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COMMENTARY

Literature- and Experience-Based Consensus for Acute Post-operative Endophthalmitis and Endogenous Endophthalmitis in Taiwan

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ABSTRACT

Clinical practices on acute post-operative and endogenous endophthalmitis (EnE) are highly variable among clinicians due to a lack of up-to-date, high-quality evidential support. An expert consensus is thus much needed. A panel consisting of ten retinal specialists in Taiwan was organized. They evaluated relevant literature and developed key questions regarding acute post-operative and EnE that are cardinal for practice but yet to have conclusive evidence. The panel then attempted to reach consensus on all the key questions accordingly. There were eight key questions proposed and their respective consensus statements were summarized as follows: Gram staining and culture are still the

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standard procedures for the diagnosis of endophthalmitis. Vitrectomy is recommended to be performed earlier than the timing proposed by the Endophthalmitis Vitrectomy Study (EVS). Routine intracameral antibiotic injection for post-cataract surgery endophthalmitis prophylaxis is not recommended because of potential compounding error hazards and a lack of support from high-quality studies. Routine fundus examination is recommended for all patients with pyogenic liver abscess. In EnE, vitrectomy is recommended if diffused and dense vitritis is present, or if the disease progresses. These consensus statements may work as handy guidance or reference for clinical practices of acute post-operative and EnE.

Keywords: Endogenous endophthalmitis (EnE); Acute post-operative endophthalmitis; Taiwan; Expert consensus

Key Summary Points

Despite the fact that many retrospective studies have investigated the management of acute post-operative endophthalmitis and endogenous endophthalmitis (EnE), to date, only one decades-old prospective randomized study has addressed the management of acute post-operative endophthalmitis.

The aim of this commentary is to provide an expert consensus on several key questions regarding acute post-operative endophthalmitis and EnE, as well as a glimpse into the Taiwanese epidemiological profiles.

Timing of vitrectomy set by the decades-old landmark study, the Endophthalmitis Vitrectomy Study, is regarded as outdated, and vitrectomy is recommended to be performed earlier and for those with better initial vision both in acute post-operative endophthalmitis and EnE.

Perspective in managing both acute post-operative endophthalmitis and EnE is changing owing to improvement of surgical technologies, introduction of new antibiotics, and other factors.

INTRODUCTION

Endophthalmitis is a disease with highly variable presentations, geographical diversity, and mixed etiologies [1]. It usually comes with severe visual loss [2]. For years, extensive studies explored its diagnosis and management [2–6]. However, due to its complexity, there was only one decades-old, prospective, randomized controlled trial being conducted, that is the

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Endophthalmitis Vitrectomy Study (EVS). It scrupulously investigated into the management of acute post-operative endophthalmitis [3, 7]. Since then, many aspects of endophthalmitis, including epidemiology [1, 8, 9], management pattern [3, 10–12], and prognosis [2, 13] have evolved through time, owing to the alteration of several factors, such as pattern of systemic infections [14–17], introduction of new antibiotics [18, 19], and advance in micro-incisional vitrectomy [20, 21]. Nowadays, clinicians still heavily depend on the implications of the EVS study, which may be outdated and not compatible with current clinical environments.

Recently, despite several large-scale retrospective studies providing insights into modern practices of endophthalmitis [22–26], their conclusions are sometimes confusing, and largely ununiformed. A panel with relevant expertise was thus organized in Taiwan with the aims to review and evaluate current evidence, and attempt to reach a consensus on several key aspects of acute post-operative endophthalmitis and endogenous endophthalmitis (EnE), and also provide insights into the current epidemiological profiles in Taiwan. With the consensus, one may find it easier to navigate through this complex disease.

MATERIALS AND METHODS

A nationwide panel of vitreoretinal experts was selected from members of the Taiwan Ocular Inflammation Society (TOIS). The aim of the selected panel is to provide a clear and up-to-date guidance and suggestion for several issues of acute post-operative endophthalmitis and EnE in Taiwan that are currently lack of high-quality evidential support. The panel comprised ten ophthalmologists in Taiwan with expertise in both endogenous and acute post-operative endophthalmitis in tertiary centers. All experts had records of relevant publications or research contributions on the subject. There are three consecutive steps in the consensus development process. The collection and selection of relevant papers was the initial step, followed by proposition and establishment of key questions according to the selected papers, and followed by consensus development on those proposed key questions. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

In the first step, an exhausting search for articles regarding acute post-operative endophthalmitis and EnE was performed on PubMed, EMBASE, and Cochrane Library databases using keywords including "endogenous endophthalmitis," OR "acute post-operative endophthalmitis" with publication year from January 2000 to December 2022. The panel organizer then filtered through the initial article list, and selected relevant articles regarding diagnostic methods, management, prophylaxis, and screening. Afterwards, selected articles were reviewed by panel members and a final set of reference articles were decided. On the other hand, to outline the Taiwanese epidemiology of acute post-operative endophthalmitis, EnE, and pyogenic liver abscess-related EnE, relevant case series were also exhaustively searched from PubMed, EMBASE, and Cochrane Library databases using the keywords "endophthalmitis," AND "Taiwan", as well as "pyogenic liver abscess," AND "endophthalmitis," AND "Taiwan," with publication year from January 2000 to December 2022. The representative case series were selected by the panel organizer, and were composed into separate tables.

In the second step, based on the reference articles and clinical experience, the panel establishes several key questions that cover issues of acute post-operative endophthalmitis and EnE but yet to have strong evidence. Each key question will be evaluated by the panel for its importance and necessity. At the end of the second step, a set of key questions was listed for consensus development.

In the third step, to reach consensus on key questions, the panel meeting was held online on January 15, 2023. For the consensus development of each key question, the Delphi method (Estimate-Talk-Estimate method) was applied, and the panel organizer acted as facilitator. One consensus statement was stated for each key question. Each statement was

discussed and modified until unanimous consent was reached.

RESULTS AND DISCUSSION

The initial literature search collected 188 articles. The panel organizer filtered through the article and selected 22 articles for further panel review. Four additional papers were advised by panel members and added into the initial set of articles under unanimous panel consent. At the end of the first step, there were a total of 26 articles left for key questions development.

Furthermore, for representative cases series, there were five case series regarding acute post-operative endophthalmitis; three case series addressing EnE; and six case series providing incidence of endophthalmitis in pyogenic liver abscess. These series were summarized into three separate tables (Tables 2, 3, 4).

In the second stage, according to the collected articles and clinical experience, the panel members developed eight key questions (Table 1). Consensus was reached in all eight key questions. Individual discussions and consensus results were demonstrated in the following sections.

KEY QUESTION 1: WHAT ARE THE INCIDENCE AND THE DOMINANT PATHOGENS OF ACUTE POST-OPERATIVE ENDOPHTHALMITIS IN TAIWAN?

