcastle-Ottawa Scale.

Corticosteroid use was associated with esophageal candidiasis in all four studies that assessed it, with an adjusted odds ratio (OR) of 2.05 (P = 0.007) in Kimchy et al., an adjusted OR of 5.80 (95% confidence interval [CI] 3.90-8.63, P < 0.001) among non-HIV patients in Takahashi et al., an unadjusted OR of 6.67 (95% CI 2.20-22.3, P = 0.001) in Yakoob et al., and an adjusted OR of 2.26 (95% CI 1.1-4.68, P = 0.027) in

Ou et al.^{1,3,5,11} Among corticosteroid users with and without HIV in Takahashi et al., a prednisone-equivalent dose of ≥ 20 mg/day was also associated with esophageal candidiasis (OR 3.09, $P = 0.019$).³ Proton pump inhibitor use was an independent risk factor in Kimchy et al. (OR 1.66, $P = 0.030$) and in Ou et al. (OR 8.86, 95% CI 5.61-13.97, $P < 0.001$), but not among non-HIV patients in Takahashi et al. (OR 1.16, 95% CI 0.82-1.65, $P = 0.388$).^{1,3,11} Broad-spectrum antibiotic use was associated with esophageal candidiasis in Yakoob et al. (OR 4.55, 95% CI 1.14-21.5, $P = 0.02$) but not after adjustment in Ou et al. (OR 0.91, 95% CI 0.57-1.42, $P = 0.664$), and its frequency did not differ significantly between cases and controls in Kimchy et al. (12.4% vs. 7.7%, $P = 0.104$).^{1,5,11}

Malignancy was associated with esophageal candidiasis in both studies that assessed it, with an unadjusted OR of 8.05 (95% CI 1.91-47.1, $P = 0.001$) for carcinoma in Yakoob et al. and an adjusted OR of 8.43 (95% CI 5.74-12.39, $P < 0.001$) in Ou et al.^{5,11} Diabetes mellitus was significant only in Yakoob et al. (OR 7.34, 95% CI 2.26-27.5, $P = 0.001$); its prevalence did not differ between cases and controls in Kimchy et al., and it was not associated with esophageal candidiasis among non-HIV patients in Takahashi et al. or after adjustment in Ou et al. (OR 0.78, 95% CI 0.52-1.19, $P = 0.255$).^{1,3,5,11} Ou et al. also identified liver cirrhosis (OR 1.74, 95% CI 1.06-2.87, $P = 0.029$) and previous gastric surgery (OR 6.81, 95% CI 3.36-13.79, $P < 0.001$) as independent risk factors.¹¹ Prior organ transplantation was an independent risk factor in Kimchy et al. (OR 5.81, $P = 0.009$), and increasing age was associated with a modestly higher risk among non-HIV patients in Takahashi et al. (OR 1.02 per year, $P = 0.008$).^{1,3}

Regarding symptoms, Takahashi et al. reported that dysphagia (OR 1.20, 95% CI 1.05-1.38) and odynophagia (OR 1.22, 95% CI 1.01-1.48) were independently associated with *Candida* esophagitis in non-HIV patients, based on the modified Gastrointestinal Symptom Rating Scale (GSRS) and after adjustment for age, sex, and PPI use.¹² In contrast, Yakoob et al. found no correlation between symptoms and endoscopic grade, and in Ou et al. 45.8% of patients with cirrhosis and 9% of those without cirrhosis were asymptomatic at diagnosis.^{5,11}

DISCUSSION

Five reports from four independent populations, spanning four countries and two decades of endoscopic practice, met the inclusion criteria.^{1,3,5,11,12} Corticosteroid use was the only factor associated with esophageal candidiasis in non-HIV patients in every study that assessed it, and malignancy was associated in both studies that examined it. In contrast, PPI use, diabetes mellitus, antibiotic use, and symptom predictors showed direct disagreement between studies rather than simple gaps in the evidence.

