

Ocular Candidiasis: A Literature Review

Elvira Esmeralda Poerwosusanta¹, Sofia Risti Widhiarty¹, Junus Fredrik Jerry Rumajar¹, Pardawan¹

¹Departement of Ophthalmology, Ansari Saleh Hospital, Banjarmasin, South Borneo, Indonesia

Correspondence: elvira.poerwo@yahoo.com

ABSTRACT

Candida species may cause catastrophic visual loss. In many cases, the progression of ocular candidiasis is slow and gradual, beginning with chorioretinitis and then moving on to vitritis and endophthalmitis. Candida species is the fourth most frequent cause of nosocomial infections, accounting for nine percent of all cases. Candidaemia may develop in chorioretinitis and endophthalmitis, leading to severe vision impairment. Endogenous Candida endophthalmitis is brought on by haematogenous inoculation of the choroid and retina through minute capillaries. The organisms subsequently multiply, producing both focal inflammation and the creation of localised abscesses. Ocular candidiasis is preventable with early use of antifungal medication. The medicine of first choice is fluconazole, although amphotericin may be used for patients who have developed resistance to fluconazole.

Keyword: *Candida; Endophthalmitis; Fluconazole; Ocular Candida.*

INTRODUCTION

Candida species may cause catastrophic visual loss. In many cases, the progression of ocular candidiasis is slow and gradual, beginning with chorioretinitis and then moving on to vitritis and endophthalmitis. Candida species is the fourth most frequent cause of nosocomial infections, accounting for nine percent of all cases. In the critical care unit, the incidence of this infection is even higher, at ten percent. Over the last two decades, there has been a rise of nearly tenfold in the number of cases with nosocomial candidaemia. On the other hand, there has been a general trend toward a decreasing incidence of ocular candidiasis among inpatients who have candidaemia.^{1,2}

Throughout the course of medical history, researchers have estimated that the incidence of ocular candidiasis ranges anywhere from 9 percent to 45 percent. Estimates that are more up to date, on the other hand, indicate that the incidence is less than 2 percent. It has been hypothesised that this tendency might be attributed to

advances in the diagnosis and treatment of candidaemia at an earlier stage.³ The authors discuss current incidence rates and risk factors at one inpatient hospital, as well as examine the epidemiology, diagnosis, and shifting treatment paradigms of ocular candidiasis in the existing body of scholarly research on the topic. Patients who have been diagnosed with systemic candidaemia are given certain recommendations for ocular examination and follow-up care.⁴

One instance of *C albicans* endophthalmitis failed caspofungin monotherapy. Following vitreous sample, caspofungin quantities were undetectable. As intravitreal caspofungin has proven beneficial in rabbits with *C albicans* endophthalmitis, it may have potential applications. In fungal endophthalmitis, vitrectomy is a treatment option in addition to medicinal care. It allows organism collection for culture and polymerase chain reaction, vitreous cavity clearance, and antifungal drug installation.⁵

Retrospective investigations have shown favourable results for individuals receiving vitrectomy, especially if the procedure is performed within one week after discovery. In addition to acute chorioretinitis and endophthalmitis, vitrectomy may be used to address persistent problems such as epiretinal membrane development. Even while previous research supports vitrectomy with intravitreal amphotericin for significant vitreal involvement, new-generation triazoles or echinocandins may alter this suggestion.^{6,7}

METHODS

The data for this systematical review were culled from full-text English publications published in the preceding ten years (range 2012-2022). The purpose of this study is to assess the management ocular candidiasis. The databases that we utilized to produce this article are Pubmed and Google Scholar. In this investigation, the PICO analysis was used to include adult ocular candidiasis patients, index was risk factor, examination, and management the patient with ocular candidiasis, without comparisons and the objective was patient outcome. The research comprised both clinical trials and randomized clinical trials.

This analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) paradigm, in which the researchers originally entered keywords into each database. The phrases "(("ocular"[All Fields] OR "oculars"[All Fields]) AND ("candidiasis"[MeSH Terms] OR "candidiasis"[All Fields] OR "candidiases"[All Fields]) AND ("manage"[All Fields] OR "managed"[All Fields] OR "management s"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "managment"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields])) AND ((y_5[Filter] AND (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter])))". The researchers received five articles, which will be discussed during the discussion (**Table 1**).