In Taiwan, according to the collected case series (Table 2), the incidence of post-cataract surgery and vitrectomy was reported to be 0.21% and 0.03%, respectively, with an overall incidence of all operation types to be 0.19% [27]. Globally, periocular commensal Gram-positive bacteria, such as *Staphylococcus* sp., are frequently reported as dominant pathogens in acute post-operative endophthalmitis [8, 16, 17, 28, 29]. However, these pathogens are not as frequent in Taiwan [30–33] (Table 2). Instead, both *Enterococcus* sp. [33, 34] and non-tuberculosis mycobacterium (NTM) [31, 32] had been reported as the major pathogens in Taiwanese reports (Table 2). These patterns deviated greatly from that of global trend. For high incidence of post-operative NTM endophthalmitis, the case-collection period of the study happened to catch up a cluster of post-operative NTM endophthalmitis. This episode thus significantly distorted the pathogens percentage [32]. Of note, there were, in total, three outbreaks of NTM-related, acute, post-operative endophthalmitis in Taiwan from 2011 to 2014 [31, 35]. The panel commented that these unusual episodes are highly associated with heavy reliance on detergent solution for cataract-surgery equipment cleaning in many Taiwanese private practices [35]. NTM contamination of operative equipment cannot be efficiently eliminated by detergent wash, and thus led to the outbreaks. The panel concluded that the introduction and widespread usage of autoclave systems in Taiwan effectively eliminated post-operative NTM endophthalmitis in recent years [35, 36].

Acute post-operative endophthalmitis with *Enterococcus* species tells a different story in Taiwan. The *Enterococcus* species was frequently met in the Taiwanese case series of acute post-operative endophthalmitis. They accounted for 29% and 38% of the culture-proven cases, respectively, in two previous cases series (Table 2) [32, 33]. In a more recent series reported by Peng et al. in 2021, *Enterococcus faecalis* claimed 20% of culture-proven cases [30]. The panel commented that the *Enterococcus* species is indeed emerging as one of major pathogens for acute post-operative endophthalmitis in modern Taiwan. The panel reasoned that several factors might contribute to the emergence of *Enterococcus* species. The fact that intracameral antibiotics prophylaxis is widely used by many ophthalmic surgeons in Taiwan may be an important factor because it removes common pathogens and selects special ones. Subtropical climate [37] and differences in procedural protocols [38] are also possible factors that shape the unique pathogen pattern in Taiwan. Furthermore, the panel is aware that publication bias is also a haunting factor in studying endophthalmitis, and all the reported

Table 1 Eight key questions and consensus statement

Mark	Key question	Consensus statement
1	What are the incidence and the dominant pathogens of acute post-operative endophthalmitis in Taiwan?	Despite the major pathogens of acute post-operative endophthalmitis are Gram-positive cocci, *Enterococcus* sp. is emerging as a frequent, and sometimes dominant pathogen in modern Taiwan
2	What is the optimal clinical approach of pathogens identification for acute post-operative endophthalmitis in Taiwan?	Gram stain (or seldomly KOH stain if fungal infection is suspected) and microbial culture are standard clinical approaches of pathogens identification for acute post-operative endophthalmitis in Taiwan. PCR is not recommended in clinical setting
3	What are the optimal timing and indications for vitrectomy in acute post-operative endophthalmitis?	For acute post-operative endophthalmitis, early vitrectomy is recommended for those with initial vision worse than 20/40, or 2–3 lines worse than anticipated vision. Furthermore, for those who received intravitreal antimicrobials injection at first but have their vision or clinical symptoms/signs deteriorate in the first 24 h or less should also undergo vitrectomy. The visual criteria stated by the EVS is regarded as outdated
4	Should intracameral antibiotics injection at the end of cataract-extraction operation be recommended for endophthalmitis prophylaxis?	The panel cannot recommend routine use of intracameral injection of antibiotics for endophthalmitis prophylaxis in cataract surgery currently due to a lack of standard antibiotics formulation
5	What are current characteristics of EnE in Taiwan, regarding predisposing factor, pathogen, primary infection focus, and epidemiology?	In Taiwan, the most common predisposing factor for endogenous endophthalmitis is diabetes mellitus; pyogenic liver abscess are the most common primary infection focus; and the most common pathogen for EnE is *Klebsiella* species. In Taiwan, the incidence of endogenous *Klebsiella* endophthalmitis from pyogenic liver abscess has been in decrease in recent years, possibly owing to improving DM control. On the other hand, increasing incidence of endogenous *Klebsiella* endophthalmitis from UTI in non-diabetic, elderly, female patient is noted
6	Whether general dilated fundus examination should be recommended for patients with certain infection focus	In Taiwan, routine dilated fundus screening for EnE is recommended for all patients with pyogenic liver abscess

Table 1 continued

Mark	Key question	Consensus statement
7	What is the optimal timing and indication of vitrectomy for bacterial EnE?	Vitrectomy in bacterial EnE is indicated when progression of vitritis or deterioration of vision are noted despite 24 h of systemic antibiotics with or without intravitreal antibiotics injection. Early vitrectomy at initial encounter is also recommended when dense vitritis blocks the view of disc and arcade vessels
8	What is recommended treatment strategy for fungal chorioretinitis and endogenous fungal endophthalmitis?	For endogenous fungal chorioretinitis, an effective, adequately penetrant, systemic antifungal agent is mandatory. For fungal chorioretinitis without vitritis, systemic antifungal is mostly sufficient. For sight-threatening chorioretinitis without vitritis, additional intravitreal injection of antifungals is recommended. For any endogenous fungal endophthalmitis with vitritis, systemic antifungal alone is regarded inadequate, and concomitant intravitreal antifungals or vitrectomy are recommended. Vitrectomy is reserved for cases with dense vitritis, significantly sight-threatening chorioretinitis or subretinal abscess, as well as progressing disease despite combined treatment with systemic and intravitreal antifungals

sp. species, *KOH* potassium hydroxide, *EVS* Endophthalmitis Vitrectomy Study, *UTI* urinary tract infection, *DM* diabetes mellitus, *PCR* polymerase chain reaction, *EnE* endogenous endophthalmitis

results should always be interpreted with caution [39].

Consensus Statement

Despite the major pathogens of acute post-operative endophthalmitis are Gram-positive cocci, *Enterococcus* sp. is emerging as a frequent, and sometimes dominant pathogen in modern Taiwan.

KEY QUESTION 2: WHAT IS THE OPTIMAL CLINICAL APPROACH OF PATHOGEN IDENTIFICATION FOR ACUTE POST-OPERATIVE ENDOPHTHALMITIS IN TAIWAN?

