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Endogenous Endophthalmitis Vitrectomy study (EEVS) - A retrospective analysis

Isha Acharya

dr.acharyaisha@gmail.com

C. L gupta eye institute https://orcid.org/0000-0002-6803-5790

Dev Agarwal

C. L gupta eye institute

Lokesh Chauhan

C. L gupta eye institute

Rohan Kapoor

C L Gupta Eye Institute https://orcid.org/0000-0001-6077-7039

Ruheen Siddiqui

C. L gupta eye institute

Amit Sharma

C. L gupta eye institute

Himanshu Prakash

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Abstract

Purpose: To compare the clinical outcomes of primary pars plana vitrectomy (PPV) combined with intravitreal antibiotics versus intravitreal antibiotics alone in endogenous endophthalmitis (EE) using a framework analogous to the Endophthalmitis Vitrectomy Study (EVS).

Methods: This retrospective single-centre study included 103 patients (107 eyes) diagnosed with EE from 2018-2025. Eyes were categorized into two groups: Group 1 underwent primary PPV with vitreous biopsy and intravitreal antibiotics, while Group 2 received vitreous biopsy with intravitreal antibiotics alone. Demographic characteristics, microbiological spectrum, presenting and final visual acuity, repeat interventions, and the impact of systemic antibiotics were analysed.

Results: 57 eyes were included in Group 1 and 50 eyes in Group 2. Mean presenting visual acuity was comparable between Group 1 (2.13 ± 0.63) and Group 2 (2.29 ± 0.45) ($p = 0.15$). Final visual acuity also did not differ significantly between Group 1 (1.67 ± 1.02) and Group 2 (1.80 ± 1.09) ($p = 0.78$). Presenting visual acuity was the strongest predictor of final visual outcome ($p < 0.001$). Pseudomonas species were the most common isolates. Repeat PPV was required significantly more often in Group 2 than Group 1 (21.7% vs 5.3%; $p = 0.01$). Systemic antibiotic use did not significantly affect final visual outcomes ($p = 0.83$). Most eyes remained within the <20/400 to perception-of-light visual category at final follow-up.

Conclusions: Presenting visual acuity is the strongest determinant of visual outcome in EE. Primary vitrectomy may reduce the need for repeat surgical intervention, although overall visual prognosis remains guarded.

Introduction

Endogenous endophthalmitis (EE) is a rare but potentially devastating intraocular infection resulting from hematogenous spread of microorganisms from a distant systemic focus with an incidence of merely 2–6% of all endophthalmitis cases.[1] Despite its low incidence, EE is associated with a poor visual prognosis, often resulting in severe visual impairment, phthisis bulbi, or even evisceration.

The management of endophthalmitis has been largely guided by the findings of the Endophthalmitis Vitrectomy Study (EVS)[2], which established treatment protocols for postoperative endophthalmitis based on presenting visual acuity. While numerous studies have corroborated and expanded upon EVS recommendations in exogenous endophthalmitis, there remains a relative paucity of robust evidence guiding the management of endogenous endophthalmitis. Existing literature on EE is limited, with most studies comprising small sample sizes and heterogeneous patient populations.

The largest series from India has been reported by Dave et al.[3], who analysed 117 patients with culture-proven EE. Their study provided valuable insights into the clinical profile, microbiological spectrum, and management outcomes of EE, however, the study was restricted to culture-positive cases, potentially underrepresenting the true clinical spectrum of EE, especially in settings with low microbiological yield.

Another larger study was conducted by Tan et al.[4] including 108 patients evaluating vitrectomy with silicone oil versus vitrectomy alone in bacterial EE.

Nonetheless, both these studies did not address a key clinical question explored in the EVS—namely, the comparative role of intravitreal antibiotics alone versus primary pars plana vitrectomy combined with intravitreal antibiotics. This lack in evidence leaves uncertainty regarding optimal initial management strategies in EE.

In this context, the present study aims to evaluate the clinical outcomes of endogenous endophthalmitis using a framework analogous to the EVS guidelines, comparing treatment approaches based on initial visual acuity. To the best of our knowledge, this represents one of the largest retrospective single centre analyses of EE from north India and second only to that of Dave et al[1,3] in India and provides valuable insights into treatment outcomes and decision-making in this challenging clinical entity.

Methods

This retrospective analysis was conducted at a tertiary eye care centre in North India involving patients diagnosed with EE assessing 8-year old records from January 2018 to December 2025. Medical records of all eligible patients were reviewed, and eyes with a clinical diagnosis of endogenous endophthalmitis were included irrespective of microbiological confirmation. Endogenous endophthalmitis was defined by clinical manifestations indicating intraocular infection in the absence of prior intraocular surgery or trauma.

