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ORIGINAL RESEARCH

Clinical presentation and prognostic factors in emergency department endophthalmitis: a 11-year retrospective study

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Abstract

Background: Endophthalmitis, a serious eye condition that poses a risk to vision and can quickly worsen, is considered a genuine urgent situation for the eyes. This research is concentrated on individuals with endophthalmitis who seek care in the emergency department (ED), with the objective of identifying the clinical signs and microbial properties that may increase the likelihood of needing evisceration. By doing so, the goal is to enhance the early detection and immediate management of this condition. **Methods**: This is a retrospective study conducted in the ED setting in a tertiary medical center in Northern Taiwan. Between January 2012 to December 2022, a total of 453 ED endophthalmitis patients were enrolled. Detailed chart reviews were done and the data collected included demographic characteristics, clinical symptoms, microbiology culture results, presenting visual acuity (VA), and the rate of evisceration. **Results**: There were 144 patients (31.8%) with endogenous endophthalmitis and 309 patients (68.2%) with exogenous endophthalmitis in the ED. The most common symptoms were blurry vision (94.3%) and red eye (88.7%). Blood culture was positive in 18.8% of cases, while vitreous or aqueous culture was positive in 59.6% of cases. The most commonly identified pathogens for endogenous and exogenous endophthalmitis were *Klebsiella pneumoniae* (20.5%) and *Staphylococcus epidermidis* (23.6%), respectively. The most significant risk factors for evisceration in both endogenous and exogenous groups were impaired initial VA and corneal ulcer. The proportion of patients with endogenous endophthalmitis who underwent evisceration (13.9%) was significantly higher than their exogenous counterparts (5.5%). **Conclusions**: Timely identification and proper management are essential for patients at risk of developing endophthalmitis in emergency settings. This is particularly important for individuals who exhibit compromised initial visual acuity and suffer from corneal ulcers. Despite intensive therapy, the long-term visual outcomes for endogenous endophthalmitis are generally worse compared to the exogenous form.

Keywords

Endogenous endophthalmitis; Exogenous endophthalmitis; Vitreous culture; Evisceration; Emergency department

1. Introduction

Endophthalmitis is defined as an intraocular infection involving the vitreous and/or aqueous humor. It is a vision-threatening disease that requires urgent medical intervention. In the absence of timely diagnosis and intervention, endophthalmitis frequently results in notable visual impairment or total loss of vision. Due to its capacity to advance quickly and result in severe consequences, it is essential to grasp the clinical features, predisposing factors, and most effective treatment approaches for endophthalmitis to enhance patient outcomes and maintain visual acuity (VA).

Endophthalmitis is further categorized as endogenous and exogenous according to the origin of the pathogens. Endogenous endophthalmitis is caused by the dissemination of pathogens through the bloodstream from distant infection sites, whereas exogenous endophthalmitis arises from external factors, such as post-traumatic incidents [1, 2], postoperative (*e.g.*, cataract extraction, glaucoma drainage implants/trabeculectomy, pars plana vitrectomy), post-intravitreous injection therapy, or secondary to corneal ulcer [3]. Endogenous endophthalmitis, which occurs at a rare rate of approximately 1.9 cases per million per year [4], is frequently linked to bloodstream infection or distant infection

sites such as pneumonia, urinary tract infection, cellulitis, liver abscess, renal abscess, osteomyelitis, endocarditis, and meningitis [5–7]. Additionally, it may manifest following non-ocular invasive procedures like dental treatments, gynecological surgeries, or anorectal surgeries [5]. Compared to exogenous endophthalmitis, endogenous endophthalmitis is often associated with poorer visual outcomes [8–12]. Administering intravitreal antibiotics promptly has been linked to improved visual prognosis and a decreased likelihood of requiring evisceration or enucleation in instances of endophthalmitis [12, 13], while delayed detection could result in substantial impairment to the patient's eyesight.

According to previous literature, the most common Gram-positive pathogens for endophthalmitis are *Staphylococcus epidermidis*, *Staphylococcus aureus*, *group B streptococcus*, *Streptococcus pneumoniae*, *Bacillus spp.* and *Listeria monocytogenes*. Frequently identified Gram-negative pathogens include *Klebsiella spp.*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter spp.* and *Neisseria meningitidis.* [8, 11]. Highly virulent bacteria include *Staphylococcus aureus*, *Streptococcus* species, *Bacillus*, *Escherichia coli*, *Klebsiella Pneumoniae* and *Pseudomonas aeruginosa*, while *Candida albicans* represents a highly pathogenic fungus [2, 10, 14, 15]. Early detection and treatment of these pathogens are imperative to prevent severe visual impairment.

The geographical location also plays a role in the diversity of microbiological profiles. In Asia, bacterial endogenous endophthalmitis is often linked to pyogenic liver abscesses triggered by *Klebsiella Pneumoniae*, particularly in individuals with diabetes mellitus [16, 17], while in the United States, the most frequent pathogens are Gram-positive bacteria, especially *Streptococcus spp.* and *Staphylococcus spp*, most frequently associated with endocarditis [8]. Underlying conditions that may predispose individuals to infection include compromised immunity, chronic obstructive pulmonary disease (COPD), and end-stage renal disease (ESRD) [13]. Endophthalmitis is occasionally associated with widespread systemic infection affecting various organs, with pyogenic liver abscess being the predominant identified origin [16, 18]. In the pediatric population, *Streptococcus pneumoniae* and *Haemophilus influenzae*, which are frequently encountered in cases of pneumonia, sinusitis, or otitis media, are more prone to be the causative agents [19].