RESULT

Nagao showed the diagnosis of ocular candidiasis was supported by the results in 54 instances (26.5 percent). 43 (79.6%) of these 54 cases were diagnosed within 7 days after a positive blood culture. More instances of ocular candidiasis were caused by *Candida albicans* ($P = 0.034$ odds ratio [OR]; 3.68 95 percent confidence interval [CI] 1.11-12.2) and had higher β -d-glucan levels ($P = 0.001$ OR; 9.99 95 percent CI 2.71-21.3). Fundoscopic evaluation should be considered during the first 7 days of medication, particularly for patients with *C. albicans* BSIs and elevated β -d-glucan levels. In addition, a follow-up fundoscopic examination should be performed before discontinuing treatment for individuals at high risk.⁸

Table 1. The literature include in this study

Author	Origin	Method	Sample Size	Period	Result
Nagao, 2012 ⁸	Japan	Retrospective study	220 patients	January 2005 and December 2011	Among ocular candidiasis cases, more cases were due to <i>Candida albicans</i> ($P = 0.034$ odds ratio [OR]; 3.68 95% confidence interval [CI] 1.11-12.2) and had higher β -d-glucan values ($P = 0.001$ OR; 9.99 95% CI 2.60-21.3). We need to consider fundoscopic examination to be performed within the first 7 days of therapy, especially for those patients who have <i>C. albicans</i> BSIs and higher β -d-glucan values. Additionally, follow-up fundoscopic examination should be considered before stopping therapy for high-risk patients.
Son, 2019 ⁹	South Korea	Prospective study	438 adults were diagnosed with candidemia	January 2014 and May 2017	Other study showed the symptoms of 11 individuals were present. Persistent candidemia (aOR = 2.55; 95% CI, 1.29-5.08; $P = 0.01$), neutropenia in the preceding 2 weeks (aOR, 2.92; 95% CI, 1.14-7.53; $P = 0.03$), and <i>C. albicans</i> infection (aOR, 2.15; 95% CI, 1.14-4.03; $P = 0.03$) were independently associated with ocular involvement. Initial examination revealed that 41.7% of the 24 neutropenic individuals had ocular involvements.
Munoz, 2017 ¹⁰	Spain	post hoc analysis of a prospective, multicenter, population-based candidemic	168 patients	2010-2011	The incidence of ocular candidiasis was comparable among patients receiving first treatment with candins (3/56; 5.4%) and other regimens (10/112; 8.2%). Multivariate analysis revealed that dialysis following candidemia (OR,

		surveillance program implemented				19.4; 95% CI, 1.7-218) and involvement of organs other than the eye were risk factors for eye involvement (OR, 5.4; 95 percent CI, 1.1-25.7). Eye involvement was not shown to be more prevalent in individuals getting echinocandins as first treatment than in those receiving other medications.
Kato, 2018 ⁷	Japan	Retrospective study	174 patients	April and March 2016	2011	Candida albicans candidemia (77.1 vs. 34.5 percent, P 0.001), neutropenia (14.3 vs. 5.8 percent, P = 0.141), CVC placement (94.3 vs. 71.2 percent, P = 0.004), and the presence of shock (28.6 vs. 14.6 percent, P = 0.145) were all more prevalent in the EFE group. C. albicans candidemia (adjusted odds ratio 6.48; [95% CI 2.63-15.95]) and CVC placement (7.55 [1.56-36.55]) were identified as significant risk variables for EFE by multivariate logistic regression analysis.
Khalid, 2014 ¹¹	USA	Retrospective study	283 patients	February 2000–March 2010		C. albicans (54 percent) was the most frequently isolated Candida species, followed by C. parapsilosis (20 percent), C. glabrata (13 percent), and C. tropicalis (13 percent) (8 percent). During the research period, the percentage of patients who were officially assessed by an ophthalmologist grew from 9 percent in 2000 to 73 percent in 2010 (P <0.0001). There was evidence of ocular candidiasis in 18 (12.5%) individuals. 5 of 18 (or 28 percent) individuals complained visual problems.
Hautala, 2021 ¹²	Finlandia	Retrospective study	304 patients	2008–2017		Any early antifungal therapy reduced the likelihood of developing endophthalmitis. Echinocandin reduced the incidence of OC in individuals with central venous catheters (CVCs) or abdominal cancer.