The patients were categorized into two groups based on the initial management strategy.

Group 1 - eyes that underwent primary pars plana vitrectomy (PPV) combined with vitreous biopsy and intravitreal antibiotics

Group 2- eyes that underwent vitreous biopsy with intravitreal antibiotic injection alone (IOAB group).

The choice of treatment was based on clinical judgment, presenting visual acuity, media clarity, and severity of intraocular inflammation and patient affordability.

Eyes with pre-existing ocular conditions that could independently affect final visual outcomes, including corneal opacities/ulcers, penetrating ocular trauma, prior vitrectomy, and retinal detachment, were excluded from the study. Baseline demographic data, including age, gender, and residence, as well as systemic risk factors such as diabetes mellitus, chronic kidney disease and recent systemic illness, were recorded. Detailed clinical evaluation included presenting visual acuity, duration of symptoms, and laterality.

Visual acuity was assessed using Snellen charts and converted to logarithm of the minimum angle of resolution (LogMAR) units for statistical analysis. In patients with bilateral involvement, the eye with

worse visual acuity was chosen for the final assessment. Additionally, children in whom visual acuity assessment was not possible were excluded from visual acuity analysis.

Patients were further stratified based on duration of presentation into early (≤ 7 days) and late (> 7 days). Presenting visual acuity was categorized into standard clinical groups (20/20–20/60, < 20/60–20/200, < 20/200–20/400, < 20/400 to perception of light, and no perception of light) for subgroup analysis.

Microbiological investigations included vitreous sampling in all cases, with additional blood and urine cultures performed wherever possible. Culture positivity and organism identification were recorded. Systemic antibiotic therapy was administered at the discretion of the treating physician based on systemic evaluation and suspected source of infection.

Outcome measures included final best-corrected visual acuity, need for repeat intravitreal injections, requirement of repeat PPV, and additional surgical interventions such as silicone oil injection and pars plana lensectomy. Decision on repeat PPV was based on factors like improvement in media clarity, worsening of condition or delayed patient consent/decision making. The impact of presenting visual acuity, timing of intervention, and use of systemic antibiotics on final visual outcomes was also evaluated.

Statistical analysis was performed to compare outcomes between the two groups. Continuous variables were expressed as mean ± standard deviation and compared using appropriate parametric tests, while categorical variables were analysed using chi-square or Fisher's exact test. A p-value of < 0.05 was considered statistically significant.

Results

A total of 103 (107 eyes) patients with EE were included in this retrospective analysis. Group 1 included 57 patients/57 eyes and group 2 had 46 patients, 50 eyes. The cohort demonstrated a slight male predominance, comprising 54 males (52.4%) and 49 females (47.6%) overall.

The mean age of presentation was comparable between the two groups, with Group 1 having a mean age of 34.95 ± 16.65 years and Group 2 having a mean age of 40.83 ± 21.02 years (*p = 0.12*).

The mean duration of symptom onset prior to presentation was longer in the surgical group (Group 1- 15.28 ± 16.37 days) compared to the non-surgical group (Group 2- 10.9 ± 13.25 days), though this difference was not statistically significant (*p = 0.15*). Distribution of early (≤ 7 days) versus late (> 7 days) presentation was comparable between groups (*p = 0.07*). Maximum duration of symptom onset was 60 days noted in two patients. Majority had unilateral presentation (with only 3.8% bilateral).

Systemic associations were frequently identified. A history of fever at presentation was noted in a substantial proportion of patients (17.5%), reflecting the systemic infective aetiology, however in the majority, cause was unidentified followed by typhoid in several of the patients (Fig. 1A). Diabetes mellitus was also a common underlying comorbidity (14.6%) while 7% patients were HCV reactive

(Fig. 1B). Patients frequently belonged to rural population (56.3%). Mean follow up duration was 157.14 ± 137 days.

Microbiological evaluation of vitreous revealed a moderate culture positivity rate (19.4%), with bacterial organisms predominating over fungal isolates. The most commonly isolated organism across cultures was pseudomonas species (7.8%) followed by staphylococcus aureus (2.9%).(Fig. 1C) Staphylococcus aureus and E.coli were most commonly identified organisms in blood and urine cultures respectively. Baseline demographic variables, including gender distribution ($p = 0.23$), residence ($p = 0.31$), and systemic disease prevalence ($p = 1.0$), were comparable between the two groups ($p > 0.5$), indicating appropriate baseline matching.