Smears and microbial cultures from the extracts of anterior chamber or vitreous had long been regarded as standard procedures for pathogen identification in endophthalmitis in the past [40, 41]. Yield rates of stains and cultures varied but are generally low [40, 42, 43]. Recently, polymerase chain reaction (PCR) came into view as a promising, rapid, and precise

Table 2 Collected cases series of acute post-operative endophthalmitis in Taiwan

Author/ year/cases number	Location, collection period	Cause	(+) culture rate[a]	Major pathogen(s)	Received PPV as part of treatment	Evisceration or enucleation	Final VA	Comments
Peng et al. [30], 2021/82	Single tertiary center, southern Taiwan 2010–2019	Post-operative	30 (37%)	*S. aureus* 7 (23%), *E. faecalis* (20%)	71 (87%)	1 (1%)	Post-cataract endophthalmitis have better final vision	Related surgeries before endophthalmitis: cataract 80%, vitrectomy 15%, intravitreal injection 5%
Hung et al. [31], 2018/12	Clusters from clinic and hospitals, southern Taiwan 2011–2016	Post-cataract-operation	–[b]	*M. abscessus* 100%	58%	42%	All eyes were atrophied or removed	NTM infection clusters/all cases included were NTM-proven
Chen et al. [32], 2017/25	Single tertiary center, northern Taiwan 2009–2015	Post-cataract operation	13 (52%)	*M. abscessus* 8 (62%), Gram-positive 4 (31%), fungal 1 (7.6%)	76%	Not discussed	5/200 or better in 14 (56%)	–
Teng et al. [33], 2016/19	Single tertiary center, southern Taiwan 2004–2015	Post-cataract operation	–[b]	*Enterococcus* sp. 38%, *S. epidermidis* 29%, *S. aureus* 9.5%	Not discussed	Not discussed	20/40 or better in 21.1%	All cases included are culture-proven

Table 2 continued

Author/ year/cases number	Location, collection period	Cause	(+) culture rate[a]	Major pathogen(s)	Received PPV as part of treatment	Evisceration or enucleation	Final VA	Comments
Wu et al. [27], 2006/56	Single tertiary center, southern Taiwan 1991–2004	Post-operative	31 (55%)	CoNS 15 (48%), *E. faecalis* 9 (29%),	8 (18%)	Not discussed	20/40 or better in 21%, 20/100 or better in 55%,	Overall incidence of acute post-operative endophthalmitis: 0.19% (56 out of 30,219)/cataract 46(82%), PK 6 (11%), filtering surgery 2 (4%), secondary intraocular lens implant 1 (2%), vitrectomy 1 (2%)

S. aureus Staphylococcus aureus, *PsA* Pseudomonas aeruginosa, *M. abscessus* Mycobacterium abscessus, *NTM* nontuberculous mycobacteria, *S. epidermidis* Staphylococcus epidermidis, *CoNS* coagulase-negative staphylococcus, *E. faecalis* Enterococcus faecalis, *PPV* pars plana vitrectomy, *VA* visual acuity, *PK* penetrating keratoplasty

[a]Positive rate of culture

[b] These two studies included only culture-proven cases, the positive rates of culture are thus omitted because their presentations are pointless and may be misleading.

alternative [44, 45]. It had been advocated for timely pathogen identification in endophthalmitis. However, the high cost and lack of accessibility prevent its clinical application in Taiwan [46]. In addition, since most acute post-operative endophthalmitis are bacterial, and most pathogens are susceptible to standard antibiotics regimen including vancomycin and ceftazidime, fast pathogen identification with expensive PCR is mostly pointless. Furthermore, many clinicians are not comfortable with narrowing the antibiotics spectrum within days of initial encounter, for fear of omitting other mixed pathogens.

Consensus Statement

Gram stain (or seldomly potassium hydroxide (KOH) stain if fungal infection is suspected) and microbial culture are standard clinical approaches of pathogen identification for acute post-operative endophthalmitis in Taiwan. PCR is not recommended in clinical setting.

KEY QUESTION 3: WHAT ARE THE OPTIMAL TIMING AND INDICATIONS FOR VITRECTOMY IN ACUTE POST-OPERATIVE ENDOPHTHALMITIS?

The EVS has long been used as a landmark study for deciding whether and when to perform a vitrectomy in acute post-operative endophthalmitis [7]. The study states that if the visual acuities of the patients are light perception or worse, then these patients will benefit from early vitrectomy performed within 6 hours. According to the study, their visual outcomes will be superior to that of the patients with similar initial visual acuities but received intravitreal antimicrobial injections instead. For those with initial vision better than light perception, vitrectomy group failed to show superior benefit in terms of final vision. Decades since the EVS, the advance of vitrectomy surgical system promised enhancing fluidics stability, less tissue traction, and much reduced sclerotomy size. This modern, micro-incisional vitrectomy technique is believed to reduce complication rates including retinal detachment, wound leakage, and expulsive hemorrhage [47]. Recently, many retrospective studies advocated that micro-incisional vitrectomy can be applied in patients with acute post-operative endophthalmitis with better initial vision and achieve better final vision [3, 10, 48]. However, after EVS, no prospective randomized control trial study was conducted to rigorously validate the viewpoint [3]. The panel agreed that because of advancing micro-incisional vitrectomy, the modern vision indication for vitrectomy should be set much earlier than that of EVS. For those with acute post-operative endophthalmitis, if the initial vision is worse than 20/40 or 2–3 lines poorer than the anticipated vision, vitrectomy should be considered. Furthermore, for those who have received intravitreal injections of antimicrobials but experience a worsening of their vision or other clinical signs within the first 24 hours, vitrectomy is also recommended.

Consensus Statement

For acute post-operative endophthalmitis nowadays, early vitrectomy is recommended for those with initial vision worse than 20/40, or 2–3 lines worse than anticipated vision. Furthermore, for those who initially received intravitreal antimicrobial injections but experience a deterioration in their vision or clinical symptoms/signs within the first 24 hours, vitrectomy should also be considered. The visual criteria outlined by the EVS are considered outdated.

KEY QUESTION 4: SHOULD INTRACAMERAL ANTIBIOTICS INJECTION AT THE END OF CATARACT-EXTRACTION OPERATION BE RECOMMENDED FOR ENDOPHTHALMITIS PROPHYLAXIS?

Prophylaxis with intracameral antibiotics at the end of cataract surgery as a routine procedure

Table 3 Collected cases series of endogenous endophthalmitis in Taiwan

Author, year Eyes/patients	Location of patient collection Collection period	Pathogens	Predisposing medication conditions	Primary infection focus	Culture positivity in ocular extract/ blood culture	Treatment pattern: IVI/ PPV/ enucleation or evisceration	Final VA
Kuo et al. [56], 2021 194/175	Single tertiary center, northern Taiwan, 2008–2015	K.p. (34%)/ PsA. (12%)/ CoNS (6.7%)/*C. albicans* (6.7%)	DM (58%)/ HTN (37%)/ ESRD (15%)/ Cirrhosis (12%)	Liver abscess (25%)/UTI (3.4%)/ Pneumonia (3.4%)	51%/35%	82%/29%/ 18.30%	17% > 6/ 60
Hsieh et al. [55][a], 2020 83/70	Single tertiary center, central Taiwan, 2007–2017	K.p. (53%), *E. coli* (101%), *S. aureus* (7.2%), PsA (7.2%), *C. albicans* (7.2%),	DM (64%)/ Malignancy (13%)/Liver cirrhosis (8.4%)/ ESRD (8.4%)	Liver abscess (41%)/UTI (12%)/ Pneumonia (4.8%)	No data available	92%/47%/ 7.2%	35% > 6/ 600
Chen et al. [57], 2017 105/86	Single tertiary center, southern Taiwan, 2002–2013	K.p. (56%), *S. aureus* (8.1%), *C. albicans* (8.1%), *E. coli* (3.5%)	DM (61%)/ HTN (35%)/ Malignancy (17%)/Liver cirrhosis (11%)	Liver abscess (69%)/UTI (8.3%)/ Pneumonia (4.2%)	34%/88%	89%/23%/ 18%	44% count finger or better