To date, previous studies have focused on endophthalmitis in inpatient settings. In contrast, there is limited literature on endophthalmitis within the emergency department (ED) context. Being a tertiary medical institution, we are referred ophthalmology cases from district and regional hospitals, as well as local clinics. In Taiwan's healthcare system, patients have the option to directly seek treatment at the ED without the need for referrals. This practice notably boosts the volume of cases, especially during periods when outpatient services are not available, such as nights or holidays. This study aims to delineate the clinical presentations and microbiological profiles that constitute key risk factors for evisceration in endophthalmitis patients presenting to the ED. The goal is to enhance early diagnosis and optimize management strategies for this vision-threatening condition at the initial point of care.

2. Materials and methods

2.1 Study setting

This is a retrospective cohort analysis. The study site is the ED of a tertiary medical center in Northern Taiwan, consisting of a 3600-bed capacity and an annual ED volume of 180,000 patient visits.

2.2 Participants and data collection

All patients who visited the emergency department From January 2012 to December 2022 with the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnostic codes corresponding to endophthalmitis were included (Fig. 1). Patients diagnosed with endophthalmitis as a primary condition and not as a pre-existing condition were considered eligible for inclusion, while those who revisited the emergency department within one month for the same issue had only the data from their initial visit included in the analysis. A senior emergency physician conducted a thorough review of patient charts to gather relevant clinical information such as symptoms, initial visual acuity, presence of other infections, underlying medical conditions, and types of treatment administered. The collected data encompassed predetermined factors, including demographic details (age, gender, ocular and systemic diseases), triage classification based on the Taiwan Triage and Acuity Scale (TTAS) [20], clinical manifestations, results of microbiological cultures, initial best corrected visual acuity (BCVA), treatment modalities including surgical procedures, and patient outcomes.

2.3 Statistical analysis

All analysis were conducted using SPSS software (Version 22; IBM Corp, Armonk, NY, USA). Categorical variables were presented using proportions and analyzed using the Chi-Square test or Fisher's exact test, where appropriate. Continuous variables were presented using mean $\pm$ standard deviation (SD). Snellen vision was converted into a logarithm of the minimum angle of resolution (logMAR) for numeric comparison. Ultra-low VA such as counting fingers (CF), hand motion (HM), light perception (LS), and no light perception (NLS) was assigned VA values 2.1 logMAR, 2.4 logMAR, 2.7 logMAR and 3.0 logMAR, respectively, following previous literature [5, 21]. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

A total of 716 ED patients were enrolled during the 11-year study period (2012–2022). After reviewing medical records, 204 patients with a primary diagnosis other than endophthalmitis were excluded. Fifty-nine individuals who returned to the emergency department within one month, which was considered part of the same medical episode, were excluded from the study. The analysis included a total of 453 patients (469 eyes), as illustrated in Fig. 1. Demographic data, along with a comparison between the endogenous and exogenous