The mean presenting visual acuity in logMAR was 2.13 ± 0.63 in Group 1 and 2.29 ± 0.45 in Group 2 suggesting a comparable baseline visual status between the two groups ($p = 0.15$). This indicates that the severity of disease at presentation was comparable, allowing for a balanced comparison of treatment outcomes. It should be noted that two children in whom visual acuity assessment was not feasible were excluded from the visual acuity analysis.

At final follow-up, both groups demonstrated improvement in visual acuity. The mean final LogMAR visual acuity was comparable between Group 1 (1.67 ± 1.02) and Group 2 (1.80 ± 1.09) (*$p = 0.78$*). However, presenting visual acuity demonstrated a highly significant association with final visual outcomes ($p < 0.001$), indicating a clear trend that eyes with better baseline vision are more likely to achieve favourable outcomes irrespective of the groups.(Fig. 2)

Distribution of final visual acuity across treatment groups did not show a statistically significant difference. However, clinically relevant trends were observed. A relatively higher proportion of eyes achieving the best visual outcome (20/20–20/60) were in the group 1 (21%) compared to the group 2 (20.5%), though insignificant ($p = 0.85$). Despite this, the majority of patients in both groups (Group 1 = 45.6%, group 2 = 40.9%, $p = 0.50$) clustered within the poorer visual acuity range of < 20/400 to perception of light, underscoring the aggressive nature of EE irrespective of treatment modality (Fig. 2). The proportion of eyes with NPL vision was also similar across subgroups with a relatively higher numbers in group 2 (group 1 = 14% and group 2 = 22.7%, p value = 0.75).

Among early versus later presenters, early presenters had a relatively higher proportion of patients (36%) achieving final visual acuity better than 20/200, compared to 27% among late presenters; however, this difference was not statistically significant ($p = 0.68$)

The mean number of repeat intravitreal injections was similar between groups (Group 1: 2.44 ± 2.58 vs Group 2: 1.89 ± 1.74; $p = 0.20$), with no statistically significant difference in distribution (*$p = 0.82$*).

However, significant differences were observed in surgical intervention requirements: Repeat PPV was significantly higher in Group 2 (21.7%) compared to Group 1 (5.3%) (*$p = 0.01$*) while silicone oil injection was significantly more common in Group 1 (44.1%) compared to Group 2 (19.4%) (*$p = 0.03$*). Notably,

among patients initially managed with IOAB who subsequently required PPV, approximately 40% achieved visual acuity better than 20/200. Rates of pars plana lensectomy (PPL) were comparable between groups (*p = 0.186*). Interestingly, none of the eyes underwent evisceration.

Systemic antibiotics were used in a similar proportion of patients in both groups, with 41.3% in Group 1 (PPV) and 42.2% in Group 2 (IOAB alone) (*p = 0.92*), indicating a uniform distribution of systemic antibiotic use across both cohorts. Final visual outcomes were comparable irrespective of systemic antibiotic use (p = 0.83) (Fig. 3). In group 1, the majority of eyes remained in the < 20/400 to PL category both without (29.8%) and with (15.7%) systemic antibiotics, with only a small proportion achieving better visual acuity. Similarly, in group 2, 22.7% of eyes without and 18.1% with systemic antibiotics remained in the same poor visual category, with no appreciable shift toward favourable outcomes. Overall, systemic antibiotic use did not significantly influence final visual outcomes in either group.

It should be noted that, although a prior sample size calculation was not performed because of the retrospective study design, a post-hoc power analysis based on the observed difference in repeat pars plana vitrectomy rates between the two groups (5.3% vs 21.7%) demonstrated an achieved statistical power of 72.1% at a two-sided significance level of 0.05.

Discussion

Endogenous endophthalmitis (EE) remains a challenging clinical entity with significant morbidity and variable outcomes. The present study represents one of the largest single-centre retrospective analyses of EE from India in recent years and, to the best of our knowledge, among the largest studies comparing primary PPV with intravitreal antibiotics alone using an EVS-based framework in endogenous disease. This is particularly relevant given the paucity of standardized guidelines for management of EE, in contrast to postoperative endophthalmitis.