K.p Klebsiella pneumoniae, *PsA Pseudomonas aeruginosa*, *CoNS* coagulase-negative staphylococcus, *C. albicans* Candida albicans, *S. aureus* Staphylococcus aureus, *DM* diabetes mellitus, *HTN* hypertension, *ESRD* end-stage renal disease, *E. coli* Escherichia coli, *IVI* intravitreal injection, *PPV* pars plana vitrectomy, *VA* visual acuity, *UTI* urinary tract infection

[a]All cases in this study were culture-proven

for prophylaxis of acute post-operative endophthalmitis is in heated debate [49, 50]. Recently, several prospective randomized controlled studies conducted and confirmed the benefit of intracameral antibiotics for prophylaxis of post-cataract endophthalmitis [49, 51]. The European Society of Cataract and Refractive Surgeons (ESCRS) 2007 study concluded that intracameral administration of compounding cefuroxime 1 mg in 0.1 ml normal saline significantly decreased the incidence of endophthalmitis after cataract surgery [49]. However, compounding error, compounding error-related ocular injuries, and drug-related adverse reactions haunt all kinds of intra-cameral antibiotics injection [52], and still, prophylaxis may fail sometimes due to insufficient dosage or inadequate spectrum coverage [53]. Furthermore, hemorrhagic occlusive retinal vasculitis (HORV) is a potential devastating

Table 4 Collected studies regarding subsequent endogenous endophthalmitis rates in patients with pyogenic liver abscess in Taiwan

Author	Publication year	Patient collection period	Geographical distribution of patient collection	Number of patients included	Per case EnE rates (%)
Keller et al. [58]	2012	2006–2008	Nationwide health registry	12,050	0.9[a]
Hu et al. [59]	2012	2006–2008	Nationwide health registry	12,727	0.84
Lin et al. [60]	2012	2000–2007	Nationwide health registry	21,307	1.36
Tsai et al. [61]	2012	2000–2004	Nationwide health registry	29,703	1.70
Sheu et al. [62]	2011	1991–2009	Single tertiary center, southern Taiwan	602	7.00
Chou et al. [63]	1996	1986–1993	Single tertiary center, southern Taiwan	352	3.10

EnE endogenous endophthalmitis
[a]Due to the study design, where patients were followed for 1 year, the ratio also indicates annual incidence

complication of intracameral vancomycin injection, which limits its application [52].

In Taiwan, off-label intracameral injection of commercialized 0.5% moxifloxacin eyedrop (Vigamox®) was administered routinely at the end of cataract operations by some clinicians. Intracameral injection of undiluted Vigamox® eye drops was found to be safe and efficient in acute post-operative endophthalmitis prevention by some retrospective studies [54]. However, to date, no large, prospective, randomized control trials have confirmed its safety and efficacy. After discussion, the panel agreed not to recommend intracameral antibiotics injection for endophthalmitis prophylaxis. The fear of compounding errors, resulting from the lack of standardized disposable antibiotic products in Taiwan, is often cited as outweighing the potential benefits.

Consensus Statement

The panel is unable to recommend the routine use of intracameral antibiotic injection for endophthalmitis prophylaxis in cataract surgery at present due to the absence of a standardized antibiotic formulation.

KEY QUESTION 5: WHAT ARE THE CURRENT CHARACTERISTICS OF ENE IN TAIWAN REGARDING PREDISPOSING FACTORS, PATHOGENS, PRIMARY INFECTION FOCUS, AND EPIDEMIOLOGY?

In total, three EnE case series have been identified in Taiwan since 2000 [55–57] (Table 3). Six studies of pyogenic liver abscess with incidence of subsequent EnE were collected from 2000 [58–63]. A decreasing trend in endophthalmitis rates in patients with pyogenic liver abscess was noted throughout the study period (Table 4).

In Taiwan, the most common predisposing factor for EnE is diabetes mellitus (58.3–63.9%) [62, 64, 65] (Table 3), similar to those of global reports [66, 67]. Pyogenic liver abscess is the most frequent site of primary infection focus in Taiwan [55, 56, 59]. Urinary tract infection (UTI) was the second; followed by pneumonia (Table 3) [55, 56, 59]. On the other hand, intravenous drug users were not a frequent source of EnE [4, 68, 69] (Table 3).

In Taiwan, 78–91% of culture-proven EnE are bacterial, while the other 8–18% are fungal

[55, 56]. *Klebsiella pneumoniae* has a particularly high percentage of pathogens (34–53%) compared to those reported in global studies (Table 3) [55, 56]. *Staphylococcus* species, *Pseudomonas aeruginosa*, and *Candida albicans* were three significant minorities with similar percentages (Table 3) [55, 56].

Up-to-date epidemiology reports for the EnE in Taiwan are scarce. Based on clinical experience, one panel member advised on the trend of recent EnE in Taiwan: The incidence of endogenous *Klebsiella* endophthalmitis is in decrease in recent years, possibly owing to much improved diabetes mellitus control in modern Taiwan. However, the incidence of non-diabetic endophthalmitis is increasing in recent years. Among these cases, there is a predominant trend toward older female patients with UTI.

Consensus Statement

In Taiwan, the most common predisposing factor for endogenous endophthalmitis is diabetes mellitus; pyogenic liver abscesses is the most common primary infection focus; and the most common pathogen for EnE is *Klebsiella* species. In Taiwan, the incidence of endogenous *Klebsiella* endophthalmitis from pyogenic liver abscess has been in decrease in recent years, possibly owing to much improved diabetes mellitus (DM) control. On the other hand, increasing incidence of endogenous *Klebsiella* endophthalmitis from UTI in non-diabetic elderly female patients is noted.

KEY QUESTION 6: SHOULD GENERAL DILATED FUNDUS EXAMINATION BE RECOMMENDED FOR PATIENTS WITH CERTAIN INFECTION FOCUS IN TAIWAN?