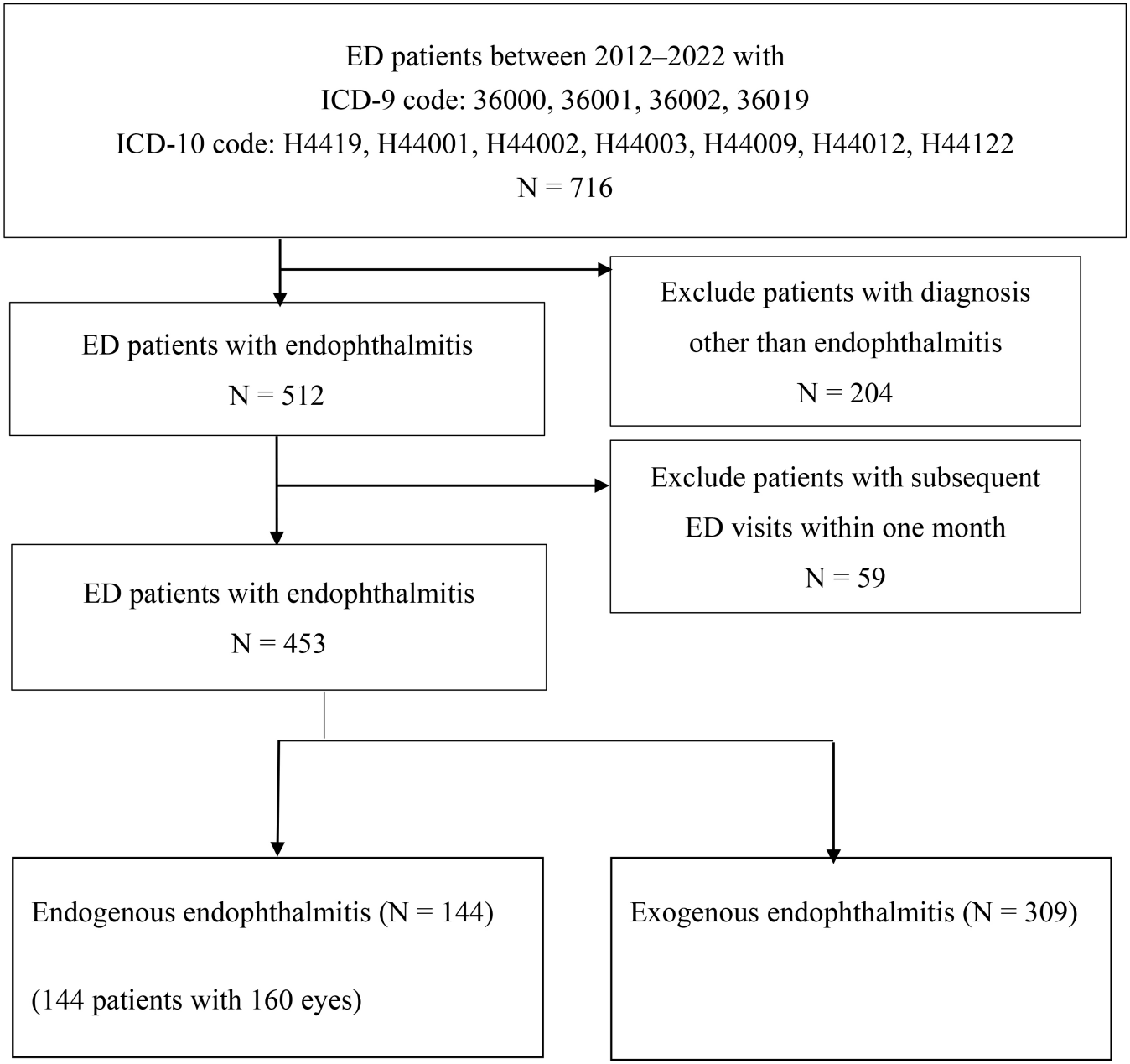

FIGURE 1. Flowchart of the recruitment of ED patients with endophthalmitis. ED: emergency department; ICD: International Classification of Diseases.

groups, are presented in Table 1. The average age of the patients was 63.8 years, comprising 256 (56.5%) males. Among them, 144 patients (31.8%) were diagnosed with endogenous endophthalmitis. Among 309 patients with exogenous endophthalmitis, 247 (79.9%) were acute onset (within 6 weeks), and 62 (20.1%) were chronic. The primary causes included postoperative (84.8%), traumatic (9.4%), corneal ulcer-related (3.9%), and post-intravitreal injection (1.9%).

Among postoperative cases, cataract surgery with intraocular lens (IOL) implantation was the most common procedure (84.4%), followed by glaucoma surgery (8.4%) and trans pars plana vitrectomy (TPPV) (4.6%). All cases in the exogenous group had unilateral involvement. The most prevalent systemic comorbidities encountered in the study were hypertension and diabetes, affecting 44% and 38.6% of patients, respectively. Among the underlying ophthalmic diseases observed, glaucoma was the most common (10.4%). In terms of treatments administered, a total of 410 patients (90.5%) underwent intravitreal antibiotic injections, with 129 patients receiving them for endogenous infections and 281 for exogenous infections. Additionally, 37 patients (8.2%) were treated with topical antibiotics, including 12 for endogenous infections and 25 for exogenous infections. Systemic antibiotics were given to 125 patients (27.6%), with 92 receiving them for endogenous infections and 33 for exogenous infections. Surgical interventions included vitrectomy in 180 cases (38.4%), with 28 cases for endogenous infections and 152 for exogenous infections, as well as evisceration in 37 cases (8.7%), with 20 cases for endogenous infections and 17 for exogenous infections.

TABLE 1. Demographic results.