An important aspect of our study is its conceptual alignment with the Endophthalmitis Vitrectomy Study (EVS)[2], while adapting its principles to the unique setting of endogenous endophthalmitis. The EVS[2] was a landmark randomized controlled trial in postoperative bacterial endophthalmitis that stratified management based on presenting visual acuity and compared immediate PPV and vitreous tap with intravitreal antibiotic injections, with or without intravenous systemic antibiotics. In contrast, our study—analogous to an Endogenous Endophthalmitis Vitrectomy Study (EEVS)—is a retrospective real-world analysis focusing specifically on endogenous disease, which differs fundamentally in its pathogenesis, microbial spectrum, and systemic associations. Unlike EVS[2], which included only postoperative cases, our cohort comprised hematogenous infections with often delayed presentation and more virulent organisms. Furthermore, while EVS evaluated four treatment arms including the role of intravenous antibiotics, our study compared two pragmatic strategies—primary PPV versus intravitreal antibiotics alone with vitreous tap in both the groups, reflecting real-world clinical decision-making in EE. A summarised difference table between EVS and EEVS has been highlighted in Table 1.

The demographic and clinical profile in our cohort was largely consistent with previously reported Indian studies.[1,3] Similar to the findings by Dave et al.[3], EE in our population frequently affected relatively young individuals, many of whom were immunocompetent and lacked identifiable systemic risk factors, with a significant proportion demonstrating negative systemic microbiological workup.

Microbiologically, bacterial organisms predominated in our study, with *Pseudomonas* species being the most common isolate, which is consistent with the findings of Ratra et al.[1], who also reported a predominance of gram-negative organisms including Pseudomonas species, while Dave et al[3] found Streptococcus pneumoniae as the commonest organism. The vitreous culture positivity rate in our study was 19.4%, which is comparable, though slightly lower, than the 27.6% reported by Ratra et al.[1] The relatively low culture yield underscores the diagnostic challenge in EE and highlights the importance of clinical diagnosis and early empirical therapy. Similar to prior studies, our cohort demonstrated a male preponderance and predominantly unilateral involvement. [1,3]

The role of vitrectomy in EE has remained controversial. The EVS[2] emphasized that the benefit of PPV was largely limited to eyes with perception of light vision, whereas, our findings suggest a broader role of early vitrectomy in EE, particularly in reducing retreatment burden and improving functional visual distribution. Greenwald et al.[5] suggested a more conservative approach and found no compelling evidence supporting the benefit of vitrectomy, particularly in cases with diffuse posterior involvement, where visual prognosis remained poor irrespective of intervention. In contrast, Chieh-Yu Lin et al.[6], in their meta-analysis on Klebsiella pneumoniae endogenous endophthalmitis (EKPE), demonstrated that vitrectomy results in greater visual acuity improvement compared to intravitreal antibiotics alone, particularly in eyes presenting with visual acuity of hand movements or worse. Negretti et al[7] also reported better visual gains following vitrectomy in EE cohort. This aligns with our observation that although final visual acuity was comparable between groups, the PPV group achieved better distribution in functional visual categories and required significantly fewer repeat surgical interventions, suggesting better initial disease control.

An additional clinically relevant observation from our study was the favourable visual outcomes achieved in a subset of patients who initially received intravitreal antibiotics alone but subsequently required vitrectomy. Nearly 40% of such eyes attained a visual acuity better than 20/200, indicating that pars plana vitrectomy can still provide meaningful visual recovery even when performed after an initial delay. This reinforces the role of vitrectomy as a valuable therapeutic option even beyond the early window, especially in eyes showing suboptimal response to initial intravitreal therapy.

Jackson et al.[8], in their 17-year prospective series along with a review of 267 reported cases, emphasized that endogenous bacterial endophthalmitis is a rare but severe condition with poor visual prognosis, often resulting in blindness. They further highlighted that many topical, subconjunctival, and systemic antibiotics fail to achieve therapeutic intraocular concentrations.[8] This may explain why patients develop EE despite appropriate systemic therapy. Our findings strongly support this concept, as

systemic antibiotic use did not significantly influence final visual outcomes in either group. This suggests that once intraocular involvement is established, management must primarily rely on intraocular interventions such as intravitreal antibiotics and/or vitrectomy rather than systemic therapy alone. Similarly, EVS[2] also reported no significant benefit of systemic antibiotics on visual outcomes in postoperative endophthalmitis cases.

However, systemic antibiotics still hold importance in addressing the primary systemic infective foci in the context of EE unlike as seen in EVS study[2] and potentially preventing recurrences. Notably, in our study, we did not observe any recurrences even on long-term follow-up. However, the lack of a structured long-term follow-up protocol limits our ability to definitively evaluate their role in preventing re-infection, which remains an important consideration for future studies. Thus, while our study is conceptually modelled on EVS, it highlights important differences in disease behaviour and management priorities in endogenous endophthalmitis.

