# The Importance of Comorbidity with Low Culture Positivity in Patients with Endophthalmitis

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## ABSTRACT

**Purpose:** This paper aims to assess the clinical outcomes in patients with endophthalmitis. The effect of comorbidities on hospitalization time, treatment management, and vision gain are also examined.

**Methods:** This retrospective study includes 40 eyes from 40 patients. Endophthalmitis was divided into two groups, exogenous and endogenous. Culture results, comorbidities, hospitalization times, treatment management, and vision gain were examined. Patients with diabetes mellitus(DM) and/or hypertension(HT) were put in Comorbidity Group 1(CG1). Patients with systemic comorbidities (inflammatory or non-inflammatory comorbidities) in addition to DM and/or HT were put in Comorbidity Group 2(CG2).

**Results:** Endophthalmitis was of exogenous origin in 25 eyes and endogenous origin in 15 eyes. The outcomes of exogenous and endogenous groups according to various parameters are as follows: Rates of culture positivity (16.0%/20.0%), pars plana vitrectomy(PPV) (56.0%/86.7%), intravitreal injection(IVI) (44.0%/13.3%), rePPV(4.0%/20.0%), two IVIs (52.0%/6.7%), more than two IVIs (20.0%/66.7%). In the exogenous group, the mean hospitalization time in CG1 and CG2 was 7.3 ± 2.5 and 10.5 ± 2.8 days, respectively. The mean number of IVIs in CG2 was 28% more than CG1. In the endogenous group, mean hospitalization time in CG1 and CG2 was 14.3 ± 10.1 and 22.0 ± 6.7 days, respectively. The mean number of IVIs in CG2 was 86% more than CG1.

**Conclusions**: The culture and antibiogram findings were low; therefore, we increased surgical procedures and repeated IVI. This study showed that patients with systemic comorbidities (inflammatory or non-inflammatory) in addition to DM and/or HT experienced longer hospitalization times and needed more IVI.


**Keywords:** Comorbidity, culture, endophthalmitis, hospitalization time

## INTRODUCTION

Endophthalmitis is sight-threatening inflammation of intraocular spaces. It is classified as exogenous or endogenous, depending on the route of infection.[1,2] Endogenous endophthalmitis is less common and occurs in 2%–40% of all endophthalmitis cases.[3,4]

Culture positivity is defined as identifying a causative agent and applying the antimicrobial agent to which the causative agent is most sensitive. A precise microbiological diagnosis allows the accurate treatment of endophthalmitis. However, due to the limitations of microbiological methods in detecting pathogens, clinicians may encounter negative results.

Comorbidity is a disease or condition that coexists with a disease but is often independent of it. Previous studies have demonstrated that comorbidity has been associated with oxidative stress/inflammation, leading to ocular, systemic, and psychiatric diseases or exacerbating diseases.[5–7]

This study aimed to examine culture results, comorbidities, hospitalization time, treatment, and vision gain of the patients with endogenous or exogenous endophthalmitis. In addition, the effect of culture results and comorbidities on hospitalization time, treatment management, and vision gain was examined.

## MATERIALS AND METHODS

40 patients who had been diagnosed with endophthalmitis between March 2016 - January 2021 in the ophthalmology clinic of Istanbul Training and Research Hospital were analyzed retrospectively. Istanbul Training and Research

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Hospital Clinical Trials Ethics Committee approved this retrospective, single-center case series. The study adhered to the tenets of the Declaration of Helsinki.

Endophthalmitis cases were identified, and patients' charts were reviewed. Patients' culture results, systemic comorbidities, hospitalization time, and endophthalmitis treatment were taken from their medical records. The patients' initial and final visual acuity (VA) was recorded using a decimal VA card. Decimal VA values were converted to *logarithm of the minimum angle of resolution* (logMAR) VA values. As in prior studies,[8,9] VA values assigned to hand motion, light perception, and no light perception were 0.5/200, 0.25/200, and 0.125/200; their logMAR values are equivalent to 2.6, 2.9, and 3.2, respectively. Vision gain was calculated in logMAR by subtracting the initial VA from the final VA. The sample was divided into two; patients with exogenous endophthalmitis (Group 1; *n*:25) and endogenous endophthalmitis (Group 2; *n*:15).