	Overall	Endogenous	Exogenous	*p*-value
Age (yr) (Mean ± SD)	63.77 ± 15.24	63.26 ± 15.80	64.01 ± 15.00	0.624
Age group (yr) (n, %)				
<18	3 (0.6%)	1 (0.7%)	2 (0.6%)	
18–65	229 (50.6%)	77 (53.5%)	152 (49.2%)	0.692
>65	221 (48.8%)	66 (45.8%)	155 (50.2%)	
Male sex (n, %)	256 (56.5%)	75 (52.1%)	181 (58.6%)	0.232
Triage level (n, %)				
Level 1	5 (1.1%)	3 (2.1%)	2 (0.7%)	
Level 2	28 (6.2%)	18 (12.5%)	10 (3.2%)	
Level 3	383 (84.6%)	110 (76.4%)	273 (88.3%)	0.001
Level 4	35 (7.7%)	13 (9.0%)	22 (7.1%)	
Level 5	2 (0.4%)	0 (0.0%)	2 (0.7%)	
Past history (n, %)				
Previous eye surgery	317 (70.0%)	35 (24.3%)	282 (91.3%)	<0.001
Glaucoma	47 (10.4%)	13 (9.0%)	34 (11.0%)	0.634
Retinal detachment	17 (3.8%)	2 (1.4%)	15 (4.9%)	0.123
Diabetes mellitus	175 (38.6%)	80 (55.6%)	95 (30.7%)	<0.001
Liver cirrhosis	16 (3.8%)	8 (5.6%)	8 (2.6%)	0.187
Hypertension	199 (44.0%)	71 (49.3%)	128 (41.4%)	0.149
Cancer	37 (8.2%)	19 (13.2%)	18 (5.8%)	0.013
End-stage renal disease	38 (8.4%)	21 (14.6%)	17 (5.5%)	0.002
Cardiovascular disease	33 (7.3%)	12 (8.3%)	21 (6.8%)	0.695
Bedridden status	25 (5.5%)	18 (12.5%)	7 (2.3%)	<0.001
Autoimmune disorders	13 (2.9%)	6 (4.2%)	7 (2.3%)	0.920
Chronic obstructive pulmonary disease	13 (2.9%)	3 (2.1%)	10 (3.2%)	0.364
Admission (n, %)	363 (80.1%)	110 (76.4%)	253 (81.9%)	0.216
Treatment (n, %)				
Intravitreal antibiotic injection	410 (90.5%)	129 (89.6%)	281 (90.94%)	0.775
Systemic antibiotics	125 (27.6%)	92 (63.9%)	33 (10.68%)	<0.001
Surgery				
*Vitrectomy	180 (38.4%)	28 (17.5%)	152 (49.2%)	<0.001
Evisceration	37 (8.2%)	20 (13.9%)	17 (5.5%)	0.004
Mortality (n, %)	4 (0.9%)	4 (2.7%)	0 (0.0%)	1.000

**: analyzed by individual eye. SD: standard deviation.*

Table 2 presents with disease presentation. The most common symptom was blurry vision (94.3%), followed by red eye (88.7%) and ocular pain (74.8%). In terms of laboratory examinations, the average white blood cell (WBC) count was 10.85 × $10^3/\mu$L, C-reactive protein (CRP) 58.8 mg/L, creatinine 1.58 mg/dL, hemoglobin 12.51 g/dL, and serum glucose 163 mg/dL. The endogenous group, compared with exogenous group, has higher triage level, poorer conscious level, greater proportion of bilateral involvement, fever, ocular swelling, underlying comorbidities (diabetes mellitus, ESRD or bedridden status), and remote infection focuses. Out of the 453 individuals included in the study, 97 patients (21.4%) exhibited detectable infections outside the eyes. The primary source of these infections was found to be bloodstream-related, which encompassed conditions like bacteremia, septic emboli, and infections associated with catheters. Other infection origins include solid organ abscesses, bone and soft tissue infections, urinary tract infections, pneumonia, empyema, meningitis, cardiovascular system infections, otorhinolaryngological infections, alimentary tract infections and vaginitis.

In terms of patient outcomes, 180 patients (38.4%) underwent vitrectomy, 37 (8.2%) underwent evisceration, and unfortunately, 4 patients (0.9%) did not survive. According our institution's policy, endophthalmitis patients underwent

TABLE 2. Disease characteristics.

	Overall	Endogenous	Exogenous	*p*-value
Glascow coma scale <15 (n, %)	31 (6.8%)	22 (15.3%)	9 (2.9%)	<0.001
Symptom duration (d) (Mean ± SD)	5.91 ± 10.74	7.81 ± 9.72	5.03 ± 11.09	0.007
Eye(s) involved (n, %)				
Right eye	200 (44.2%)	57 (39.6%)	143 (46.3%)	<0.001
Left eye	237 (52.3%)	71 (49.3%)	166 (53.7%)	
Both eyes	16 (3.5%)	16 (11.1%)	0 (0.0%)	
Initial visual acuity* (Mean ± SD)	2.23 ± 0.66	2.32 ± 0.66	2.19 ± 0.66	0.043
Clinical presentation (n, %)				
Fever	54 (11.9%)	45 (31.2%)	9 (2.9%)	<0.001
Blurry vision	427 (94.3%)	130 (90.3%)	297 (96.1%)	0.023
Red eye	402 (88.7%)	130 (90.3%)	272 (88.0%)	0.585
Ocular pain	339 (74.8%)	93 (64.6%)	246 (79.6%)	0.001
Tearing	100 (22.1%)	21 (14.6%)	79 (25.6%)	0.012
Foreign body sensation	59 (13.0%)	14 (9.7%)	45 (14.6%)	0.202
Ocular discharge	100 (22.0%)	43 (29.9%)	57 (18.5%)	0.009
Ocular swelling	129 (28.5%)	56 (38.9%)	73 (23.6%)	0.001
Headache	26 (5.7%)	9 (6.3%)	17 (5.5%)	0.919
Corneal ulcer	99 (21.9%)	40 (27.8%)	59 (19.1%)	0.050
Other infection site(s)	97 (21.4%)	87 (60.4%)	10 (3.2%)	<0.001
Laboratory exam (Mean ± SD)				
White blood cell count ($10^3/\mu$L)	10.85 ± 4604.09	11.63 ± 5286.21	10.10 ± 3694.11	0.007
C-reactive protein (mg/L)	58.80 ± 78.32	88.61 ± 90.20	21.54 ± 34.20	<0.001
Creatinine (mg/dL)	1.58 ± 2.11	1.55 ± 1.75	1.61 ± 2.40	0.817
Hemoglobin (g/dL)	12.51 ± 2.37	11.59 ± 2.29	13.39 ± 2.12	<0.001
Serum glucose (mg/dL)	163.59 ± 81.47	181.84 ± 92.88	144.92 ± 63.10	0.003
Blood culture positive (n, %)	32 (7.1%)	30 (20.83%)	2 (0.6%)	<0.001
Vitreous/aqueous culture positive* (n, %)	257 (54.8%)	83 (51.9%)	174 (56.3%)	0.414
Pathogen* (n, % of culture positive eyes)				
Gram-positive bacteria	90 (35.0%)	15 (18.1%)	75 (43.1%)	<0.001
Gram-negative bacteria	69 (26.9%)	33 (39.8%)	36 (20.7%)	
Fungus	25 (9.7%)	13 (15.7%)	12 (6.9%)	
Multiple bacteria	36 (14.0%)	11 (13.3%)	25 (14.4%)	
Multiple fungus	3 (1.2%)	0 (0.0%)	3 (1.7%)	
Bacteria and fungus	34 (13.2%)	11 (13.3%)	23 (13.2%)	