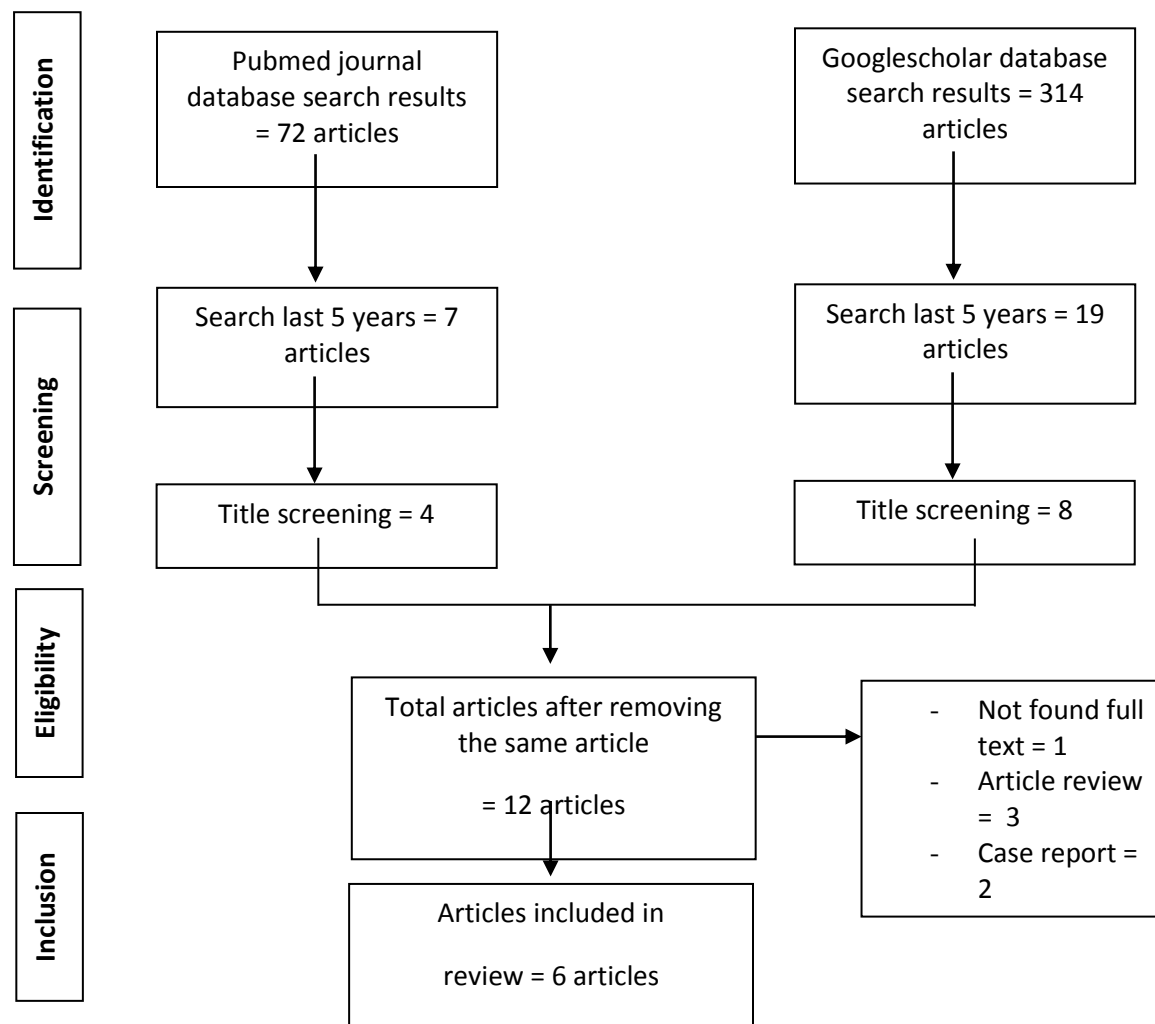


Figure 1. Article search flowchart

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Munoz *et al* showed the incidence of ocular candidiasis was comparable among patients receiving first treatment with candins (3/56; 5.4%) and other regimens (10/112; 8.2%). Multivariate analysis revealed that dialysis following candidemia (OR, 19.4; 95% CI, 1.7-218) and involvement of organs other than the eye were risk factors for eye involvement (OR, 5.4; 95 percent CI, 1.1-25.7). Eye involvement was not shown to be more prevalent in individuals getting echinocandins as first treatment than in those receiving other medications.¹⁰

Candida albicans candidemia (77.1 vs. 34.5 percent, $P = 0.001$), neutropenia (14.3 vs. 5.8 percent, $P = 0.141$), CVC placement (94.3 vs. 71.2 percent, $P = 0.004$), and the presence of shock (28.6 vs. 14.6 percent, $P = 0.145$) were all more prevalent in the EFE group. *C. albicans* candidemia (adjusted odds ratio 6.48; [95% CI 2.63-15.95]) and CVC placement (7.55 [1.56-36.55]) were identified as significant risk variables for EFE by multivariate logistic regression analysis.⁷

Khalid showed *C. albicans* was the most frequently isolated *Candida* species, followed by *C. parapsilosis*, *C. glabrata*, and *C. tropicalis*. During the research period, the percentage of patients who were officially assessed by an ophthalmologist grew from 9 percent in 2000 to 73 percent in 2010 ($P < 0.0001$). There was evidence of ocular candidiasis in 18 (12.5%) individuals. 5 of 18 (or 28 percent) individuals complained visual problems. In multivariable analysis, no ocular candidiasis predictors were detected.¹¹ Other study showed early antifungal therapy reduced the likelihood of developing endophthalmitis. Echinocandin reduced the incidence of OC in individuals with central venous catheters (CVCs) or abdominal cancer.¹²