The most important finding of our study was that presenting visual acuity emerged as the strongest determinant of final visual outcome, irrespective of the treatment modality employed similar to the results of some of the prior studies[9,10]. Eyes with superior baseline vision exhibited a markedly higher likelihood of attaining positive visual results, emphasizing the critical importance of early diagnosis and timely intervention. Similar results were documented in the EE cohort by few other studies also.[3,7,9]

An additional clinically relevant observation in our study was the trend toward better visual outcomes among patients presenting early. A higher proportion of early presenters achieved a final visual acuity better than 20/200 compared to late presenters, although this difference did not reach statistical significance. This suggests that while early presentation may confer a clinical advantage, the aggressive nature of endogenous endophthalmitis may limit the final outcomes.

Visual prognosis in EE continues to remain poor.[9,11] Rosiah Muda et al.[11], in their 9-year retrospective study, also reported that EE frequently leads to severe visual impairment and that poor presenting visual acuity is significantly associated with worse final outcomes. This was strongly reflected in our cohort, where the majority of patients remained within the < 20/400 to perception of light category despite appropriate management.

Nonetheless, this study has few limitations including its retrospective single-centre design, which introduces the potential for selection bias, as treatment allocation was based on clinical judgment rather than randomization. Although baseline characteristics were comparable between groups, unmeasured confounders may have influenced outcomes. Unlike the Endophthalmitis Vitrectomy Study (EVS), this study was not designed as a randomized controlled trial and therefore cannot establish superiority of one treatment strategy over another. Rather, it reflects real-world management patterns in endogenous endophthalmitis, a condition for which high-quality prospective evidence remains limited. The microbiological and systemic disease profile of our cohort, including the relatively higher proportion of typhoid- and tuberculosis-associated cases, reflects regional epidemiological patterns in North India and

may differ from that reported in Western populations. Nevertheless, this study represents one of the largest comparative analyses of endogenous endophthalmitis from India and provides valuable real-world evidence regarding prognostic factors and treatment outcomes in this uncommon but vision-threatening condition.

Conclusion

Based on our findings and correlation with existing literature, several important conclusions can be emphasized. First, presenting visual acuity appears to be the strongest determinant of final visual outcome, irrespective of treatment modality. Second, primary vitrectomy offers the advantage of reducing the need for repeat interventions compared to intravitreal antibiotics alone, likely due to better clearance of infective load and inflammatory mediators. Third, while systemic antibiotics are essential for managing the systemic source of infection, they do not appear to influence final visual outcomes once intraocular infection is established, highlighting the importance of intraocular therapy. Finally, despite advances in management, the overall visual prognosis of EE remains guarded, with a large proportion of patients experiencing severe and often irreversible visual loss.

Declarations

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process: None

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Informed consent statements: This retrospective study was approved by the Institutional Ethics Committee and adhered to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

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Conflict of interests: The authors declare that they have no conflict of interest.

Author Contributions -Isha Acharya (IA), Dev Agarwal (DA), Lokesh Chauhan (LC), Rohan Kapoor (RK), Ruheen Siddiqui (RS), Amit Sharma (AS), Himanshu Prakash (HP)

- Conceptualization and study design: IA
- Data collection: DA, AS, HP
- Data analysis and interpretation: IA, LC, RK, RS
- Manuscript drafting: IA
- Critical revision of manuscript: All authors
- Final approval of manuscript: All authors
- Accountability: All authors

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Table

Table 1
Summary of key differences in the EVS and EEVS studies;

Study design	EVS (Endophthalmitis Vitrectomy Study)[2]	EEVS (Endogenous Endophthalmitis Vitrectomy Study)
	Prospective, multicentre randomized controlled trial	**Retrospective, single-centre observational study**
Sample size	420 patients	103 patients
Study population	Postoperative bacterial endophthalmitis (after cataract surgery or secondary intraocular lens implantation)	Endogenous endophthalmitis
Microbial profile	Predominantly gram-positive coagulase negative organisms	Predominantly gram-negative-pseudomonas species
Study framework	2×2 factorial design	Two-group real-world comparison
Treatment arms	4 arms (PPV/Tap ± Intravenous antibiotics)	PPV + IOAB vs IOAB alone
Systemic antibiotics	No visual benefit	No visual benefit; systemic control role
Role of vitrectomy	Benefit in perception of light (PL only) vision	Broader benefit, fewer repeat surgeries
Primary outcomes	Visual acuity & media clarity	Visual acuity & repeat interventions
Significant Outcomes	In **PL-only group**, the difference between PPV and TAP was statistically significant over the entire range of vision.	**Baseline visual acuity** was the strongest determinant achieve favourable outcomes irrespective of the groups
Visual prognosis	Good-Moderate recovery	Poor overall