**: analyzed by individual eye. SD: standard deviation.*

evisceration rather than enucleation, as the former provides better cosmetic outcome. Of 37 evisceration cases, 13 were classified as primary (5 endogenous, 8 exogenous) based on emergency surgery within 24–48 hours of presentation. The remaining 24 cases, comprising 15 cases of endogenous origin and 9 cases of exogenous origin, underwent secondary evisceration between 3 days and over a month after their visit to the ED. The percentage of patients who required evisceration was notably higher in the endogenous endophthalmitis group (13.9%) compared to the exogenous endophthalmitis group (5.5%). Moreover, the endogenous group exhibited a significantly higher rate of positive blood cultures (20.1% *vs.* 0.6%), while the exogenous group showed a slightly elevated rate of positive vitreous/aqueous cultures (56.3% *vs.* 52%).

Table 3 demonstrates the blood and vitreous/aqueous culture results. In the endogenous group, 109 patients (75.7%) underwent blood cultures, and 137 eyes (85.6%) received vitreous or aqueous cultures. In the exogenous group, 56 patients (18.1%) underwent blood cultures, and 294 eyes (95.1%) received vitreous or aqueous cultures. Blood culture was positive in 18.8% of cases, while vitreous or aqueous culture was positive in 59.6% of cases. The most commonly identified

TABLE 3. Summary of the culture results (proportion of culture positive cases).

Blood Culture	Endogenous (n = 109)			Exogenous (n = 56)	
	Pathogen	Count (%)		Pathogen	Count (%)
1st	*Klebsiella pneumoniae*	10 (34.5%)	1st	*Staphylococcus aureus*	1 (50.0%)
2nd	*Staphylococcus aureus*	6 (20.7%)	1st	*Staphylococcus caprae*	1 (50.0%)
3rd	*Group B Streptococcus*	3 (10.3%)			
4th	*Staphylococcus caprae*	2 (6.9%)			
	Escherichia coli	2 (6.9%)			
	Staphylococcus capitis	2 (6.9%)			
	Total	29 (100.0%)		Total	2 (100.0%)
Vitreous/aqueous Culture	Endogenous (n = 137)			Exogenous (n = 294)	
	Pathogen	Count (%)		Pathogen	Count (%)
1st	*Klebsiella pneumoniae*	17 (20.5%)	1st	*Staphylococcus epidermidis*	41 (23.6%)
2nd	*Pseudomonas aeruginosa*	14 (16.9%)	2nd	*Pseudomonas aeruginosa*	21 (12.1%)
3rd	*Staphylococcus epidermidis*	6 (7.2%)	3rd	*Enterococcus faecalis*	15 (8.6%)
3rd	*Staphylococcus aureus*	6 (7.2%)	4th	*Staphylococcus aureus*	9 (3.3%)
5th	*Penicillium*	5 (6.0%)	5th	*Penicillium*	8 (4.6%)
6th	*Group B streptococcus*	4 (4.8%)	6th	*Streptococcus pneumoniae*	6 (3.5%)
6th	*Chrysonilia*	4 (4.8%)	6th	*Cladosporium*	6 (3.5%)
8th	*Aspergillus*	3 (3.6%)	6th	*Aspergillus*	6 (3.5%)
	Total	83 (100.0%)		Total	174 (100.0%)
Pathogen by Category	Endogenous (n = 83)			Exogenous (n = 174)	
	Pathogen	Count (%)		Pathogen	Count (%)
1st	Gram-negative bacteria	33 (39.8%)	1st	Gram-positive bacteria	75 (43.1%)
2nd	Gram-positive bacteria	15 (18.1%)	2nd	Gram-negative bacteria	36 (20.7%)
3rd	Mono-fungal	13 (15.7%)	3rd	Multi-bacterial	25 (14.4%)
4th	Multi-bacterial	11 (13.3%)	4th	Bacterial and fungal	23 (13.2%)
4th	Bacterial and fungal	11 (13.3%)	5th	Mono-fungal	12 (6.9%)
6th	Multi-fungal	0 (0.0%)	6th	Multi-fungal	3 (1.7%)

