Original Article

Pediatric endogenous endophthalmitis: Clinical features and treatment outcomes

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Context: Forty-eight pediatric patients treated for endogenous endophthalmitis were analyzed. Redness and vitritis were the common symptom and sign, respectively; infection with Gram-negative bacilli was frequent. Children under 5 and with systemic illness had poorer visual prognosis. **Purpose:** To Analyze the demographics, clinical-microbiological profiles, and treatment outcomes of pediatric patients with endogenous endophthalmitis. **Methods:** We conducted a retrospective analysis of electronic medical records covering 8 years from 2016 to 2023 at a tertiary eye care center in India, focusing on patients of age <18 years diagnosed with endogenous endophthalmitis. Data extraction included demographic variables, clinical presentations, microbiological analyses, therapeutic interventions, and visual outcomes. **Results:** The analysis included 48 patients with an average age of 5.4 ± 4.98 years and an equal gender ratio. During the study period, 48 children with endogenous endophthalmitis were treated; it was 5% (48 of 961) of all endophthalmitis patients and 20.8% (48 of 231) of pediatric endophthalmitis patients. Common symptoms included redness (62.5%), reduced vision (20.8%), leucocoria (27.08%), pain (22.91%), and watering/discharge (29.16%). Clinical signs included vitritis (89.58%) and anterior chamber exudates/hypopyon (47.91%). Vitreous culture positivity was 54.05%; common isolates were Gram-negative bacilli (35%), Gram-positive cocci (25%), and Gram-positive bacilli and fungi (20% each). Systemic infection was present in 72.9% (35 of 48) of patients, with respiratory tract infection being the most common (39.5%). All eyes received intravitreal antibiotic injections, and 28 (75.7%) received vitrectomy. Children under 5 with systemic illness had a worse visual prognosis. Unfavorable outcomes were associated with Gram-positive bacilli and fungal infection. Approximately 45% of eyes worsened to phthisis. **Conclusions:** Any redness in a child with systemic infection warrants prompt ophthalmic evaluation. Children under 5 with systemic illness are associated with a worse visual prognosis. Unfavorable outcomes are linked to Gram-positive bacilli and fungal infection.

Key words: Endogenous endophthalmitis, microbiology, pediatric

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Endogenous endophthalmitis is a rare but serious condition. The incidence is 2–8% of all varieties of endophthalmitis.[1-7] It is caused by the spread of microorganisms from a primary infection site via the bloodstream to the eye's posterior segment.[8] The right eye is more commonly affected due to the direct route through the right carotid artery.[9] Damage is likely caused by a septic embolus that enters the posterior segment vasculature. The infection can extend from the choroid and retina to the vitreous cavity and the eye's anterior chamber. A direct spread of organisms can also occur from contagious sites via the optic nerve. Endogenous endophthalmitis is less often reported than postoperative and traumatic endophthalmitis and more so in children. The treatment outcome in endogenous endophthalmitis is invariably poor.[10,11] In addition to under-reporting, it is also misdiagnosed in children. We analyzed 8 years (2016–2023) of data on endogenous endophthalmitis in children we treated in a large tertiary referral eye care facility in India.

Methods

a. **Study Design:** We collected data retrospectively from the electronic medical records using the keywords 'endogenous endophthalmitis', 'vitreous biopsy', 'intraocular antibiotics', and 'vitreous culture'. The inclusion criteria were patients under 18 at the presentation time and a clinical diagnosis of endogenous endophthalmitis. We presumed it endogenous when there was no evident external source of infection, such as history or evidence of trauma, ophthalmic surgery, and contiguous spread of infection from keratitis or scleritis. We

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excluded patients with inadequate data. A comprehensive history was obtained to rule out noninfectious pan uveitis and document systemic history related to febrile illness or previous hospitalization. The collected data included patient demographics (age, gender), chief complaints, presenting and final visual acuities, results of a comprehensive examination of the anterior and posterior segments of the eye, ultrasonography and/or ultrasound biomicroscopy if performed, and the microbiology workup of all relevant body fluids, including vitreous/aqueous biopsy, systemic examination, interventions details, and the outcome.