Figures

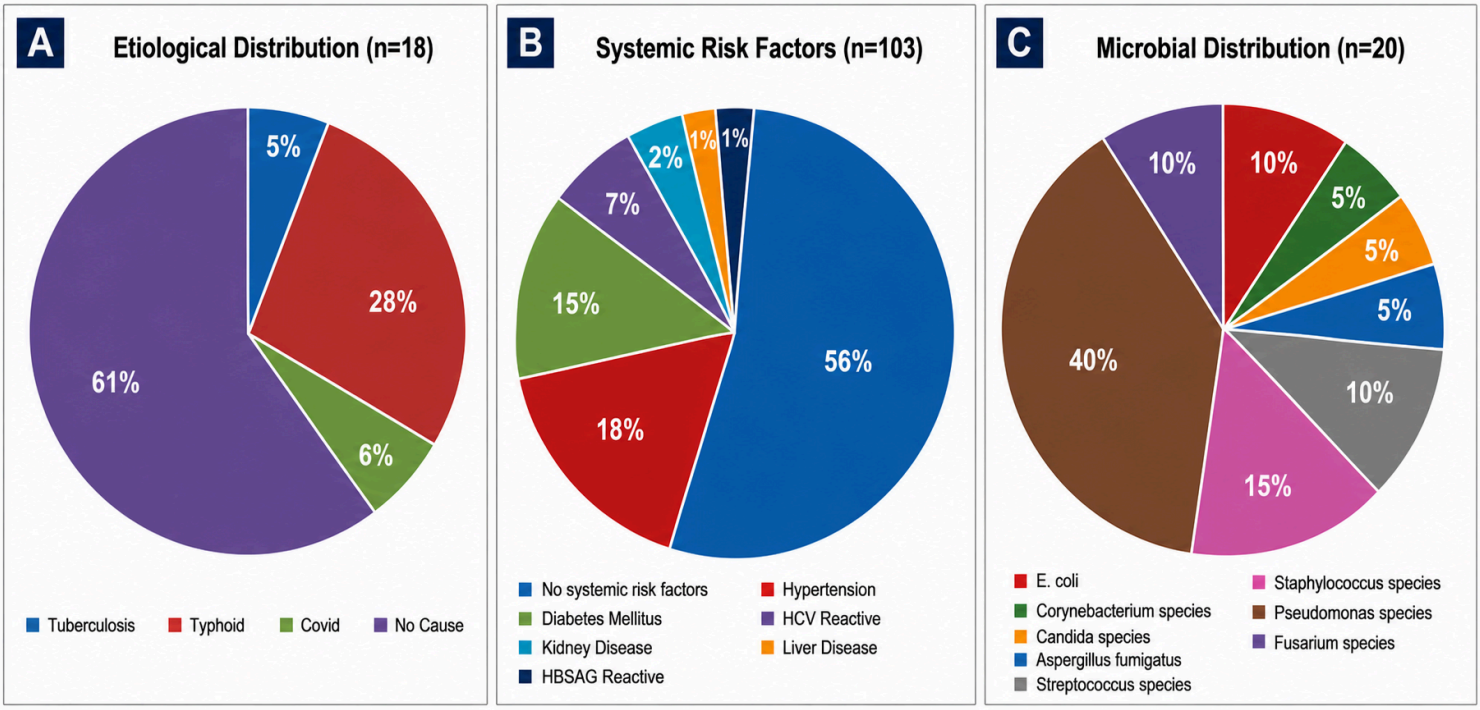

Figure 1

Pie charts depicting the distribution of etiological factors, systemic risk factors, and microbial profile among patients with endogenous endophthalmitis.

(A) Etiological distribution (n = 18) showing no identifiable cause in 61% of cases, followed by typhoid (28%), COVID-19 (6%), and tuberculosis (5%).

(B) Systemic risk factors (n = 103), with no systemic risk factors observed in 56% of patients, followed by hypertension (18%), diabetes mellitus (15%), HCV reactivity (7%), kidney disease (2%), liver disease (1%), and HBsAg reactivity (1%).

(C) Microbial distribution (n = 20), demonstrating *Pseudomonas* species as the most common isolate (40%), followed by *Staphylococcus* species (15%), *E. coli* (10%), *Streptococcus* species (10%), *Fusarium* species (10%), *Corynebacterium* species (5%), *Candida* species (5%), and *Aspergillus fumigatus* (5%).