intraocular pathogens for endogenous and exogenous endophthalmitis were *Klebsiella pneumoniae* (20.5%) and *Staphylococcus epidermidis* (23.6%), respectively. In the exogenous group, Gram-positive bacteria ranked first (43.1%), followed by Gram-negative bacteria (20.7%), and multi-bacterial (14.4%). Conversely, the endogenous group exhibited a higher prevalence of Gram-negative bacteria (39.8%) compared to Gram-positive bacteria (18.1%). Furthermore, fungal infections were more prevalent in the endogenous group (15.7%) than in the exogenous group (8.5%). In terms of multi-bacterial or mixed bacterial fungal infections, both groups showed similar rates. The predominant pathogen identified in blood cultures overall was *Klebsiella pneumoniae* (6.1%), followed by *Staphylococcus aureus* (4.2%).

Table 4 shows multivariate logistic regression analysis of risk factors for evisceration in endophthalmitis patients. The most significant risk factors for evisceration in the endogenous group were impaired initial VA (odds ratio (OR) = 39.436, $p = 0.0019$) and corneal ulcer (OR = 5.143, $p = 0.0012$). In the exogenous group, these two risk factors were also present, along with ocular discharge (OR = 7.447, $p = 0.0001$) and ocular swelling (OR = 18.349, $p < 0.0001$). Age (OR = 1.046, $p = 0.0128$), foreign body sensation (OR = 4.259, $p = 0.0198$), hypertension (OR = 5.018, $p = 0.006$) and glaucoma (OR = 4.834, $p = 0.0128$) are statistically significant risk factors of evisceration for endogenous endophthalmitis, while fever (OR = 10.214, $p = 0.0022$), cardiovascular disease (OR = 4.977, $p = 0.0101$) are independent predictors for the exogenous group. Undergoing a vitrectomy seems to serve as a highly effective safeguard against evisceration in the exogenous group. The various types of pathogens did not demonstrate any substantial association with the risk of evisceration.

TABLE 4. Analysis of risk factors for evisceration.

	Endogenous			Exogenous		
Variable	Odds Ratio	95% CI	*p*-value	Odds Ratio	95% CI	*p*-value
Age	1.046	(1.010, 1.084)	0.0128	1.020	(0.983, 1.057)	0.2965
Gender (Male)	1.146	(0.444, 2.959)	0.7785	1.316	(0.474, 3.654)	0.5987
Mean arterial pressure	0.992	(0.967, 1.018)	0.5335	1.005	(0.980, 1.030)	0.7115
Glascow coma scale <15	5.238	(1.827, 15.020)	0.0021	17.662	(4.237, 73.612)	<0.0001
Initial symptoms						
Initial visual acuity	39.436	(3.886, 400.216)	0.0019	275.284	(22.561, ∞)	<0.0001
Fever	0.345	(0.096, 1.242)	0.1035	10.214	(2.311, 45.147)	0.0022
Red eye	0.964	(0.199, 4.667)	0.9636	0.615	(0.168, 2.250)	0.4626
Ocular pain	0.626	(0.241, 1.629)	0.3370	0.445	(0.158, 1.253)	0.1252
Foreign body sensation	4.259	(1.259, 14.405)	0.0198	0.353	(0.046, 2.724)	0.3177
Ocular discharge	2.758	(1.053, 7.222)	0.0389	7.447	(2.699, 20.550)	0.0001
Ocular swelling	2.727	(1.037, 7.175)	0.0421	18.349	(5.106, 65.941)	<0.0001
Corneal ulcer	5.143	(1.914, 13.822)	0.0012	17.380	(5.427, 55.666)	<0.0001
Previous Medical History						
Previous ocular surgery	0.750	(0.233, 2.413)	0.6296	0.196	(0.063, 0.605)	0.0047
Diabetes mellitus	0.481	(0.184, 1.261)	0.1369	0.935	(0.320, 2.733)	0.9025
Hypertension	5.018	(1.587, 15.872)	0.0060	2.485	(0.870, 6.945)	0.0898
Cancer	1.191	(0.313, 4.526)	0.7973	1.011	(0.126, 8.083)	0.9917
End stage renal disease	0.614	(0.132, 2.865)	0.5349	1.078	(0.134, 8.649)	0.9435
Cardiovascular disease	0.541	(0.066, 4.433)	0.5668	4.977	(1.465, 16.911)	0.0101
Glaucoma history	4.834	(1.399, 16.705)	0.0128	2.687	(0.824, 8.768)	0.1014
Received Vitrectomy	0.812	(0.221, 2.983)	0.7535	0.058	(0.008, 0.446)	0.0062
Positive Ocular culture	4.358	(1.387, 13.692)	0.0117	6.273	(1.409, 27.926)	0.0159
Culture Pathogen						
Gram-positive bacteria	2.769	(0.459, 16.706)	0.9228	2.771	(0.453, 16.965)	0.9491
Gram-negative bacteria	7.826	(2.240, 27.342)	0.8885	22.167	(4.534, 108.379)	0.9022
Mono-fungal	1.500	(0.154, 14.591)	0.9431	<0.001	-	0.9523
Multi-bacterial	6.750	(1.276, 35.701)	0.8934	5.783	(0.775, 43.128)	0.9325
Multi-fungal*	-	-	-	<0.001	-	0.9720
Bacterial-fungal	<0.001	-	0.9000	<0.001	(0.263, 34.766)	0.9741