### Inclusion and exclusion criteria

Patients with exogenous and endogenous endophthalmitis were included in this study. Traumatic endophthalmitis cases and those associated with scleritis or keratitis were excluded. These patients' VA is generally decreased; they have pain and show signs of intraocular inflammation on examination (generally ≥ 2+ anterior segment cellular reaction and/or posterior segment vitritis). Patients who did not have a vitreous/aqueous culture or were treated with topical steroids without additional interventions were excluded.

### Microbiological techniques

Intraocular samples collected in the operating room from patients under anesthesia were aqueous and vitreous humor obtained by vitreous taps or vitreous biopsies. The samples were processed within half an hour by first inoculating them onto culture media and then a direct smear examination of Gram-stained samples.

The collected samples were cultivated in the operating room in various mediums (Fluid thioglycollate medium, Blood agar, Chocolate agar, Eosin methylene blue agar, and Sabouraud dextrose agar). Gram stain results of vitreous/aqueous cultures were available within 1 day, and culture plates were generally completed within 3–5 days. Blood cultures were also prepared for endogenous cases.

Since PCR analysis for microbial DNA is not available in our institute, PCR could not be performed.

### Endophthalmitis treatment protocol

Suspected endophthalmitis was defined as any case that the examining physician evaluated the clinical status as infection and performed a vitreous/aqueous tap, followed by PPV and/or IVI.

IVI was applied as the primary treatment if the patient's retinal reflex was good at the first clinic visit and their macula, optic disc, and retinal vascular structures could be observed. If the patient's retinal reflex was blurred, and their macula, optic disc, and retinal vascular structures could not be observed, PPV was applied as the primary treatment. The patient's clinical course was closely monitored for 24 h after IVI. If the patient responded to the treatment, IVI was repeated after 48–72 h; otherwise, PPV was performed. Kuhn et al.[10] suggested this management scheme as "complete and early vitrectomy." In addition to IVI or PPV, topical fortified antibiotic drops were prescribed. The drug administered intravitreally was also given as fortified drops. Topical steroids were administered after the patient responded to antibiotic therapy (i.e., when anterior chamber reaction and vitreous condensation decreased). Systemic and intravitreal steroids were not used. Topical cyclopentolate was used for a mydriatic effect. In groups 1 and 2, the systemic antibiotic treatments of all patients were started and maintained by consulting with the infectious diseases department. Intravitreally given drugs were also administered systemically. The patients were discharged after complete regression of anterior and posterior segment findings; patients' recovery time was defined as hospitalization time.

In the surgical procedure, 23-gauge PPV was performed following fibrin/exudate removal from the anterior chamber; then posterior hyaloid was removed, and 1000 centistoke silicone oil was injected. Intravitreal antibiotics and antifungal injections were administered at the end of the vitrectomy surgery.

Endophthalmitis was accepted as culture-positive in the case of a positive Gram stain and/or positive growth was reported on culture plates. Endophthalmitis was considered culture-negative when both the Gram stain and culture plates were negative.

All the patients had DM and/or HT as systemic comorbidities. Patients with DM and/or HT were put in CG1. Patients with systemic comorbidities (inflammatory comorbidity or non-inflammatory comorbidity) in addition to DM and/or HT were put in CG2.

The culture results, comorbidities, hospitalization time, treatment management, and vision gains of the groups were examined. The effect of culture results and comorbidities on hospitalization time, treatment management, and vision gain was analyzed.

### Statistical Analyses

Statistical Package for the Social Sciences (SPSS) version 22.0 was used in statistical analysis. Descriptive statistics are shown as the minimum, maximum, and mean ± standard deviation. Shapiro–Wilk test was used to check normal distribution. As the parameters failed to meet normal distribution, non-parametric tests were used for statistical analysis. Wilcoxon test was used to compare initial and final VA in the groups. Mann-Whitney U test was used to compare CG1 and CG2 in terms of hospitalization time, number of IVIs, and visual gain. Chi-square test was used to compare CG1 and CG2 in terms of primary therapy, PPV requirement, and RePPV requirement. The confidence interval was taken as 95%; therefore, p-values lower than 0.05 indicated a statistically significant difference.

## RESULTS

### Demographic characters

### Group 1 (Exogenous Endophthalmitis)

25/40 eyes with endophthalmitis were of exogenous origin (62.5%). This group was composed of 16 male and 9 female patients, with a mean age of 63.9 ± 12.2 (44–89). The mean onset of signs and symptoms was 21.8 ± 29.0 (1–120) days. The mean follow-up was 13.0 ± 12.3 (1–41) months.