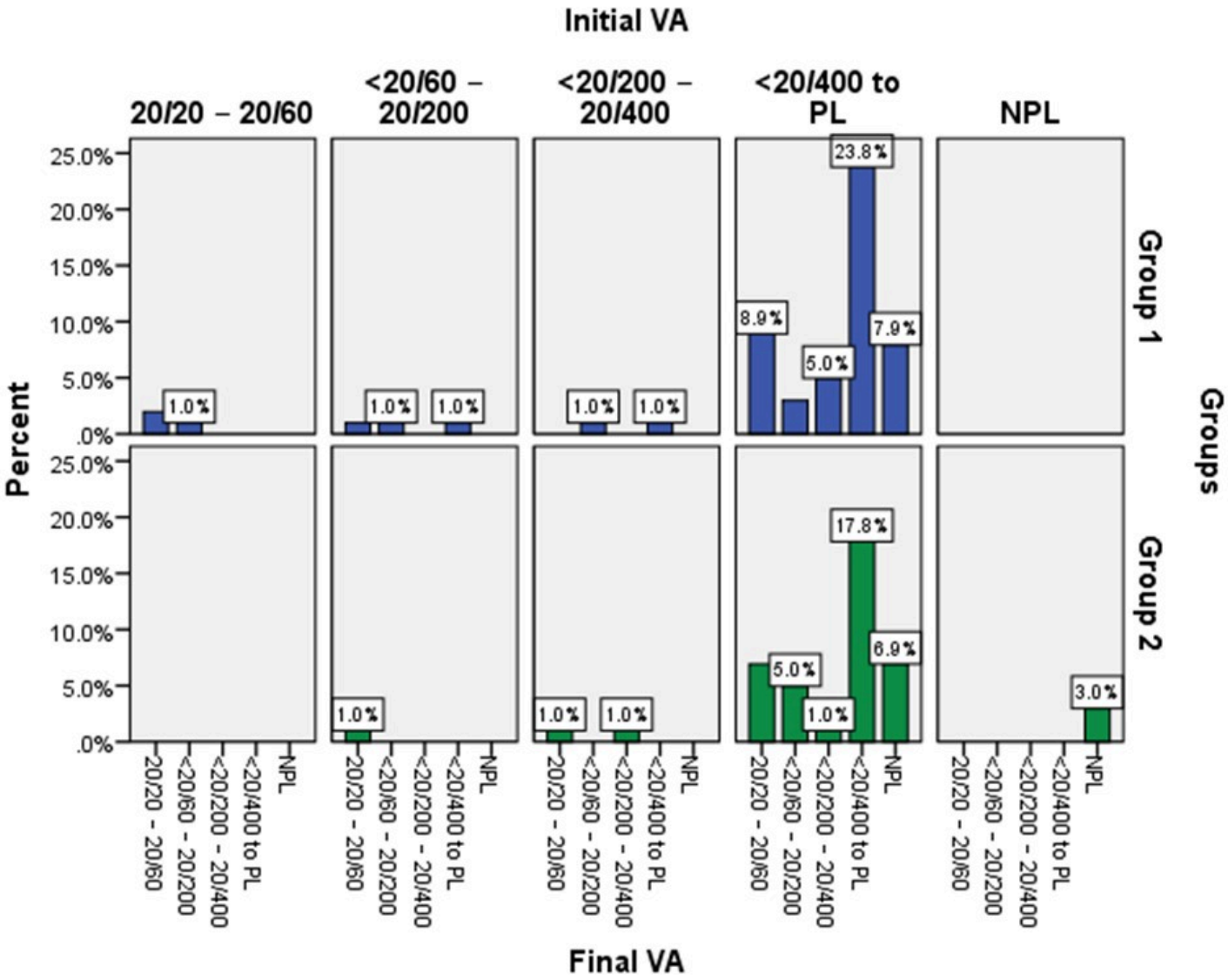

Figure 2

Distribution of final visual acuity (VA) stratified by initial visual acuity in the two treatment groups
Stacked Bar graphs depicting the percentage distribution of final VA outcomes across different baseline VA categories for Group 1 and Group 2 - Final VA categories include 20/20–20/60, <20/60–20/200, <20/200–20/400, <20/400 to perception of light (PL), and no perception of light (NPL). Most eyes in both groups presented with severe visual impairment (<20/400 to perception of light [PL]). In Group 1, the highest proportion of eyes remained within the <20/400 to PL category at final follow-up, while a smaller proportion achieved visual improvement to better visual acuity categories. In Group 2, a similar distribution was observed, although a small proportion progressed to no perception of light (NPL). Percentages within each bar indicate the proportion of eyes in the corresponding visual acuity transition category. Additionally eyes with better presenting VA demonstrated a trend toward more favourable final outcomes in both groups.