**Endogenous group: no multi-fungal cases. CI: confidence interval.*

4. Discussion

This 11-year retrospective study (2012–2022), conducted at a tertiary medical center in Taiwan, aimed to analyze the clinical findings, risk factors, microbiology, and prognosis of both endogenous and exogenous endophthalmitis in ED setting. Although there have been investigations into triggering factors, manifestations, prevalent and uncommon pathogens, treatment approaches, and predictive elements of visual results in hospital settings, there is a dearth of research concentrating on endophthalmitis specifically in the ED environment. Our study is the first to investigate the clinical features and prognostic factors of both endogenous and exogenous endophthalmitis specifically in the ED setting.

In contrast to the exogenous group, patients in the endogenous group typically exhibit a higher triage level and lower conscious level upon initial presentation at the Emergency Department. These characteristics suggest a higher likelihood of concurrent systemic infection with unstable hemodynamics. A cross-sectional study involving 6400 ED patients diagnosed with endogenous endophthalmitis in the United States identified various factors linked to mortality, such as immunodeficiency, heart failure, hepatic infection, and liver cirrhosis [22]. In our study, the endogenous type of endophthalmitis is more frequently associated with bilateral involvement, fever, periorbital swelling, underlying comorbidities (such as diabetes mellitus, end-stage renal disease, impaired neurological function, or bedridden status), and distant infection sources. The results from the laboratory revealed increased systemic inflammation

in endogenous cases, characterized by raised levels of white blood cells, C-reactive protein, and serum glucose ($p < 0.001$). Positive blood cultures were significantly more frequent in endogenous cases ($p < 0.001$). Pathogen analysis showed that endogenous infections were more commonly associated with Gram-negative bacteria and fungi, while exogenous infections predominantly involved Gram-positive bacteria ($p < 0.001$). The results highlight the systemic characteristics of endogenous infections in contrast to the localized aspects of exogenous cases. Research conducted earlier has indicated that endogenous endophthalmitis is associated with a worse visual prognosis when compared to exogenous endophthalmitis [8–11]. Our study supports this finding by revealing a higher rate of evisceration in the endogenous group ($p = 0.004$). The mortality rate is 2.8% in the endogenous group, compared to zero deaths in the exogenous group. Additionally, the exogenous group has a significantly higher rate of vitrectomy (49.2% *vs*. 17.5%) but a lower rate of evisceration (5.5% *vs*. 13.9%).

In our study, the most common pathogens for endogenous and exogenous endophthalmitis are *Klebsiella pneumoniae* and *Staphylococcus epidermidis*, respectively. *Pseudomonas aeruginosa* ranks second in both categories. According to a meta-analysis conducted by Naik *et al*. [23], a review of 20 studies revealed that the occurrence rate of culture-negative endophthalmitis varied between 40% and 70%. On the contrary, our findings reveal that the rates of culture-negative results in vitreous or aqueous samples are 38.7% for endogenous endophthalmitis and 40.8% for exogenous endophthalmitis. Studies conducted earlier suggest that fungal endophthalmitis typically exhibits a more favorable visual prognosis compared to bacterial endophthalmitis [13]. However, in our study, evisceration rates did not differ significantly between bacterial and fungal infections.

In terms of endogenous endophthalmitis, the pathogen is highly geographically specific. In Southeast Asia, *Klebsiella pneumoniae* is a predominant pathogen for both liver abscesses and endogenous endophthalmitis, particularly in diabetic patients [13, 17, 18]. According to research carried out in Malaysia, *Klebsiella* species are responsible for approximately 80%–90% of culture-positive cases of endogenous endophthalmitis [6]. Conversely, a study in New Zealand revealed that Gram-positive bacteria were the predominant pathogens in endogenous endophthalmitis, with fungi and Gram-negative bacteria following closely [4]. Our study aligns with prior findings from Asia, indicating a stable pathogen prevalence trend over numerous decades, despite the influence of Westernized living habits and the impact of the COVID-19 pandemic on contemporary Asian societies.