Due to the hematogenous nature of EnE, anterior chamber reactions are sometimes mild when the posterior pole has fulminant presentations [70, 71]. This characteristic is in contrast to that of acute post-operative endophthalmitis (Fig. 1), and poses challenges in early diagnosis. Consequently, routine dilated fundus screening for certain patient populations has long been debated. The efficacy of fundus screening for EnE varies among different etiologies and also depends on incidences and several other factors

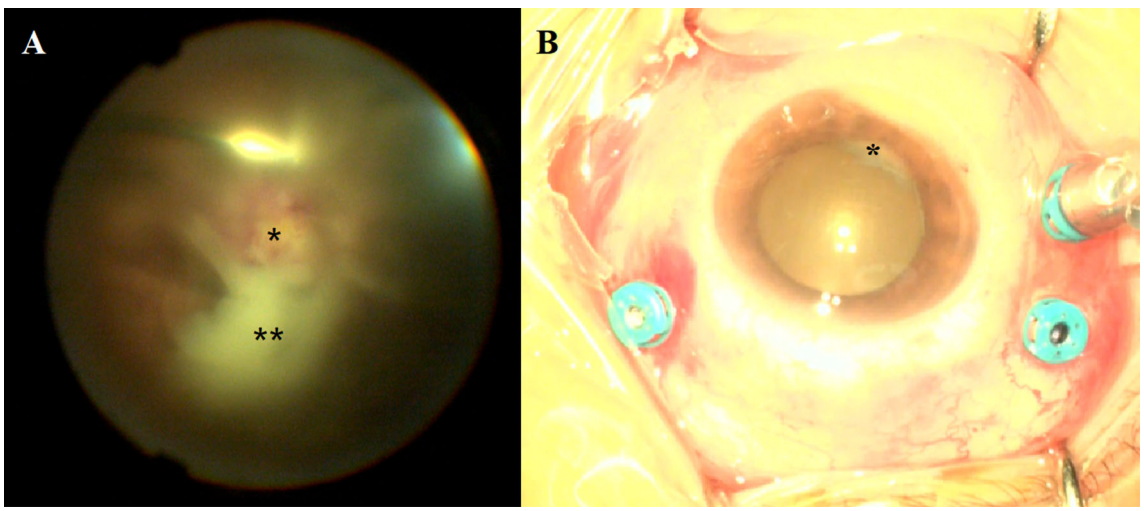

Fig. 1 Discrepancy between the presentations of anterior and posterior segments in endogenous endophthalmitis. In a case of pyogenic liver abscess-related endogenous *Klebsiella* endophthalmitis, the posterior segment revealed dense vitritis (**), massive sub-macular abscess (*) with diffused retinal vessel sheathing (**A**); while at the same time only mild hypopyon presented in the anterior chamber (*) (**B**)

[72]. Fundus screening is widely advocated for pyogenic liver abscess because of its relative high incidence of EnE [6, 73]. In Taiwan, EnE developed in 0.9–1.36% of patients with pyogenic liver abscesses according to the nationwide health registration database [58–60]. Their disease courses are usually fulminant, and only a small proportion of patients left with functional vision [55–57] (Table 2). The panel thus recommended dilated fundus screening for all patients with pyogenic liver abscess.

Consensus Statement

In Taiwan, routine dilated fundus screening for EnE is recommended for all patients with pyogenic liver abscess.

KEY QUESTION 7: WHAT ARE THE OPTIMAL TIMING AND INDICATION OF VITRECTOMY FOR BACTERIAL ENE

Systemic antimicrobials with adequate ocular penetrance, with or without intravitreal injection of antibiotics, are standard treatment in bacterial EnE [2, 74]. On the other hand, vitrectomy for the management of bacterial EnE has gained additional roles in recent years [75–77]. In Taiwan, 82–92% of eyes received intravitreal injection, while 23–47% of eyes received vitrectomy [55–57] (Table 3).

To date, no prospective randomized controlled study has assessed the benefits of vitrectomy in cases of bacterial endophthalmitis. Several retrospective studies advocate the benefit of vitrectomy in bacterial EnE with initial better vision [25, 77]. A wide variety of timings and indications for vitrectomy in EnE were proposed [2, 78]. On the other hand, several studies challenged the sufficiency of antibiotic concentration with systemic antibiotics alone in severe cases [79]. Studies commented that even for those antibiotics with good blood–retinal barrier penetration, whether their initial concentrations achieving therapeutic level in the first several hours are still questionable [80, 81]. Consequently, the panel concluded that micro-incisional vitrectomy in bacterial EnE is recommended when progression of vitritis or deterioration of vision are noted despite 24 h of systemic antibiotics with or without intravitreal antibiotic injection. Early vitrectomy at initial encounter is also recommended when dense vitritis blocks the view of disc and arcade vessels.

Consensus Statement

Vitrectomy in bacterial EnE is indicated when progression of vitritis or deterioration of vision are noted despite 24 h of systemic antibiotics with or without intravitreal antibiotic injection. Early vitrectomy at initial encounter is also recommended when dense vitritis blocks the view of disc and arcade vessels.

KEY QUESTION 8: WHAT IS THE RECOMMENDED TREATMENT STRATEGY FOR FUNGAL CHORIORETINITIS AND ENDOGENOUS FUNGAL ENDOPHTHALMITIS?

Endogenous fungal endophthalmitis (EFE) applies a slightly different treatment strategy compared to its bacterial counterpart [82, 83]. Fungal chorioretinitis without vitritis is regarded as an early form of EFE [84], which can be successfully treated with effective systemic antifungal agents alone [83]. The main issues in debate are similarly whether and when to perform intravitreal antifungal injection or vitrectomy, which still lacks support from prospective studies to date [85]. Systemic antifungals with additional intravitreal injection of Amphotericin B or voriconazole is recommended in EFE with sight-threatening chorioretinitis without vitritis, or EFE with vitritis [83, 86]. Because vitrectomy still comes with possible complications, such as retinal detachment, epiretinal membrane, ocular hypertension, suprachoroidal hemorrhage [10, 87], it is recommended to be reserved for those cases with dense vitritis, those with significant macular-threatening chorioretinitis or subretinal

abscess, and those with progress in terms of vision or signs despite combined systemic and intravitreal antifungals.

Consensus Statement

For endogenous fungal chorioretinitis, an effective, adequately penetrant, systemic antifungal agent is mandatory. For fungal chorioretinitis without vitritis, systemic antifungal is usually sufficient. For sight-threatening chorioretinitis without vitritis, additional intravitreal injection of antifungals is recommended. For any endogenous fungal endophthalmitis with vitritis, systemic antifungal alone is regarded as inadequate, and concomitant intravitreal antifungals or vitrectomy are recommended. Vitrectomy is reserved for cases with dense vitritis, significantly sight-threatening chorioretinitis or subretinal abscess, as well as progressing disease despite combined treatment with systemic and intravitreal antifungals.

LIMITATIONS

The panel is fully aware of the study's limited scope, which primarily focuses on the situation in Taiwan. The epidemiology section showed unique profiles that are deviated from that of global trend. Explanations were thus provided accordingly. On the other hand, despite the consensus on topics of diagnosis and management were tailored to the real-world conditions in Taiwan, they were based on modern and global evidence. More specifically, the consensus for the Key questions 1, 5, and 6 mainly addressed issues in Taiwan, while the recommendations for the Key questions 2, 3, 4, 7, and 8 are more geographically independent. When it comes to endophthalmitis, the disease and practice patterns vary greatly among territories, and too many topics are left without uniformed conclusions. We thus believe that this study provides not only important perspectives for clinicians and scholars in Taiwan, but also valuable references for those in East Asia, Southeast Asia, and even around the world.