Visual acuity was measured using the illuminated Snellen acuity chart placed at 4 meters. Vision less than 6/60 was measured by showing the fingers of the hand at different distances (recorded as count fingers, CF at a distance measured in meters). When the patients could not recognize the fingers, the vision was measured by shining an illuminated indirect ophthalmoscope at the highest intensity to the eye from a distance of one meter (recoded as Light Perception, LP). For young children unable to read numbers, preferential-looking tests (e.g. Teller Acuity Cards® and Cardiff Acuity Test®) and picture charts were utilized.

b. **Sample collection and Microbiology:** Vitreous samples were obtained from the patients during surgery with or without aqueous samples. Aqueous humor from the anterior chamber was aspirated through the corneal limbus with a 29 g needle on a 1 mL syringe. Care was taken to properly orient the needle in the anterior chamber to avoid accidental lens touch or iris capture at the needle tip. Vitreous specimens were collected using a 25-gauge vitrectomy cutter through the pars plicata route (in children under 3) and pars plana in older children. After aspirating 0.3 to 0.5 mL, vitreous was examined under a direct microscope using Gram, Giemsa, and 0.1% Calcofluor white stain to detect bacteria, fungus, and yeasts. Cultures were performed on various media: 5% sheep blood chocolate agar, 5% sheep blood agar, brain heart infusion broth, thioglycollate broth, Sabouraud dextrose agar (SDA), potato dextrose agar (PDA), and Robertson's cooked meat broth. SDA and PDA were incubated at 27°C for up to 2 weeks to support fungal growth, while all other media were incubated at 37°C for 1 week for bacterial cultures. A positive culture was defined by the growth of the same organism on two or more liquid media or confluent growth on a single solid medium.

   For blood samples, 5–10 mL was aseptically collected and inoculated into blood culture bottles (Hi Media, Mumbai, India), incubated at 37°C for 1 week, with growth confirmed by subculture on blood agar. Midstream urine samples were collected aseptically and cultured on blood and MacConkey agar within 1 hour, with growth of $>10^5$ cfu/mL considered significant. The Vitek 2 compact system (bioMérieux, France) was used for bacterial and yeast identification; the fungal species were identified by sporulation and growth patterns. Antibiotic sensitivity testing for bacterial isolates was done using the Kirby–Bauer disc-diffusion method on Mueller–Hinton blood agar.

c. **Treatment Decision.** The specific ophthalmic treatment was either Tap-Inj (vitreous biopsy + intravitreal antimicrobial injection) or Vit-Inj (vitrectomy + intravitreal antimicrobial injection). The treating retina specialists made the decision tailored to each child; it was primarily influenced by the Endophthalmitis Vitrectomy Study (EVS) recommendations.[12] In brief, the treatment was as follows: Intravitreal injection: The empirical choice of antibiotics was vancomycin and ceftazidime, and later, when repeated susceptibility-adjusted antibiotics. Pars plana vitrectomy was performed using the 23/25 G vitrectomy system.

   Vitrectomy technique: A 25 G pars plana (pars plicata for children under 3) vitrectomy was performed in all patients under strict aseptic precautions and general anesthesia. Vitreous samples were aspirated before starting the infusion. Lensectomy was performed when indicated, and the vitrectomy approach was tailored based on the clinical situation. In most cases, a safe vitrectomy aimed at debulking vitreous opacities. Extensive vitrectomy with vitreous base excision was performed only when necessary, such as in cases with severe vitreous traction or organized membranes. The vitrectomy was carried out with a cutting rate of 5000 cuts per minute. At the end of the procedure, the ports were sutured with polyglactin (vicryl) 7-0 sutures. For children under 6 months of age, the three ports were placed 0.5 mm behind the limbus, and for children aged 1 to 3 years, the ports were placed 1 mm behind the limbus at age 1, with an additional 1 mm increase for each subsequent year, up to 3 years. In children older than 4 years, a standard three-port 25 G pars plana vitrectomy was performed with ports located 3.5 mm behind the limbus.