In exogenous endophthalmitis, most of which is surgery-related, our study identified *Staphylococcus epidermidis* as the most common pathogen, consistent with previous literature [12, 24]. However, our results contrast with a separate study conducted in Taiwan by Cheng *et al*. [25], who found that *Pseudomonas aeruginosa* was the predominant bacterial strain in cases of acute postoperative endophthalmitis. In this study, *Enterococcus faecalis* ranked as the third most common bacterial species in exogenous endophthalmitis. This finding aligns with trends reported in a 2024 Taiwanese study on acute postoperative exogenous endophthalmitis [26], although the proportion in our study (8.62%) is markedly lower than the reported 20%–38%. The discrepancy may be attributed to the inclusion of non-postoperative exogenous endophthalmitis in our study, potentially lowering the proportion of *Enterococcus*. It also hints at potential temporal variations within the identical geographical area. Unlike highly virulent pathogens such as *Staphylococcus aureus*, *Bacillus*, *Streptococcus*, *Pseudomonas* and *Escherichia coli* [2, 14, 27], *Staphylococcus epidermidis* is less pathogenic. This likely explains the better visual prognosis in the exogenous group compared to the endogenous group.

Research conducted in the past has pointed out that *Candida* species are the predominant fungal isolates in endogenous endophthalmitis, representing as high as 78% of cases, suggesting a higher prevalence of yeasts compared to molds [15]. In contrast, our study found *Penicillium* as the most frequently cultured fungus, followed by *Chrysonilia*, *Candida* and *Aspergillus*. For exogenous endophthalmitis, *Penicillium* was also the most common, with *Cladosporium* and *Aspergillus* ranking second and third, respectively. This observation could be attributed to the challenges in cultivating *Candida* species or to regional differences. In general, the incidence of evisceration does not show a correlation with the quantity of pathogen species present in either the internal or external categories. Our assertion is that the virulence of the predominant pathogen, rather than the quantity of concurrent pathogen species, plays a pivotal role in conditions that pose a threat to vision.

In the current study, evisceration was used as an indicator of the worst visual prognosis. One possible substitute endpoint that could have been considered was the reduction in VA. However, it was not chosen because of its lack of precision, which may be impacted by the timing and manner of assessment, along with the potential for data truncation throughout the observation period. Important factors associated with the risk of evisceration in endophthalmitis encompass changes in awareness (Glasgow Coma Scale <15), initial VA reduction, eye discharge, swelling around the eyes, corneal ulceration, and positive results from ocular culture tests. This finding underscores the need for heightened vigilance in assessing patients with prominent ocular surface manifestations, particularly in those whose VA cannot be assessed due to altered mental status. Patients with a history of ocular surgery are less likely to require evisceration. This observation could be attributed to the increased incidence of exogenous endophthalmitis cases in this research, which typically show a more favorable visual prognosis in comparison to endogenous cases. Opting for early vitrectomy (within 24 hours) has been linked to improved visual results and a reduced risk of subsequent evisceration, aligning with conclusions drawn from earlier research [26, 28–30]. Based on our study, a foreign body sensation may suggest a potential association with an increased risk of evisceration in patients with endogenous endophthalmitis. Similarly, fever could be considered a concerning indicator in cases of exogenous endophthalmitis. While fever is not frequently seen in cases of exogenous endophthalmitis, it should be given significant consideration if detected. Our study has identified a strong association between reduced initial visual acuity [14, 30, 31], which is a known predictor of unfavorable visual

prognosis in both endogenous and exogenous endophthalmitis, and the likelihood of requiring evisceration.

The strength of this study lies in its focus on emergency department patients as the research subjects and its comparison of the clinical characteristics and prognosis between endogenous and exogenous endophthalmitis groups, which has been rarely addressed in previous literature. However, being a study conducted at a single center, our findings may predominantly represent the demographics of the specific region and may not be universally applicable to other contexts. The restricted sample size in our research might lead to selection bias and diminish the statistical efficacy. Moreover, employing evisceration as the endpoint of our investigation may not serve as a responsive indicator to comprehensively encompass the fundamental elements of clinical and visual outlook. However, it remains an important indicator of severe ocular outcomes.

5. Conclusions

When patients exhibit noticeable ophthalmological symptoms like blurred vision, redness in the eyes, and eye pain, it is crucial for Emergency Department physicians to promptly rule out the possibility of acute endophthalmitis. Particularly, patients who have had recent eye surgeries or who also have concurrent conditions such as bacteremia, urinary tract infections, or liver abscesses should receive special consideration. Despite early and aggressive treatment in the ED, the visual prognosis for endogenous endophthalmitis remains poorer compared to exogenous cases.

ABBREVIATIONS

ED, emergency department; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; ESRD, end-stage renal disease; VA, visual acuity; BCVA, best corrected visual acuity; logMAR, logarithm of the minimum angle of resolution; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; TTAS, Taiwan Triage and Acuity Scale; SD, standard deviation; CF, counting fingers; HM, hand motion; LS, light perception; NLS, no light perception; IOL, intraocular lens; TPPV, trans pars plana vitrectomy; WBC, white blood cell; OR, odds ratio; CI, confidence interval.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

PL and HFY—conceived and designed the study, undertook data acquisition, carried out data analysis and data interpretation. CHC—provided statistical expertise. PL—wrote the manuscript draft. HFY, JWY and CJS—undertook critical revision of the manuscript for important intellectual content. All authors participated and contributed to the critical revision of the manuscript and gave final approval of version submitted for publication.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Chang Gung Memorial hospital, Taiwan (IRB No. 202300051B0). The requirement for informed consent was waived by the aforementioned institution/IRB due to the retrospective nature of the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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