21/25 eyes had acute endophthalmitis (<6 weeks), and 4/25 eyes had chronic endophthalmitis (>6 weeks). Endophthalmitis developed after cataract surgery (phacoemulsification) in 12 eyes, after PPV in 6 eyes, and after IVI in 7 eyes.

Intraoperative complications in surgical procedures were documented in 1/25 eyes (nucleus drop in cataract surgery). There was no intraoperative complication in other surgical procedures.

### Group 2 (Endogenous Endophthalmitis)

There were 15/40 eyes (37.5%) with endogenous endophthalmitis. This group consisted of 12 male and 3 female patients with a mean age of 66.9 ± 12.9 (47–96). The mean follow-up was 6.6 ± 9.0 (1–27) months.

### Findings in Group 1 (Exogenous Endophthalmitis)

#### 1) Culture results

4/25 eyes (16%) had culture positivity: *Stenotrophomonas maltophilia* was observed in two eyes, *Pseudomonas aeruginosa* in one eye and *Bacillus cereus* in one eye.

#### 2) Comorbidity

There were 13 patients in CG1 and 12 patients in CG2. Regarding CG2, chronic obstructive pulmonary disease was observed in 4 patients, coronary artery disease in 2 patients, chronic kidney failure in 2 patients, thrombophlebitis in 1 patient, cholecystitis in 1 patient, chronic pyelonephritis in 1 patient, and asthma in 1 patient. Immunodeficiency (hereditary/acquired) causes were not present in any of the CG2's patients.

#### 3) Hospitalization

The mean hospitalization time was 8.9 ± 3.1 (4–14) days ($n$ = 25). The mean hospitalization time was 7.3 ± 2.5 (4–12) days in CG1 ($n$ = 13) and 10.5 ± 2.8 (6–14) days in CG2 ($n$ = 12). There was a statistically significant difference between the two groups ($p$ = 0.010); CG2's hospitalization time was 43% longer than CG1.

#### 4) Treatment management

21/25 eyes with exogenous endophthalmitis underwent IVI as the primary treatment, whereas 4/25 eyes underwent PPV as the primary treatment. The course of eyes treated with IVI was evaluated for 24 h. PPV was administered to 10 eyes that did not respond to IVI. Overall, 14/25 eyes (56%) underwent PPV and 11/25 eyes (44%) IVI.

7/25 eyes (28%) received one IVI, 13/25 eyes (52%) two IVIs, and 5/25 eyes (20%) more than two IVIs. The mean number of IVIs was 2.08 ± 1.07 (1–5).

8/25 eyes were treated with intravitreal vancomycin (1 mg/0.1 ml), ceftazidime (2.25 mg/0.1 ml), and 17/25 eyes with intravitreal vancomycin (1 mg/0.1 ml), ceftazidime (2.25 mg/0.1 ml), and amphotericin B (5 µg/0.1 ml). After 48–72 h, IVI was repeated if necessary. Intravitreal ciprofloxacin (100 µg/0.1 ml) injections were performed in 2 eyes as *S. Maltophilia,* susceptible to ciprofloxacin, was isolated. Intravitreal ceftazidime (2.25 mg/0.1 ml) injections were performed in 1 eye as *P. Aeruginosa,* susceptible to ceftazidime, was isolated. Intravitreal ciprofloxacin (100 µg/0.1 ml) injections were performed in 1 eye as *B. Cereus,* susceptible to ciprofloxacin, was isolated. 1 eye did not respond adequately to vancomycin (1 mg/0.1 ml), ceftazidime (2.25 mg/0.1 ml), and amphotericin B (5 µg/0.1 ml); therefore, vancomycin (1 mg/0.1 ml), meropenem (500 µg/0.1 ml), and amphotericin B (5 µg/0.1 ml) were administered after consulting the infectious diseases department. Finally, a clinical response was obtained.

Intravitreally given drug was also given systemically as an adjuvant upon consulting the infectious diseases department.

1 eye underwent rePPV (4%), which was a case where the posterior hyaloid could not be removed, which resulted in an incomplete vitrectomy in the first surgery. rePPV was planned for this eye. The posterior hyaloid was removed, and a complete vitrectomy was performed later. *P. aeruginosa* was isolated in this eye.