d. **Systemic Evaluation:** Past medical records were analyzed to identify any systemic infection focus, such as sepsis, pneumonia, enterocolitis, meningitis, and encephalitis. Previous culture reports of body fluid and antibiotic susceptibility, if any. All patients received a detailed pediatrician evaluation. Blood and urine samples were sent for microbiology workup, and significance was categorized as was done for the vitreous. A fellowship-trained uvea specialist also evaluated patients in case there was a dilemma between endogenous endophthalmitis and uveitis. A detailed history from the caregivers was used to determine injury or exposure to contaminants. A thorough clinical evaluation looked for signs of trauma, such as external wounds, bruising, or fractures, under a slit lamp biomicroscope or examination under anesthesia with a microscope, as appropriate. Endogenous infection was considered when there was no evidence of trauma on physical examination.

   Data Analysis: The collected data were entered into MS Excel, and statistical analysis was performed using SPSS software (version 22.0). To determine their visual prognosis, we categorized patients based on the type of culture growth and the specific interventions they received.

e. **Study definition:** To facilitate a comprehensive analysis, we further categorized our cohort into three subgroups: triple-negative, single-positive, and double-positive. These were defined as follows: Triple-negative: All patients tested negative for blood, urine, and vitreous microscopy/culture. In these patients, the diagnosis of endogenous endophthalmitis was based on clinical assessment. Single-positive or double-positive: Patients tested positive for one or two body fluids – blood, urine, and vitreous.

f. **Outcome Measures:** The outcome at the last visit was considered for the final analysis. We defined a favorable outcome as the preservation of the globe, intraocular pressure ≥5 mm Hg, an attached retina, no

active inflammation, and a final best corrected visual acuity (BCVA) < LogMAR 1 (20/200 Snellen equivalent). Final BCVA > LogMAR 1, retinal detachment, or phthisis was an unfavorable outcome.

g. **Ethical Considerations:** The study followed the Declaration of Helsinki and obtained necessary approvals from the institutional review board or ethics committee (2024-188-BHR6). One of the parents provided written informed consent. Patient confidentiality and privacy were strictly maintained throughout the study.

Results

Demography

We included 51 pediatric patients with unilateral clinically suspected endogenous endophthalmitis. Three patients were later ruled out for a confirmed diagnosis of retinoblastoma. In the study period 2016–2023, we treated 961 patients with endophthalmitis, and 231 of them were under 18. Thus, the incidence was 5% (48 of 961) of all endophthalmitis and 20.8% (48 of 231) of pediatric endophthalmitis. The average age of the patients was 5.4 ± 4.98 years (range: 18 days to 16 years), the boys-to-girls ratio was 1:1; 72.9% (35 of 48) patients had an underlying systemic illness (most common: respiratory tract infection, 39.5%) [Table 1].

Table 1: Patient characteristics and demographics

Characteristic	Values
Total patients	48
Age in years (mean±SD)	5.4±4.98
Gender	
Male	24
Female	24
Laterality	
Unilateral	48
Right eye	22
Left eye	26
Underlying Systemic Predisposing Conditions (*n*=number of patients)	35
Respiratory tract infection	19
Fever post immunization	2
Gastrointestinal infection	2
Blood dyscrasia	2
Urinary tract infection	3
Sepsis	3
Scalp abscess	1
Skin infection (Fungus)	1
Congenital heart disease	1
Septic arthritis	1
Time to Presentation to Hospital in days (mean±SD)	15.6±14.7
Total Duration of Follow-up in days (mean±SD)	405.92±547.37
Vitreous biopsy performed in	37
Clinical signs (*n*=number of eyes)	
Lid Edema	10
Corneal Edema	8
Keratic Precipitates	5
AC Exudates/Hypopyon	23
AC Reaction	15
Posterior Synechiae	11
Neovascularisation of Iris	4
Iris Bombe	3
Cataract	17
Exudates over Lens Capsule	6
Vitritis Grade 4	43
Retinal Detachment	6
Retinoblastoma	3