Reported prevalence varied more than twenty-fold, from 0.34% in the review of 15,000 endoscopies in Pakistan by Yakoob et al. to 8.99% in the biopsy-confirmed United States cohort of Kimchy et al.^{1,5} Ou et al. reported 0.39% among 43,217 non-HIV patients undergoing endoscopy in Taiwan, and Takahashi et al. reported 1.6% among 78,624 non-HIV patients who underwent endoscopy between 2002 and 2014 and 2.9% among the 5,581 non-HIV patients in the 2009-2014 subcohort who completed a symptom questionnaire.^{3,11,12} This wide variation likely reflects differences in case ascertainment rather than true biological variation. Yakoob et al. identified cases from ICD-9-coded records over five years of mixed inpatient and outpatient referrals; Kimchy et al. confirmed cases by esophageal biopsy in a five-hospital United States system; Ou et al. relied mainly on endoscopic appearance, with biopsy in 12 of 168 cases; and Takahashi et al. drew cases from a single referral center in Tokyo, Japan, where endoscopy is frequently performed for gastric cancer screening.^{1,3,5,11} The validity of a prevalence estimate depends on the population from which it is derived, and these populations were not equivalent.

Corticosteroid use was associated with increased odds of esophageal candidiasis in every study that assessed this factor. Kimchy et al. reported an adjusted OR of 2.05 (95% CI not reported, $P = 0.007$) in a United States case-control cohort.¹ Takahashi et al., restricting their multivariable model to non-HIV patients, found

an adjusted OR of 5.80 (95% CI 3.90-8.63, $P < 0.001$).³ Yakoob et al. reported an unadjusted OR of 6.67 (95% CI 2.20-22.3, $P = 0.001$), and Ou et al. reported an adjusted OR of 2.26 (95% CI 1.1-4.68, $P = 0.027$).^{5,11} These four studies, conducted in different populations, all showed positive associations, a rare consistency in the observational literature on esophageal candidiasis. The pattern also fits the broader literature on glucocorticoid-associated fungal infection, in which susceptibility appears to depend on both dose and duration of exposure and is mediated by impaired phagocyte function, including defective macrophage phagolysosomal fusion.^{13,14} This mechanism does not depend on HIV status, which makes a dose-dependent effect on esophageal *Candida* colonization in non-HIV patients biologically plausible even without non-HIV-specific confirmation.

Proton pump inhibitor use did not show consistent findings across studies. Kimchy et al. and Ou et al. identified significant associations, with adjusted ORs of 1.66 ($P = 0.03$) and 8.86 (95% CI 5.61-13.97), respectively.^{1,11} In contrast, Takahashi et al. found no association among non-HIV patients (adjusted OR 1.16, 95% CI 0.82-1.65, $P = 0.388$).³ A plausible biological mechanism exists, because acid suppression raises gastric pH and may facilitate *Candida* colonization of the stomach and distal esophagus. A 2023 mycobiome study found a higher relative abundance of gastric *Candida* in patients receiving PPIs, with no further increase between short-term and long-term users.¹⁵ Because this mechanism should operate regardless of HIV status, differences in immune status are unlikely to explain the discrepancy between the studies. Confounding by indication is a more probable explanation. Cases in Kimchy et al. had higher rates of organ transplantation and immunosuppressive drug use than controls, and reflux esophagitis coexisted in 83.9% of patients with esophageal candidiasis in Ou et al., so PPI use may partly reflect the indication for endoscopy rather than a causal exposure.^{1,11}