**5) Visual and anatomical results**

The initial VA was 2.28 ± 0.56 (1–2.9) logMAR, and the final VA was 0.98 ± 0.69 (0–2.6) logMAR. There was a statistically significant difference between the initial and final VA ($p = 0.000$). In 16/25 eyes (64%), the final VA was 0.1 (decimal VA) and got better.

The low VA in 8/9 eyes whose final VA was less than 0.1 (decimal VA) was due to primary diseases besides endophthalmitis. 1/9 eye had severe *P. aeruginosa* endophthalmitis. Phthisis bulbi occurred due to a late complete vitrectomy in this eye. Primary diseases of 8 eyes are shown in **Table 1**.

Overall, no retinal detachment was observed. Phthisis bulbi was observed in 1 eye (*P. aeruginosa* endophthalmitis due to late complete vitrectomy). Evisceration and enucleation were not required.

**6) The effect of culture results**

The effect of culture results on hospitalization time, treatment management, and vision gain could not be evaluated because the number of culture-positive cases was low in Group 1.

**7) Comparison of CG1 and CG2**

There was no statistically significant difference between CG1 and CG2 in primary therapy, PPV requirement, RePPV requirement, number of IVIs, and vision gain in Group 1. However, CG2's hospitalization time was 43% longer than CG1 ($p = 0.010$). The mean number of IVIs in CG2 was 28% more than CG1. The comparison of CG1 and CG2 in Group 1 is shown in detail in **Table 2**.

**Findings in Group 2 (Endogenous Endophthalmitis)**

**1) Culture results**

3/15 eyes (%20) had positive ocular culture. *Candida albicans* were isolated in 2 eyes, and *Aspergillus spp* in 1 eye. None of the patients had positive blood culture.

**Table 1**: *Primary diseases of 8/9 eyes whose final VA was less than 0.1 in Group 1.*

| **Primary Diseases** | n |
|---|---|
| Recurrent retinal detachment vitrectomized | 2 |
| Diabetic retinopathy with optic disc pale and pan photocoagulation | 2 |
| Tractional retinal detachment vitrectomized | 1 |
| Age-related macular degeneration vitrectomized due to subretinal hemorrhage | 1 |
| Bullous keratopathy | 1 |
| Complicated cataract surgery (nucleus drop) | 1 |
| n: Number of eyes | |

**Table 2:** Comparison of CG1 and CG2 in terms of hospitalization time, primary therapy, PPV requirement, RePPV requirement, number of IVIs, and vision gain in Group 1.

| **Parameters** | **Groups** | **CG1** | **CG2** | **p** |
|---|---|---|---|---|
| **Hospitalization time(days)** | **Exogenous** | 7.3±2.5(4-12) | 10.5±2.8(6-14) | **p* = 0.010** |
| **Primary therapy** | **Exogenous** | PPV (n:2)<br>IVI(n:11) | PPV(n:2)<br>IVI(n:9) | p** = 0.930 |
| **PPV requirement** | **Exogenous** | PPV(n:6)<br>IVI(n:7) | PPV(n:8)<br>IVI(n:4) | p** = 0,302 |
| **RePPV requirement** | **Exogenous** | n:1 | n:0 | P** =0.327 |
| **Number of IVIs** | **Exogenous** | 1.69± 0,75(1-3) | 2.17± 1,46(1-5) | p* = 0.650 |
| **Vision gain (logMAR)** | **Exogenous** | -1.23± 0,58 | -1.37±0,87 | p* = 0.936 |

p*: Mann-Whitney U test, p**: Chi-square test, n: Number of eyes, IVI: Intravitreal injection, PPV: Pars plana vitrectomy, RePPV:Repeat pars plana vitrectomy, CG1: Comorbidity group 1, CG2: Comorbidity group 2

**2) Comorbidity**

There were 3 patients in CG1 and 12 in CG2. Regarding CG2, chronic kidney failure was observed in 4 patients, chronic pyelonephritis in 3 patients, rectal cancer (immunodeficiency) in 1 patient, hypothyroidism in 1 patient, arrhythmia in 1 patient, prosthetic heart valve in 1 patient, and coronary artery disease in 1 patient.

**3) Hospitalization**

The mean hospitalization time was 20.4 ± 7.8 (8–30) days in Group 2 ($n$ = 15). The mean hospitalization time was 14.3 ± 10.1 (8–26) days in CG1 ($n$ = 3) and 22.0 ± 6.7 (12–30) days in CG2 ($n$ = 12). The difference was not statistically significant (p = 0.180). However, hospitalization time in CG2 was 53% longer than CG1.