Clinical features

The common presenting symptoms were redness (n = 30; 62.5%), reduced vision (n = 10; 20.8%), white spot at the pupil (n = 13; 27.08%), pain (n = 11; 22.91%), and watering/discharge (n = 14; 29.16%). The average interval to reporting to the hospital was 15.6 ± 14.7 days. In this cohort, the left eye was more involved (54.16%). The presenting visual acuity (PVA) was no light perception of light (NLP) in 6 eyes (12.5%), a third of them (n = 15, 31.25%) had LP, but inaccurate projection (LP+, PR inaccurate), a third (n = 18, 37.5%) of them had hand motion (HM) to Log MAR 1 (Snellen 20/200), and 8.33% (n = 4) eyes had vision better than Log MAR 1 but less than Log MAR 0.3 (Snellen 20/40). Vision could not be recorded in 10.4% of eyes (n = 5, uncooperative).

The common clinical signs at presentation were vitritis (89.6%), anterior chamber exudates/hypopyon (47.9%), lens opacity (35.4%), and retinal detachment, confirmed on B-scan (12.5%). Three patients referred to us with a suspicion of endogenous endophthalmitis were later diagnosed as retinoblastoma (confirmed with MRI) [Table 1]. Most of the triple-negative patients had clear cornea (n = 7; 87.5%) on presentation but with significant anterior chamber reaction (n = 4; 50%) and vitritis (n = 7; 87.5%). Three-quarters of patients in the triple-negative group had a systemic illness, and the average time to report to the hospital was 17.62 ± 18.07 days [Table 2].

Microbiology

Vitreous biopsy could be performed in 37 of 48 patients (77.1%); the family of the remaining 11 patients refused consent (n = 7) or refused any intervention after explaining a guarded visual prognosis (n = 4). Vitreous microscopy was positive in 15 instances (40.5%); it was Gram-positive cocci (6 eyes, 40%), Gram-positive bacilli, and Gram-negative bacilli and fungi (3 eyes each, 20% each). The vitreous culture was positive in 20 instances (54.1%); it was Gram-negative bacilli (7 eyes, 35%), Gram-positive cocci (5 eyes, 25%), and Gram-positive bacilli and fungi (4 eyes each, 20% each). There was also one instance of *Mycobacterium tuberculosis* infection [Table 3].

The culture was single-positive (blood, urine, or vitreous) in 67.6% (n = 25) instances and triple-negative in 21.7% (n = 8) instances. Urine culture was positive in 6 of 37 (16.2%) patients, and *Escherichia coli* was the most common organism (n = 4; 66.6%). The vitreous and urine cultures grew the same organism in one patient only. It was *Klebsiella pneumoniae*; this patient did well after treatment [Table 3]. Blood culture was positive in 2 of 37 (5.4%) patients, and the vitreous and blood cultures grew the same organism in one patient – Fusarium solani.