DISCUSSION

Candidaemia may develop in chorioretinitis and endophthalmitis, leading to severe vision impairment. Endogenous *Candida* endophthalmitis is brought on by haematogenous inoculation of the choroid and retina through minute capillaries. The organisms subsequently multiply, producing both focal inflammation and the creation of localised abscesses. The subsequent spread to the vitreous body may result in endophthalmitis and detachment of the retina. Subacute onset of impaired vision with low-grade discomfort, photophobia, and injection are common first symptoms.^{11,13}

Endogenous candidal chorioretinitis often manifests as isolated, white, deep chorioretinal lesions without direct vitreal involvement. Lesions may be solitary or many, posterior or peripheral, and singular or numerous. Chronic transretinal or epiretinal inflammation may result in the production of epiretinal membranes. Vitritis is defined by the extension of inflammation into the vitreous. Endophthalmitis is characterised by vitreous abscesses or "puff balls." Hypopyon, scleritis, and optic nerve involvement may develop in endophthalmitis. Chorioretinal lesions are characterised by granulomatous inflammation with visible organisms in the centre, surrounded by a zone of varying suppuration.^{11,13,14}

Recent study has shown that a shift in the distribution of *Candida* species from *C. albicans* to *Candida non-albicans* is the cause of candidemia. In a prior investigation of a similar kind, *C. albicans* was identified as the primary cause of candidemia. Nagao *et al.* examined health data from 2005 to 2011 and discovered *C. albicans* in 52.5% of patients.⁸ Son *et al.* examined health data from 2014 to 2017 and discovered *C. albicans* in 42.2 percent of patients. *C. albicans* was the dominant pathogen in our investigation, as it was discovered in 41.1 percent of patients, comparable to a previous publication.⁹

Recent trends indicate a rise in the use of echinocandins as the antifungal of choice for first therapy. Munoz *et al.* examined health data from 2010 to 2011 and discovered that 33.3% of patients were prescribed echinocandins.¹⁰ In the meanwhile, Kato *et al.* examined medical data from 2011 to 2016 and discovered that echinocandins were picked for 80.1% of patients. In our research, 83.6% of patients were prescribed echinocandins,

the greatest rate among prior studies. Thus, our data demonstrate the most recent clinical characteristics of OC, which are mirrored by a rise in the use of echinocandin as a first-line therapy for candidemia.⁷

Early antifungal therapy reduced the likelihood of developing endophthalmitis. Echinocandin reduced the incidence of OC in individuals with central venous catheters (CVCs) or abdominal cancer. In patients without neutropenia, they guidelines recommended during the study years administration of either empirical intravenous fluconazole (800 mg starting dose, followed by 400 mg daily) or intravenous echinocandin (casposfungin or micafungin according to generally accepted dosing) whenever Candida BSI is suspected. In patients with neutropenia with suspicion of candidemia, echinocandin was recommended. For the study period, casposfungin (70 mg starting dose, followed by 50 mg (<80 kg) or 70 mg (>80 kg) daily) has been used.¹²

In-patients were less likely to develop ocular candidiasis due to early detection of candidemia and quick systemic antifungal medication, according to Feman et al. Our patient may be protected against ocular candidiasis with fluconazole. Intravenous amphotericin has been indicated as a therapy for *C. albicans*, *C. krusei*, and *C. glabrata* resistant to fluconazole. Due to its low intravitreal penetration and systemic adverse effects, however, systemic amphotericin is not appropriate for immunocompromised people. Intravenous fluconazole was beneficial for systemic candidemia, but systemic amphotericin was ineffective due to the patient's poor general health.¹⁵⁻¹⁷

Voriconazole is a broad-spectrum, second-generation fluconazole derivative that has a 96 percent bioavailability and has been proven to reach therapeutically relevant concentrations in the vitreous body after oral dosing. Biju et al. found that oral administration of voriconazole was an effective treatment for candida endophthalmitis; however, this technique was ineffective for our patient. It has been shown that intravitreal liposomal amphotericin B injection is an effective therapy for endogenous candida endophthalmitis. Within 24 hours of injection, voriconazole is removed from the vitreous cavity, necessitating frequent intravitreal injections to maintain therapeutic concentrations in the eye.^{15,16}

In order to eliminate the need for several intravitreal injections, we chose to provide intravitreal amphotericin B instead of voriconazole due to the patient's overall poor health. Voriconazole is exclusively prescribed in South Korea for fungal infections that do not respond to amphotericin B or fluconazole. However, intravitreal amphotericin was ineffective for our patient, but voriconazole was successful and required just a single injection.¹⁵⁻¹⁷

CONCLUSION

Ocular candidiasis is preventable with early use of antifungal medication. The medicine of first choice is fluconazole, although amphotericin may be used for patients who have developed resistance to fluconazole.

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