CONCLUSIONS

Consensus was reached for eight key questions regarding acute post-operative endophthalmitis and EnE in Taiwan. The *Enterococcus* species is emerging as a major pathogen for acute post-operative endophthalmitis. Stain and culture are still recommended as standard procedures for pathogen identification. For acute post-operative endophthalmitis, timing of vitrectomy set by EVS study is regarded as unsuitable for clinical practice nowadays. With the advancement of micro-incisional vitrectomy in current times, vitrectomy is recommended for cases with better initial vision, and can also be applied once the disease progresses. On the other hand, routine use of intracameral antibiotics for infection prophylaxis is not recommended for cataract operation due to safety concerns. In terms of EnE, the incidence of pyogenic liver abscess-related EnE is in decrease, and an increasing trend of *Klebsiella* endophthalmitis in non-diabetic elderly female with UTI was noted. Routine fundus screening is recommended for all patients with pyogenic liver abscess. Early vitrectomy with more liberal visual criteria is also recommended in cases of both bacterial and fundal EnE.

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Declarations

Conflict of Interest. Cheng-Yung Lee, Shwu-Jiuan Sheu, San-Ni Chen, Cheng-Kuo Cheng, Hsi-Kung Kuo, De-Kuang Hwang, Chien-Hsiung Lai, Wei-Chun Chan, Yi-Ting Hsieh, and Chang-Hao Yang declare that they have no competing interests.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

REFERENCES

1. Keynan Y, Finkelman Y, Lagacé-Wiens P. The microbiology of endophthalmitis: global trends and a local perspective. Eur J Clin Microbiol Infect Dis. 2012;31(11):2879–86.

2. Sadiq MA, Hassan M, Agarwal A, Sarwar S, Toufeeq S, Soliman MK, et al. Endogenous endophthalmitis: diagnosis, management, and prognosis. J Ophthalmic Inflamm Infect. 2015;5(1):32.

3. Muqit MM, Mehat M, Bunce C, Bainbridge JW. Early vitrectomy for exogenous endophthalmitis following surgery. Cochrane Database Syst Rev. 2022;11(11):Cd013760.

4. Regan KA, Radhakrishnan NS, Hammer JD, Wilson BD, Gadkowski LB, Iyer SSR. Endogenous endophthalmitis: yield of the diagnostic evaluation. BMC Ophthalmol. 2020;20(1):138.

5. Fileta JB, Scott IU, Flynn HW Jr. Meta-analysis of infectious endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. Ophthalmic Surg Lasers Imaging Retina. 2014;45(2):143–9.

6. Hussain I, Ishrat S, Ho DCW, Khan SR, Veeraraghavan MA, Palraj BR, et al. Endogenous endophthalmitis in *Klebsiella pneumoniae* pyogenic liver abscess: Systematic review and meta-analysis. Int J Infect Dis. 2020;101:259–68.

7. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. Arch Ophthalmol. 1995;113(12):1479–96.

8. Callegan MC, Engelbert M, Parke DW 2nd, Jett BD, Gilmore MS. Bacterial endophthalmitis: epidemiology, therapeutics, and bacterium-host interactions. Clin Microbiol Rev. 2002;15(1):111–24.

9. Weng TH, Chang HC, Chung CH, Lin FH, Tai MC, Tsao CH, et al. Epidemiology and mortality-related prognostic factors in endophthalmitis. Invest Ophthalmol Vis Sci. 2018;59(6):2487–94.

10. Negretti GS, Chan W, Pavesio C, Muqit MMK. Vitrectomy for endophthalmitis: 5-year study of outcomes and complications. BMJ Open Ophthalmol. 2020;5(1): e000423.

11. Martínez-Vázquez C, Fernández-Ulloa J, Bordón J, Sopeña B, de la Fuente J, Ocampo A, Rubianes M. Candida albicans endophthalmitis in brown heroin addicts: response to early vitrectomy preceded and

followed by antifungal therapy. Clin Infect Dis. 1998;27(5):1130–3.

12. Wakabayashi T, Miller SC, Patel SN, Fliotsos MJ, Justin GA, Agrawal R, et al. Global current practice patterns for the management of exogenous endophthalmitis: a survey by the American Society of Ophthalmic Trauma. Curr Eye Res. 2022;47(5): 802–8.

13. Conrady CD, Feist RM, Vitale AT, Shakoor A. Long-term visual outcomes of endophthalmitis and the role of systemic steroids in addition to intravitreal dexamethasone. BMC Ophthalmol. 2020;20(1): 181.

14. Mir TA, Papudesu C, Fang W, Hinkle DM. Incidence of drug use-related endogenous endophthalmitis hospitalizations in the United States, 2003 to 2016. JAMA Ophthalmol. 2021;139(1):18–26.

15. Uppuluri A, Zarbin MA, Bhagat N. Trends in endogenous endophthalmitis in rural and urban settings in the United States. Ophthalmic Epidemiol. 2022. https://doi.org/10.1080/09286586.2022.2094965.

16. Aaberg TM Jr, Flynn HW Jr, Schiffman J, Newton J. Nosocomial acute-onset postoperative endophthalmitis survey. A 10-year review of incidence and outcomes. Ophthalmology. 1998;105(6):1004–10.

17. Han DP, Wisniewski SR, Wilson LA, Barza M, Vine AK, Doft BH, Kelsey SF. Spectrum and susceptibilities of microbiologic isolates in the Endophthalmitis Vitrectomy Study. Am J Ophthalmol. 1996;122(1):1–17.

18. Grzybowski A, Turczynowska M, Schwartz SG, Relhan N, Flynn HW Jr. The role of systemic antimicrobials in the treatment of endophthalmitis: a review and an international perspective. Ophthalmol Ther. 2020;9(3):485–98.

19. Brockhaus L, Goldblum D, Eggenschwiler L, Zimmerli S, Marzolini C. Revisiting systemic treatment of bacterial endophthalmitis: a review of intravitreal penetration of systemic antibiotics. Clin Microbiol Infect. 2019;25(11):1364–9.

20. Czajka MP, Byhr E, Olivestedt G, Olofsson EM. Endophthalmitis after small-gauge vitrectomy: a retrospective case series from Sweden. Acta Ophthalmol. 2016;94(8):829–35.

21. Shao EH, Yates WB, Ho IV, Chang AA, Simunovic MP. Endophthalmitis: changes in presentation, management and the role of early vitrectomy. Ophthalmol Ther. 2021;10(4):877–90.

22. Flores-Sánchez BC, Bloch E, Sanghi P, da Cruz L. Safety profile and surgical outcomes of early vitrectomy in eyes with unexplained fundus-obscuring vitreous haemorrhage. Eye (Lond). 2023. https://doi.org/10.1038/s41433-023-02475-2.

23. Dib B, Morris RE, Oltmanns MH, Sapp MR, Glover JP, Kuhn F. Complete and early vitrectomy for endophthalmitis after cataract surgery: an alternative treatment paradigm. Clin Ophthalmol. 2020;14:1945–54.

24. Gounder PA, Hille DM, Khoo YJ, Phagura RS, Chen FK. Endogenous endophthalmitis in western Australia: a sixteen-year retrospective study. Retina. 2020;40(5):908–18.