The antibiotic susceptibility pattern was as follows: In decreasing order, the Gram-positive cocci were susceptible to chloramphenicol, vancomycin, and moxifloxacin at 100%, 80%, and 60%, respectively; in decreasing order, the Gram-negative bacilli were susceptible to colistin, ceftazidime,

Table 2: Patient characteristics and demographics of triple negative patients

Characteristic	Value
Total patients	8
Age (mean±SD) in years	4.63±4.66
Gender	
Male	3
Female	5
Underlying Systemic Predisposing Conditions	6
Respiratory tract infection	2
Gastrointestinal infection	1
Urinary tract infection	1
Sepsis	2
Laterality	
Right eye	2
Left eye	6
Time to Presentation to Hospital in days (mean±SD)	17.62±18.07
Total Duration of Follow-up in days (mean±SD)	471.87±710
Clinical findings at presentations	
Keratic Precipitates	1
AC Exudates/Hypopyon	2
AC Reaction	4
Cataract	2
Vitritis	7
Retinal Detachment	1
Intervention	
Intravitreal injections	7
Pars plana vitrectomy	6
Outcome	
Favorable	2
Unfavorable	6

amikacin, and moxifloxacin at 100%, 60%, 40%, and 40%, respectively [Supplementary Table 1]. As a result of these findings, the antibiotic regimen for Gram-negative bacilli was altered from empirical Ceftazidime to Colistin on six occasions.

Intervention and outcome

In this cohort, 37 patients were treated, and 11 were not treated for lack of consent [Fig. 1]. All eyes received intravitreal antibiotic injections, and 28 (75.7%) received vitrectomy. Intravitreal antimicrobial injections were repeated in 22 (59.5%) eyes; the average injection number was 1.91 ± 0.95 per patient. In this cohort, only 16.6% (n = 8) patients had a favorable outcome, and 37.5% (n = 18) eyes developed phthisis. The outcome of all four patients with Gram-positive bacilli or fungi was poor. Three of five Gram-positive cocci-infected eyes had a favorable outcome. Also, children under 5 had a poorer outcome (P = 0.03). Six of eight triple-negative cases, all but one with positive urine culture, and two patients with positive blood culture had an unfavorable outcome. There was no significant difference in the outcomes of patients with triple-negative versus single-positive on culture [Table 4].

Fig. 1 provides a concise summary of the patients and outcomes.

Discussion

The present study analyzes 8 years of data on pediatric endogenous endophthalmitis in a large tertiary eye care facility. The demography (average age 5.4 years, equal affection of boys and girls), symptoms (redness and reduced vision), signs (hypopyon, vitreous exudates), and systemic illness (73%) were nearly like other reports[3,10,11,13-16] [Supplementary Table 2]. The variability in visual acuity recording can be attributed, in part, to the young age of the patient cohort (the average age was 5 years). This restricts the clinical correlation between visual acuity and chief complaints in this population.

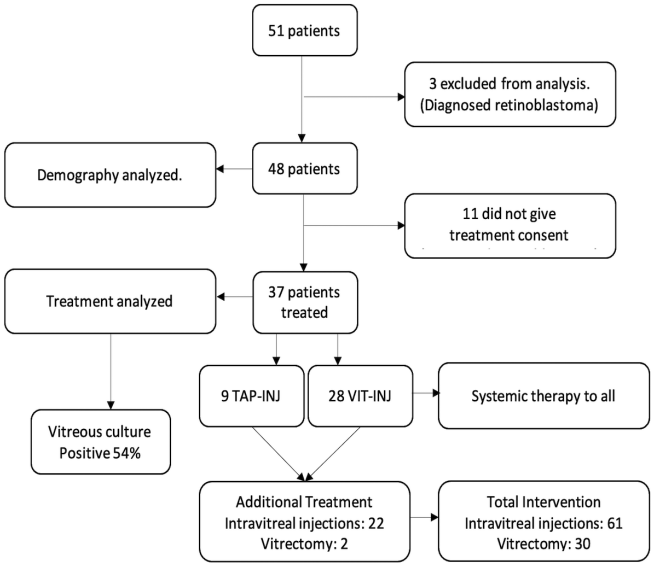

Figure 1: Brief outline of methodology and study intervention

Three retinoblastoma patients in this cohort were mistakenly referred. A good history and detailed examination (indirect ophthalmoscopy, ultrasonography, and, if needed, CT/MRI) help. Clinically, lid edema, congestion, and hypopyon are observed in infectious endophthalmitis and retinoblastoma, but the early occurrence of posterior synechiae points to endophthalmitis. Other masquerading conditions in children are Coats' disease, *Toxocara* infection, panuveitis, and persistent hyperplastic primary vitreous. Because of nonverbal and less articulated children, a delay in diagnosis is not unusual; it could be up to 26% of patients.[5,17]