In overall ($n$ = 40), the mean hospitalization time was 8.6 ± 5.1 (4–26) days in CG1 ($n$ = 16) and 16.2 ± 7.7 (6–30) days in CG2 ($n$ = 24). There was a statistically significant difference between the two groups ($p$ = 0.000). Hospitalization time in CG2 was 88% longer than CG1. The mean hospitalization times of the groups are shown in **Table 3.**

**4) Treatment management**

5/15 eyes with endogenous endophthalmitis underwent IVI as primary treatment, 10/15 eyes underwent PPV as primary treatment. The course of eyes treated with IVI was evaluated for 24 h. PPV was administered to 3 eyes that did not respond to IVI. A total of 13/15 eyes (86.7%) underwent PPV and 2/15 eyes (13.3%) IVI.

4/15 eyes (26.7%) received one IVI, 1/15 eye (6.7%) two IVIs, and 10/15 eyes (66.7%) more than two IVIs. The mean number of IVIs was 2.80 ± 1.37 (1–5).

All eyes were treated with intravitreal vancomycin (1 mg/0.1 ml), ceftazidime (2.25 mg/0.1 ml), amphotericin B (5 µg/0.1 ml). After 48-72 h, IVI was repeated if necessary. Intravitreal amphotericin B (5 µg/0.1 ml) injections were performed in 2 eyes as *C. albicans,* susceptible to amphotericin B, were isolated. Intravitreal voriconazole (100 µg/0.1 ml) injections were performed in 1 eye as *Aspergillus spp,* susceptible to voriconazole B, was isolated. 1 eye did not respond adequately to vancomycin (1 mg/0.1 ml), ceftazidime (2.25 mg/0.1 ml), and amphotericin B (5 µg/0.1 ml); therefore vancomycin (1 mg/0.1 ml), meropenem (500 µg/0.1 ml), and amphotericin B (5 µg/0.1 ml) were administered by consulting to the infectious diseases department. Finally, a clinical response was obtained.

Intravitreally given drug was also given systemically as an adjuvant upon consulting the infectious diseases department.

3/15 eyes (20%) underwent rePPV. These eyes have given an inadequate response to PPV and IVI.

**5) Visual and anatomical results**

The initial VA was 2.13 ± 0.8 (0.1–3.2) logMAR, and the final VA was 1.32 ± 1.26 (0.1–3.2) logMAR. There was a statistically significant difference between initial and final VA ($p$ = 0.018). In 8/15 eyes (53.3%), the final VA was 0.1 (decimal VA) and got better.

There was no retinal detachment and phthisis. Evisceration and enucleation were not required in any eye.

**6) The effect of culture results**

The effect of culture results on hospitalization time, treatment management, and vision gain could not be evaluated because the number of culture-positive cases was low in Group 2.

**7) Comparison of CG1 and CG2**

There was no statistically significant difference between CG1 and CG2 in terms of hospitalization time, primary therapy, PPV requirement, RePPV requirement, number of IVIs, and vision gain in Group 2. However, hospitalization time in CG2 was 53% longer than CG1. Also, the mean number of IVIs in CG2 was 86% more than CG1. The comparison of CG1 and CG2 in Group 2 is shown in detail in **Table 4**.

**Table 3:** *Mean hospitalization times of Group 1 (exogenous-origin), Group 2 (endogenous-origin), and overall.*

| | CG1 hospitalization time (days) | CG2 hospitalization time (days) | Difference | p |
|---|---|---|---|---|
| **Exogenous group n: 25** | 7.3 ± 2.5 (4-12) n:13 | 10.5 ± 2.8 (6-14) n:12 | %43 | **p* = 0.010** |
| **Endogenous group n: 15** | 14.3 ± 10.1 (8-26) n:3 | 22.0 ± 6.7 (12-30) n:12 | %53 | p* = 0.180 |
| **Overall n: 40** | 8.6 ± 5.1 (4-26) n:16 | 16.2 ± 7.7 (6-30) n:24 | %88 | **p* = 0.000** |

p*: Mann-Whitney U test, n: Number of patients, CG1: Comorbidity group 1, CG2: Comorbidity group 2, Difference: The difference in percentage between the CG1 and CG2