25. Ho IV, Fernandez-Sanz G, Levasseur S, Ting E, Liew G, Playfair J, et al. Early pars plana vitrectomy for treatment of acute infective endophthalmitis. Asia Pac J Ophthalmol (Phila). 2019;8(1):3–7.

26. Soliman MK, Gini G, Kuhn F, Iros M, Parolini B, Ozdek S, et al. International practice patterns for the management of acute postsurgical and postintravitreal injection endophthalmitis: European Vitreo-retinal Society endophthalmitis study report 1. Ophthalmol Retina. 2019;3(6):461–7.

27. Wu PC, Kuo HK, Li M, Lai IC, Fang PC, Lin SA, et al. Nosocomial postoperative endophthalmitis: a 14-year review. Graefes Arch Clin Exp Ophthalmol. 2006;244(8):920–9.

28. Buzard K, Liapis S. Prevention of endophthalmitis. J Cataract Refract Surg. 2004;30(9):1953–9.

29. Speaker MG, Milch FA, Shah MK, Eisner W, Kreiswirth BN. Role of external bacterial flora in the pathogenesis of acute postoperative endophthalmitis. Ophthalmology. 1991;98(5):639–49 (**discussion 50**).

30. Peng KL, Kung YH, Tsai HS, Wu TT. Treatment outcomes of acute postoperative infectious endophthalmitis. BMC Ophthalmol. 2021;21(1): 384.

31. Hung JH, Ko WC, Chen CY, Lin SH, Wu CL, Hsu SM, et al. Postoperative *Mycobacteroides abscessus* subsp. *abscessus* endophthalmitis: clinical analysis of 12 clustered adults and a proposed therapeutic algorithm. J Microbiol Immunol Infect. 2020;53(5): 766–77.

32. Chen YH, Chen JT, Tai MC, Chou YC, Chen CL. Acute postcataract endophthalmitis at a referral center in northern Taiwan: Causative organisms, clinical features, and visual acuity outcomes after treatment: a retrospective cohort study. Medicine (Baltimore). 2017;96(49): e8941.

33. Teng YT, Teng MC, Kuo HK, Fang PC, Wu PC, Chen CH, et al. Isolates and antibiotic susceptibilities of

endophthalmitis in postcataract surgery: a 12-year review of culture-proven cases. Int Ophthalmol. 2017;37(3):513–8.

34. Cheng JH, Chang YH, Chen CL, Chen YH, Lu DW, Chen JT. Acute endophthalmitis after cataract surgery at a referral centre in Northern Taiwan: review of the causative organisms, antibiotic susceptibility, and clinical features. Eye (Lond). 2010;24(8): 1359–65.

35. Hsu CR, Chen JT, Yeh KM, Hsu CK, Tai MC, Chen YJ, Chang YH. A cluster of nontuberculous mycobacterial endophthalmitis (NTME) cases after cataract surgery: clinical features and treatment outcomes. Eye (Lond). 2018;32(9):1504–11.

36. Phillips MS, von Reyn CF. Nosocomial infections due to nontuberculous mycobacteria. Clin Infect Dis. 2001;33(8):1363–74.

37. Kim SH, Yu MH, Lee JH, Yoon JS, Rah SH, Choi M. Seasonal variation in acute post-cataract surgery endophthalmitis incidences in South Korea. J Cataract Refract Surg. 2019;45(12):1711–6.

38. Li J, Morlet N, Ng JQ, Semmens JB, Knuiman MW. Significant nonsurgical risk factors for endophthalmitis after cataract surgery: EPSWA fourth report. Invest Ophthalmol Vis Sci. 2004;45(5): 1321–8.

39. Taban M, Behrens A, Newcomb RL, Nobe MY, Saedi G, Sweet PM, McDonnell PJ. Acute endophthalmitis following cataract surgery: a systematic review of the literature. Arch Ophthalmol. 2005;123(5): 613–20.

40. Sharma S, Jalali S, Adiraju MV, Gopinathan U, Das T. Sensitivity and predictability of vitreous cytology, biopsy, and membrane filter culture in endophthalmitis. Retina. 1996;16(6):525–9.

41. Nam KY, Lee JE, Lee JE, Jeung WJ, Park JM, Park JM, et al. Clinical features of infectious endophthalmitis in South Korea: a five-year multicenter study. BMC Infect Dis. 2015;15:177.

42. Bhikoo R, Wang N, Welch S, Polkinghorne P, Niederer R. Factors associated with positive microbial culture in patients with endophthalmitis based on clinical presentation and multimodal intraocular sampling. Asia Pac J Ophthalmol (Phila). 2020;9(1): 4–8.

43. Kung WH, Lai CT, Lin CJ, Bair H, Chen HS, Lin JM, Chen WL. Positive culture results and longer duration between onset and microincision vitrectomy have adverse effects on post-cataract surgery endophthalmitis outcome. J Formos Med Assoc. 2020;119(1 Pt 3):385–91.

44. Chiquet C, Bron AM, Lundström M, Maurin M. Acute postoperative endophthalmitis: Microbiology from the laboratory to the bedside. Surv Ophthalmol. 2022;67(6):1698–710.

45. Huang Q, Fu A, Wang Y, Zhang J, Zhao W, Cheng Y. Microbiological diagnosis of endophthalmitis using nanopore targeted sequencing. Clin Exp Ophthalmol. 2021;49(9):1060–8.

46. Hong BK, Lee CS, Van Gelder RN, Garg SJ. Emerging techniques for pathogen discovery in endophthalmitis. Curr Opin Ophthalmol. 2015;26(3): 221–5.

47. Williams GA. 25-, 23-, or 20-gauge instrumentation for vitreous surgery? Eye. 2008;22(10):1263–6.

48. Kuhn F, Gini G. Vitrectomy for endophthalmitis. Ophthalmology. 2006;113(4):714.

49. Group EES. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. J Cataract Refract Surg. 2007;33(6):978–88.

50. George NK, Stewart MW. The routine use of intracameral antibiotics to prevent endophthalmitis after cataract surgery: how good is the evidence? Ophthalmol Ther. 2018;7(2):233–45.

51. Gower EW, Lindsley K, Tulenko SE, Nanji AA, Leyngold I, McDonnell PJ. Perioperative antibiotics for prevention of acute endophthalmitis after cataract surgery. Cochrane Database Syst Rev. 2017;2(2):Cd006364.

52. Titiyal JS, Kaur M. Role of intracameral antibiotics in endophthalmitis prophylaxis following-cataract surgery. Indian J Ophthalmol. 2020;68(5):688–91.

53. Shorstein NH, Liu L, Carolan JA, Herrinton L. Endophthalmitis prophylaxis failures in patients injected with intracameral antibiotic during cataract surgery. Am J Ophthalmol. 2021;227:166–72.

54. Grzybowski A, Brona P, Zeman L, Stewart MW. Commonly used intracameral antibiotics for endophthalmitis prophylaxis: a literature review. Surv Ophthalmol. 2021;66(1):98–108.

55. Hsieh MC, Chen SN, Cheng CY, Li KH, Chuang CC, Wu JS, et al. Clinicomicrobiological profile, visual outcome and mortality of culture-proven endogenous endophthalmitis in Taiwan. Sci Rep. 2020;10(1):12481.