Endogenous endophthalmitis may present as the primary sign of bacteremia or fungemia but it is often diagnosed in patients already receiving treatment for systemic infection. Even then, routine ophthalmological screening is not medically justified or economically viable due to low incidence (less than 0.5% of patients with fungemia and 0.04% with bacteremia).[18] Predictors of endogenous endophthalmitis include infectious meningitis, endocarditis, visceral organ abscesses, immunodeficiency comorbidities (HIV/AIDS, lymphoma/leukemia, diabetes with systemic complications), intensive care unit admission, and longer hospital stays. The importance of site-specific culture reports, such as joint aspirate or abscess cultures, cannot be overstated in understanding systemic infections and their ocular implications. In our study, the patient with septic arthritis (patient #12) was diagnosed from the joint aspirate culture; it grew *Streptococcus* species, but a vitreous biopsy could not be performed because the patient was too ill. Similarly, the scalp abscess (patient # 9) demonstrated a clear correlation, with *Staphylococcus aureus* identified in both the abscess aspirate and vitreous cultures.

Table 3: Microbiological analysis

	Isolate	Vitreous culture (Positivity=20/37, 54.05%)	Urine culture (Positivity=6/37, 16.21%)	Blood culture (Positivity=2/37, 5.4%)	Analysis of individual groups of organisms
GPC	*Staphylococcus aureus*	2	-	-	Vitreous culture (Positivity=5/37, 13.51%) Urine culture (Positivity=0) Blood culture (Positivity=1/37, 2.7%)
	Streptococcus Mitis	1	-	-	
	Granulicatella Adiacens	2	-	-	
	Streptococcus haemolyticus	-	-	1	
GPB	*Bacillus spp*	4	-	-	Vitreous culture (Positivity=4/37, 10.81%) Urine culture (Positivity=0) Blood culture (Positivity=0)
GNB	*Ochrobactrum anthropic*	1	-	-	Vitreous culture (Positivity=7/37, 18.91%) Urine culture (Positivity=5/37, 13.51%) Blood culture (Positivity=0)
	Pseudomonas Stutzeri	1	-	-	
	Pseudomonas aeruginosa	2	-	-	
	Klebsiella pneumoniae	3	1	-	
	Escherichia coli	-	4	-	
ZIEHL NEELSEN POSITIVE	*Mycobacterium tuberculosis (ZN positive)*	1	-	-	Vitreous culture (Positivity=1/37, 2.7%) Urine culture (Positivity=0) Blood culture (Positivity=0)
FUNGI	*Rhodotorula mucilaginosa*	1	-	-	Vitreous culture (Positivity=4/37, 10.81%) Urine culture (Positivity=1/37, 2.7%) Blood culture (Positivity=1/37, 2.7%)
	Fusarium solani	1	-	1	
	Curvularia lunata	1	-	-	
	Aspergillus flavus	1	-	-	
	Candida albicans	-	1	-	

GPB, Gram-positive Bacilli; GPC, Gram-positive cocci; GNB, Gram-negative Bacilli

However, given the retrospective nature of the study, comprehensive culture data from all primary sites were unavailable; it is a limitation of this study.