**Table 4:** Comparison of CG1 and CG2 in terms of hospitalization time, primary therapy, PPV requirement, RePPV requirement, number of IVIs, and vision gain in Group 2

| Parameters | Groups | CG1 | CG2 | p |
|---|---|---|---|---|
| **Hospitalization time(days)** | **Endogenous** | 14.3±10.1(8-26) | 22.0±6.79(12-30) | p* = 0.180 |
| **Primary therapy** | **Endogenous** | PPV(n:2)<br>IVI(n:1) | PPV(n:8)<br>IVI(n:4) | p** = 1.000 |
| **PPV requirement** | **Endogenous** | PPV(n:3) | PPV(n:10)<br>IVI(n:2) | p** = 0.448 |
| **RePPV requirement** | **Endogenous** | n:1 | n:2 | P** =0.519 |
| **Number of IVIs** | **Endogenous** | 1.66±1.15(1-3) | 3.08± 1.31(1-5) | p*= 0.136 |
| **Vision gain (logMAR)** | **Endogenous** | -0.43± 0.80 | -0.90±1.12 | p* = 0.536 |

p*: Mann-Whitney U test, p**: Chi-square test, n: Number of eyes, IVI: Intravitreal injection, PPV: Pars plana vitrectomy, RePPV:Repeat pars plana vitrectomy, CG1: Comorbidity group 1, CG2: Comorbidity group 2

## DIRCUSSION

In this study, the clinical outcomes of endophthalmitis were evaluated. The effect of various comorbidities on hospitalization, treatment management, and vision gain was also analyzed.

### Group 1 (exogenous endophthalmitis)

The culture positivity rate in large series was reported to be 45%–75%,[11–16]. This rate was increased by polymerase chain reaction (PCR) in exogenous endophthalmitis.[14] 4/25 eyes (16%) had culture positivity. On the other hand, there are several common causes of culture- negativity. Identification of the causal pathogen from culture media may be limited due to the early administration of broad-spectrum or prophylactic antimicrobial drugs and organisms that are fastidious or slow-growing. Also, the differences in methods of taking culture samples may affect the culture results. Aqueous and vitreous samples were obtained in our study, such as the culture sample in the Endophthalmitis Vitrectomy Study (EVS).[17] The samples were placed on culture mediums (Fluid thioglycollate medium, Blood agar, Chocolate agar, Eosin methylene blue agar, and Sabouraud dextrose agar) in the operating room. Despite this, our culture-positive rate was low compared with those described in the literature.[11–16]

In a multicenter study on postoperative endophthalmitis, conducted by the European Vitreo-Retinal Society (EVRS) endophthalmitis study group in 2019, 45% and 54% of the culture positivity were observed in two different groups; 26.1% of the eyes required two IVIs, and 12.2% more than two IVIs.[16] In this study, 16% of the cultures were positive, 52% of the eyes required two IVIs, and 20% more than two IVIs. More repeat intravitreal injections were needed in this study than in the multicenter study conducted by the EVRS endophthalmitis study group. This was due to the low culture positivity rate and the failure to detect the most sensitive antibiotics.

In the literature, different visual outcomes related to endophthalmitis have been reported. In EVS,[17] 82% of eyes had a final VA of 0.1 or better, whereas, in this study, 64% of eyes had a final VA of 0.1 or better. The lower vision in eyes with a final VA less than 0.1 observed in this study may be attributed to underlying primary diseases in addition to endophthalmitis, as indicated in **Table 1**. Phthisis bulbi occurred only in one eye due to late complete vitrectomy, and the final VA remained under 0.1.

The hospitalization time in CG2 was 43% longer than CG1, and the mean number of IVIs in CG2 was 28% more than CG1. Since the culture results and antibiotic sensitivity were unavailable, CG2 having underlying diseases in addition to HT and/or DM needed a significantly longer time to recover.

### Group 2 (endogenous endophthalmitis)

In a study by Connell et al.,[2] 64.1% of eyes had a positive ocular culture; 46.8% had a final VA of 0.1 or better, and 7.8% were enucleated. In two studies by Jackson et al.,[18,19] 58% of eyes had a positive ocular culture; 56% of patients had a positive blood culture; 26%–49% of eyes had a final VA of 0.1 or better; 19%–25% of the eyes were enucleated and eviscerated. In a study by Ratha et al.,[20] 58.6 % of eyes had a positive ocular culture; 29.5% had a final VA of 0.1 or better, and 19.7 % were eviscerated. In this study, in Group 2, 20% of eyes had a positive ocular culture; 0% of patients had a positive blood culture; 53.3% of eyes had a final VA of 0.1 or better, and 0% of eyes needed evisceration and enucleation. Compared to the results of the other studies, our results are superior, although our culture isolation rate is relatively low. In a study by Jackson et al.,[18] PPV+