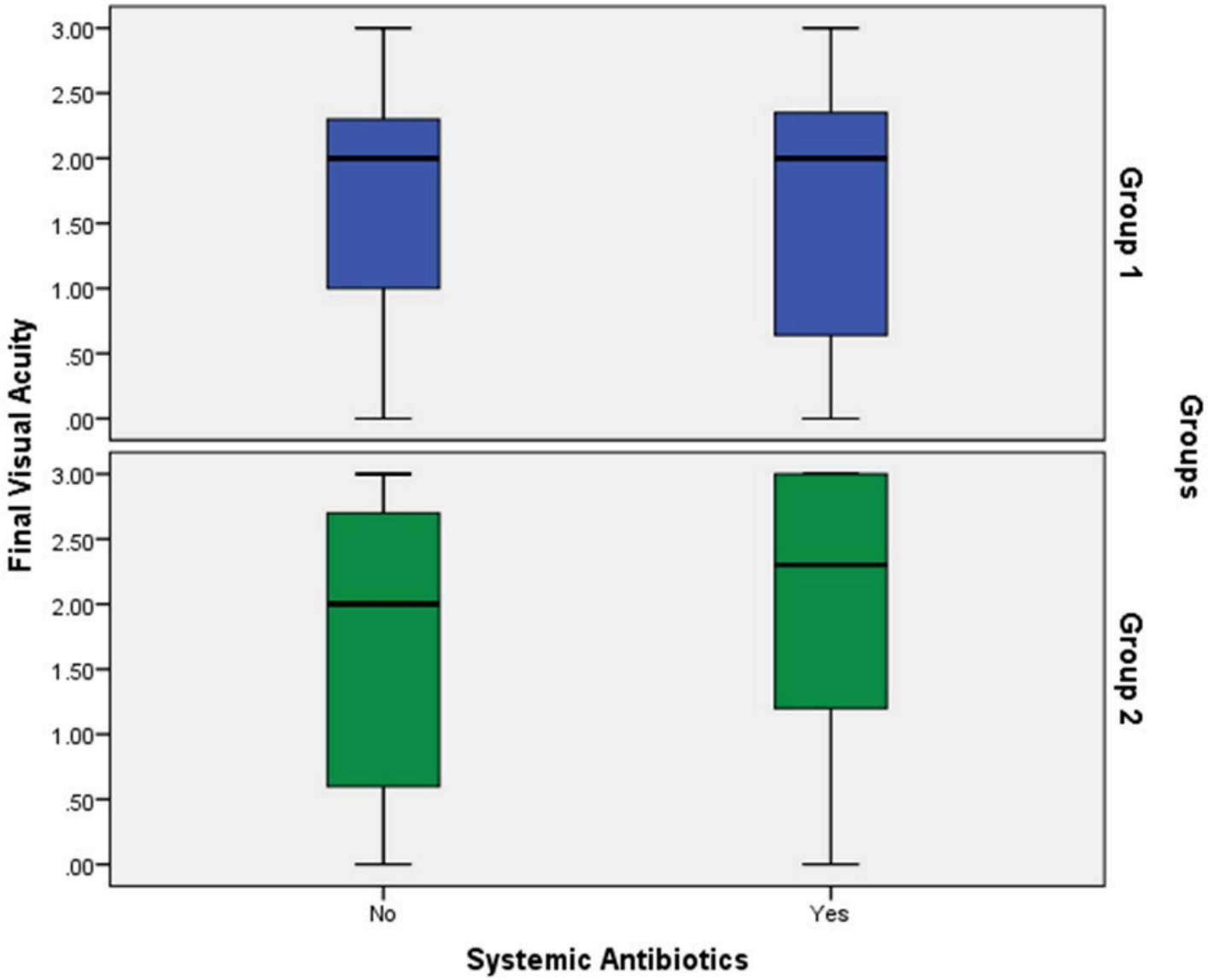

Figure 3

Comparison of final visual acuity (LogMAR) based on systemic antibiotic use in the two treatment groups.

Box-and-whisker plots showing the distribution of final best-corrected visual acuity (LogMAR) in Group 1 and Group 2, stratified by the use of systemic antibiotics (Yes versus No). The median, interquartile range, and range are depicted for each subgroup. Across both groups, the distribution of final visual acuity was comparable between patients who received systemic antibiotics and those who did not, with no appreciable difference in median LogMAR values. These findings suggest that systemic antibiotic use did not significantly influence final visual outcomes in either treatment group.