Most of our patients were referred to us by pediatricians after ocular symptoms were observed. The systemic infections were primarily managed by the referring physician. The underlying systemic predisposing conditions identified in our cohort are shown in Table 1. The most common cause was respiratory tract infections (n = 19, including one with tuberculosis). Despite our best efforts, triple-negative culture results were observed in eight patients. While the vitreous culture positivity rate was reasonable (54.05%), culture positivity from other body fluids was lower (16.2% for urine and 5.4% for blood). In India, three other studies have also reported low rates of positive blood cultures (0 to 3.4%).[9,19,20] This could be related to systemic antibiotic therapy before being presented to ophthalmology services. Also, the same microorganism may not be causing systemic and vitreous infection. In this study, only in two instances did the vitreous and blood or urine cultures grow in the same organism. Gram-negative bacilli were the most common (*Klebsiella pneumoniae* in vitreous, *Escherichia coli* in urine) in this cohort. Also, *Bacillus cereus* grew in four cases, usually associated with open globe injury[21] and intravenous drug abuse endophthalmitis in adults.[22] In our cohort, there were a few less commonly reported bacteria, such as *Ochrobactrum anthropic, Granulicatella adiacens, Streptococcus mitis*, and fungi, such as *Rhodotorula mucilaginosa* and *Curvularia lunata*. The incidence of fungal infection at 20% is higher than an earlier report of 15% in adult EE in our institute,[20] though up to 22% of fungal endophthalmitis after catract surgery is reported in India.[23] Candida was isolated in the urine culture of patients with urinary tract infection; *Aspergillus* was linked to respiratory tract infection, while *Fusarium* was isolated in a child with blood dyscrasia (acute lymphoblastic leukemia). The common sources of systemic infection in our cohort were respiratory tract infections, urinary tract infections, and sepsis. Given the typical presence of septic foci (73% in our cohort), the important therapeutic component was the administration of systemic antibiotics, intravitreal therapy, and vitrectomy [Supplementary Table 2].

The triple-negative, single-positive, and double-positive classifications stratify patients based on systemic and local infection profiles. Triple-negative cases relied on clinical diagnosis, indicating possible fastidious organisms or prior antibiotic use, suppressing cultures or the inability in detecting the organism with the available microbiological techniques. Single-positive for urine or blood and double-positive for both urine and blood suggest the presence of infection that may originate from systemic sources not isolated in the vitreous. These cases could reflect ongoing systemic infection. Cases where the vitreous is single-positive and cultures are triple-negative create uncertainty in the physician's mind when diagnosing endogenous endophthalmitis. Although there was no significant difference in final outcomes based on culture

Table 4: Univariate outcome analysis: Favorable vs unfavorable

Variable	Subgroups	Favorable outcome (Final BCVA<LOGMAR1, Attached retina) Total- 8 patients	Unfavorable outcome (Final BCVA ≥ LOGMAR1, Detached retina/phthisis) Total 40 patients	*P**
Demographic profile and presentation				
Age	≤5 years	2	28	0.03
	>5 years	6	12	
Gender	Male	6	18	0.24
	Female	2	22	
Systemic illness	Yes	2	33	0.002
	No	6	7	
Average duration of presentation to hospital	≤7 days	6	15	0.11
	>7 days	2	25	
Clinical features				
Cornea clarity	Yes	5	30	0.66
	No	3	10	
Hypopyon/Anterior chamber exudates	Yes	5	17	0.44
	No	3	23	
Culture analysis				
Based on culture of various tissue fluids	Triple negative	2	6	0.25
	Single positive	4	21	
	Double positive	2	2	
Based on vitreous culture	Gram-positive cocci	3	3	0.211
	Gram-positive bacilli	0	4	
	Gram-negative bacilli	2	6	
	Fungi	0	4	
Intervention				
Vitrectomy	Yes	5	23	0.67
	No	3	9	
Intravitreal antibiotics	Yes	7	30	0.49
	No	1	2	