56. Kuo G, Yen CL, Lu YA, Chen CY, Sun MH, Lin Y, et al. Clinical and visual outcomes following endogenous endophthalmitis: 175 consecutive cases from a tertiary referral center in Taiwan. J Microbiol Immunol Infect. 2022;55(1):114–22.

57. Chen SC, Lee YY, Chen YH, Lin HS, Wu TT, Sheu SJ. *Klebsiella pneumoniae* infection leads to a poor visual outcome in endogenous endophthalmitis: a 12-year experience in southern Taiwan. Ocul Immunol Inflamm. 2017;25(6):870–7.

58. Keller JJ, Tsai MC, Lin CC, Lin YC, Lin HC. Risk of infections subsequent to pyogenic liver abscess: a nationwide population-based study. Clin Microbiol Infect. 2013;19(8):717–22.

59. Hu CC, Ho JD, Lou HY, Keller JJ, Lin HC. A one-year follow-up study on the incidence and risk of endophthalmitis after pyogenic liver abscess. Ophthalmology. 2012;119(11):2358–63.

60. Lin YT, Liu CJ, Chen TJ, Fung CP. Long-term mortality of patients with septic ocular or central nervous system complications from pyogenic liver abscess: a population-based study. PLoS ONE. 2012;7(3): e33978.

61. Tsai FC, Huang YT, Chang LY, Wang JT. Pyogenic liver abscess as endemic disease Taiwan. Emerg Infect Dis. 2008;14(10):1592–600.

62. Sheu SJ, Kung YH, Wu TT, Chang FP, Horng YH. Risk factors for endogenous endophthalmitis secondary to *Klebsiella pneumoniae* liver abscess: 20-year experience in southern Taiwan. Retina. 2011;31(10):2026–31.

63. Chou FF, Kou HK. Endogenous endophthalmitis associated with pyogenic hepatic abscess. J Am Coll Surg. 1996;182(1):33–6.

64. Ang M, Jap A, Chee SP. Prognostic factors and outcomes in endogenous *Klebsiella pneumoniae* endophthalmitis. Am J Ophthalmol. 2011;151(2): 338–44.

65. Sheu SJ, Chen YS, Lin HS, Chen SL, Tsai PJ. A lack of ongoing diabetes is an important factor in preserving eyes from late or suboptimally treated endogenous endophthalmitis secondary to *Klebsiella pneumoniae* liver abscess. Taiwan J Ophthalmol. 2015;5(1):23–7.

66. Pillai GS, Remadevi KK, Anilkumar V, Radhakrishnan N, Rasheed R, Ravindran GC. Clinical profile and outcome of endogenous endophthalmitis at a quaternary referral centre in south India. Indian J Ophthalmol. 2020;68(5):827–33.

67. Muda R, Vayavari V, Subbiah D, Ishak H, Adnan A, Mohamed SO. Endogenous endophthalmitis: a 9-year retrospective study at a tertiary referral hospital in Malaysia. J Ophthalmic Inflamm Infect. 2018;8(1):14.

68. Tirpack AR, Duker JS, Baumal CR. An outbreak of endogenous fungal endophthalmitis among intravenous drug abusers in New England. JAMA Ophthalmol. 2017;135(6):534–40.

69. Connell PP, O'Neill EC, Amirul Islam FM, Buttery R, McCombe M, Essex RH, et al. Endogenous endophthalmitis associated with intravenous drug abuse: seven-year experience at a tertiary referral center. Retina. 2010;30(10):1721–5.

70. Gan LY, Ye JJ, Zhou HY, Min HY, Zheng L. Microbial spectrum and risk factors of endogenous endophthalmitis in a tertiary center of Northern China. Int J Ophthalmol. 2022;15(10):1676–82.

71. Wang H, Chang Y, Zhang Y, Yang R, Shi H, Zhang M. Bilateral endogenous fungal endophthalmitis: a case report. Medicine (Baltimore). 2023;102(16): e33585.

72. Aggarwal R, Ranganathan P, Pramesh CS. Research studies on screening tests. Perspect Clin Res. 2022;13(3):168–71.

73. Tan YM, Chee SP, Soo KC, Chow P. Ocular manifestations and complications of pyogenic liver abscess. World J Surg. 2004;28(1):38–42.

74. Jackson TL, Paraskevopoulos T, Georgalas I. Systematic review of 342 cases of endogenous bacterial endophthalmitis. Surv Ophthalmol. 2014;59(6): 627–35.

75. Nam KY, Lee JE, Lee JE, Jeung WJ, Park JM, Park JM, et al. Clinical features of infectious endophthalmitis in South Korea: a five-year multicenter study. BMC Infect Dis. 2015;15(1):177.

76. Lim HW, Shin JW, Cho HY, Kim HK, Kang SW, Song SJ, et al. Endogenous endophthalmitis in the Korean population: a six-year retrospective study. Retina. 2014;34(3):592–602.

77. Connell PP, O'Neill EC, Fabinyi D, Islam FM, Buttery R, McCombe M, et al. Endogenous endophthalmitis: 10-year experience at a tertiary referral centre. Eye (Lond). 2011;25(1):66–72.

78. Do T, Hon DN, Aung T, Hien ND, Cowan CL Jr. Bacterial endogenous endophthalmitis in Vietnam: a randomized controlled trial comparing vitrectomy with silicone oil versus vitrectomy alone. Clin Ophthalmol. 2014;8:1633–40.

79. Sami K, Neil K, Mandi DC, Gholam AP. Endogenous endophthalmitis: etiology and treatment. In: Alejandro RG, Julio CHC, editors. Infectious eye diseases. Rijeka: IntechOpen; 2021. p. 6.

80. Axelrod JL, Klein RM, Bergen RL, Sheikh MZ. Human vitreous levels of selected antistaphylococcal antibiotics. Am J Ophthalmol. 1985;100(4): 570–5.

81. Vedantham V, Lalitha P, Velpandian T, Ghose S, Mahalakshmi R, Ramasamy K. Vitreous and aqueous penetration of orally administered moxifloxacin in humans. Eye. 2006;20(11):1273–8.

82. Durand ML. Bacterial and fungal endophthalmitis. Clin Microbiol Rev. 2017;30(3):597–613.

83. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. Clin Infect Dis. 2016;62(4):e1-50.

84. Invernizzi A. Fungal endophthalmitis. In: Gupta V, Nguyen QD, LeHoang P, Herbort CP, editors. The uveitis atlas. New Delhi: Springer India; 2016. p. 1–9.

85. Celiker H, Kazokoglu H. The role of pars plana vitrectomy in the management of fungal endogenous endophthalmitis. Eur J Ophthalmol. 2020;30(1): 88–93.

86. Riddell JT, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. Clin Infect Dis. 2011;52(5): 648–53.

87. Lafontaine PO, Rouberol F, Cornut PL, Bron AM, Thuret G, Romanet JP, et al. Complications of pars plana vitrectomy in acute endophthalmitis. Investig Ophthalmol Vis Sci. 2005;46(13):5489.