intravitreal+systemic treatment was administered to 20% of eyes; 9% of eyes underwent PPV required evisceration and enucleation, and 26% of eyes did not undergo PPV required evisceration and enucleation. In a study by Connell et al.,[2] PPV was administered to 43.75% of the eyes; enucleation was not performed in the PPV group, and 16.1% of the eyes were enucleated in the nonPPV group. In a study by Ratha et al.,[20] 62.3% of eyes underwent PPV, and 13.1% of eyes required rePPV.

In this study, PPV was administered to 13/15 eyes (86.7%) and rePPV to 3/15 eyes (20%). All patients received intravitreal and systemic treatment. PPV combined with intravitreal and systemic treatment increased vision gain and decreased evisceration/enucleation in endogenous endophthalmitis. Culture-positivity rate (20%) increased rePPV rate (20%) in endogenous endophthalmitis cases. If the culture results were more accurate, rePPV need could have been reduced with more sensitive antibiotherapy, antifungal therapy.

The hospitalization time in CG2 was 53% longer than in CG1, and the mean number of IVIs in CG2 was 86% more than CG1. Since the culture results and antibiotic sensitivity were unavailable, CG2 having underlying diseases in addition to HT and/or DM needed a significantly longer recovery time.

This study showed that PPV combined with intravitreal and systemic treatment increased vision gain and decreased evisceration/enucleation in endogenous endophthalmitis. Due to the failure to isolate microorganisms in the culture, the repeat IVI rate was higher on exogenous endophthalmitis, and the rePPV rate was higher on endogenous endophthalmitis than in the literature. The studies in the literature have not investigated the effect of comorbidity and lack information about the total recovery times of the cases.

In endophthalmitis literature, the studies investigating comorbidity in patients with endophthalmitis reported that DM, HT, and leukemia/lymphoma are the most common comorbidities in endogenous endophthalmitis[21–23]. In the study of Weng et al.,[24] DM and HT have been reported as the most common comorbidities in endophthalmitis patients. Studies involving the relationship between the comorbidities of endophthalmitis cases and hospitalization time are lacking. In the study of Weng et al.[24,] patients with renal disease, septicemia, pneumonia, and the tumor had a higher mortality rate. In addition, hospitalization time in the mortality group was higher than survival group. However, the relationship between comorbidities and hospitalization time has not been reported.

Duric et al.[5] reported that systemic comorbidity (inflammatory comorbidity (inflammatory bowel disease) or non-inflammatory comorbidity (coronary artery disease)) increases psychological and physiological stress in patients. Cytokine release due to stress, such as interleukin IL-1b, IL-6, and TNF-α, increases inflammation. In addition, oxidative stress and inflammation trigger each other.[25,26] Kawashima et al.[6] showed that systemic comorbidity increases oxidative stress, and due to oxidative stress, ocular diseases associated with oxidative stress and inflammation, such as dry eye, increase. Fang et al.[7] showed that systemic comorbidity is associated with the prolonged clinical course of critical patients and prolonged hospitalization time in patients with COVID-19. In addition, Guan et al.[27] reported that a higher number of comorbidities is correlated with poorer clinical outcomes due to prolonged inflammation in patients with COVID-19. Our study showed that patients with systemic comorbidities (inflammatory or non-inflammatory) in addition to DM and/or HT experienced longer hospitalization times due to prolonged inflammation. The hospitalization time is the recovery time and was higher in CG2 than in CG1 in both exogenous and endogenous groups and overall.

There is no study involving the relationship between comorbidities and hospitalization time in endophthalmitis cases. This study will be the first one addressing this subject. The research findings suggest that patients with systemic comorbidities (inflammatory or non-inflammatory) in addition to DM and/or HT experience longer hospitalization times.

### Study Limitations

The current study's limitations are the retrospective design, the limited number of patients, and the failure to assess the effect of culture results on hospitalization time, treatment management, and vision gain due to the low number of culture-positive cases.

## CONCLUSIONS

Due to low culture and antibiogram findings, we had to increase surgical procedures and repeat IVI. This study showed that patients with systemic comorbidities (inflammatory or non-inflammatory) in addition to DM and/or HT experienced longer hospitalization times and needed more IVI.

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