Other risk factors showed similarly inconsistent support. Diabetes mellitus was significant only in the univariate analysis of Yakoob et al. (OR 7.34, 95% CI 2.26-27.5); its prevalence did not differ significantly between cases and controls in Kimchy et al. (35.6% vs. 28.7%, $P = 0.135$), and it lost significance after adjustment in Ou et al. (OR 0.78), a pattern consistent with confounding by coexisting conditions.^{1,5,11} Broad-spectrum antibiotic use followed the same pattern, with an unadjusted OR of 4.55 in Yakoob et al. and an adjusted OR of 0.91 in Ou et al.^{5,11} Malignancy, by contrast, remained strongly associated after adjustment in Ou et al. (OR 8.43), which supports the unadjusted estimate of 8.05 in Yakoob et al., although the latter was based on only ten exposed cases and had a wide confidence interval (1.91-47.1).^{5,11} Liver cirrhosis (OR 1.74), previous gastric surgery (OR 6.81), and prior organ transplantation (OR 5.81) were each examined in only one study, and Ou et al. attributed the cirrhosis association to depletion of CD4⁺ T cells in patients with cirrhosis.^{1,11} Increasing age reached statistical significance only in the larger non-HIV cohort of Takahashi et al. (OR 1.02 per year, $P = 0.008$), a modest effect that becomes clinically relevant only over extended periods.³ Esophageal candidiasis can also occur without recognized risk factors; in a Tanzanian endoscopy cohort that was excluded from this review because risk factors were not analyzed separately by HIV status, 4 of 20 HIV-negative patients with esophageal candidiasis had no comorbidity, although all four reported alcohol use.¹⁰

Symptom data suggest an association, although the studies addressing this issue used incompatible methods, which is itself informative. Takahashi et al., using a nine-item symptom scale with good internal consistency and excluding organic gastrointestinal disease, found that dysphagia (adjusted OR 1.20) and odynophagia (adjusted OR 1.22), but not heartburn or epigastric pain, independently predicted *Candida* esophagitis in non-HIV patients.¹² In contrast, Yakoob et al. observed no correlation between symptoms and endoscopic severity, and nearly half of the patients with cirrhosis in Ou et al. were asymptomatic.^{5,11} One possible explanation for the specific association of dysphagia and odynophagia with *Candida* esophagitis is that *Candida*-induced mucosal inflammation may impair esophageal motility, and esophageal motility abnormalities have been proposed as a cause of non-obstructive dysphagia.¹⁶ The design of Takahashi et al., which excluded confounding organic disease and used a standardized symptom scale, was structured to detect

such effects, whereas the retrospective chart review of Yakoob et al. lacked these methodological safeguards. Therefore, the absence of a signal in a less sensitive design does not negate the findings of Takahashi et al., although the high proportion of asymptomatic cases among patients with cirrhosis indicates that symptoms cannot be relied on to exclude infection.^{5,11,12}

Several limitations affect the interpretation of these findings. First, two of the five included reports were derived from the same endoscopy unit and the same patient cohort recruited between September 2009 and April 2014; one analyzed risk factors and the other symptoms.^{3,12} The evidence is therefore derived from four independent samples rather than five. Second, three of the five reports were retrospective, introducing risks of incomplete exposure ascertainment and unmeasured confounding, and quality appraisal showed recurring weaknesses in control selection and in the reporting of non-response.^{1,5,11} Third, the studies assessed different, only partially overlapping sets of exposures, used different reference populations, and spanned different eras of clinical practice, from 1997-2001 in Pakistan to 2015-2020 in the United States, which precluded meaningful pooling of effect estimates into a summary odds ratio.^{1,5} Fourth, the search used a single concise string without synonyms such as HIV-negative, immunocompetent, or *Candida* esophagitis, and reference lists were not searched, so eligible studies indexed under other terms may have been missed, including an Iranian study of HIV-negative adults.⁴

CONCLUSION AND RECOMMENDATIONS

Corticosteroid exposure and malignancy were the most consistently reported risk factors for esophageal candidiasis among non-HIV patients in the available literature. Other factors, including PPI use, diabetes mellitus, broad-spectrum antibiotic exposure, liver cirrhosis, previous gastric surgery, older age, and upper gastrointestinal symptoms, showed variable or single-study associations. Esophageal candidiasis may also occur in patients without an identifiable predisposing condition, suggesting that additional host and local esophageal factors may contribute to disease susceptibility. Given the limited number of studies, their methodological weaknesses, and the overlap between study populations, these findings should be interpreted cautiously. Future reviews should use broader search strategies, and prospective multicenter studies with standardized case definitions and systematic assessment of medication exposure, comorbidities, and other potential risk factors are warranted.

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