results, we noted a trend toward worse outcomes in patients with positive vitreous cultures, especially those with Gram-positive bacilli. However, due to the small sample size and potential confounding factors, these findings should be interpreted with caution [Table 4]. While these categories may not always alter immediate management, they offer insights into infection dynamics, atypical pathogens, and diagnostic limitations, guiding further research to refine strategies for diagnosing and managing endogenous endophthalmitis. Our study indicates that the management strategy in children under the triple- or double-positive category must address both ocular pathology and systemic infection. Conversely, children under the triple-negative or single-positive category are possibly transient bacteremia/fungemia or had received near adequate treatment with systemic antibiotics and currently need targeted ocular intervention. In endogenous endophthalmitis, systemic therapy and specific ocular therapy such as intravitreal antimicrobials and vitrectomy are required.[24] Based on the antibiotic susceptibility sensitivity report and multidrug-resistant Gram-negative bacilli resistant to ceftazidime and imipenem, the primary intravitreal antibiotics, ceftazidime and vancomycin, were changed to colistin on six occasions in this cohort. Systemic antibiotics include fluoroquinolones, aminoglycosides, third-generation cephalosporins, and clindamycin. In repeated doses, systemic fluoroquinolones are known to cross the blood-ocular barrier.[25] Generally, intravenous ceftazidime is a good choice to begin treatment before obtaining the susceptibility report. Intravenous vancomycin may not be a good choice due to its restricted ability to cross the blood-ocular barrier.[26] Systemic antibiotics are recommended for a week to 10 days, and systemic antifungals (Amphotericin B, Voriconazole) require 6 weeks or longer treatment duration.[27]

Despite appropriate interventions, the outcome in this series of patients was not very favorable, less than another report on children in India.[10] The risk of poor outcome was related to younger age (<5 years; $P = 0.03$) and infecting microorganisms (Gram-positive bacilli and fungal infection, but the sample size was too small to reach statistical significance; $P = 0.21$). In our series, nearly 40% of the eyes developed phthisis bulbi. This may also be related to delayed presentations and systemic comorbidities.

The limitations are that (1) the retrospective nature may have introduced selection bias and resulted in incomplete data; (2) the relatively small number of patients and single-center setting may limit the generalizability of our

findings to other populations; (3) the lack of a comparison group also restricts definitive conclusions; (4) reliance on medical records may have led to missing information, potentially affecting result accuracy, the absence of consistent data on intravenous fluid or drug administration prior to the onset of endophthalmitis, limiting our ability to assess its potential role as a risk factor in this cohort and finally; and (5) different diagnostic and treatment protocols over the 8 years could have influenced patient outcomes. Also, the retrospective design prevented the assessment of long-term follow-up and visual outcomes.

The strengths are that our study provides a valuable demographic and clinical profile of pediatric endogenous endophthalmitis. The findings re-emphasize the importance of early diagnosis and appropriate management.

Conclusion

Early diagnosis is important. While a detailed evaluation of children with a red eye may not be practical, all systemically ill children must be examined when they develop a red eye or complain of reduced vision.

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Supplementary Table 1: The antibiotic sensitivity report (19 available reports)

Antibiotics	GPC (5/37)						GPB (4/37)						GNB (10/37)					
	S		I		R		S		I		R		S		I		R	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Vancomycin	4	80	1	20	0	0	4	100	-	-	-	-	NA	NA	NA	NA	NA	NA
Ceftazidime	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	4	40	-	-	6	60
Cefazoline	2	40	-	-	3	60	3	75			1	25	1	10	NA	NA	NA	NA
Chloramphenicol	5	100	-	-	-	-	2	50	1	25	1	25	5	50	1	10	1	10
Amikacin	NA	NA	NA	NA	NA	NA	1	25	-	-	3	75	6	60	-	-	4	40
Ofloxacin	3	60	-	-	2	40	4	100	-	-	-	-	5	50	3	30	2	20
Gatifloxacin	3	60	-	-	2	40	4	100	-	-	-	-	6	60	2	20	2	20
Moxifloxacin	3	60	-	-	2	40	4	100	-	-	-	-	3	30	3	30	4	40
Ciprofloxacin	1	20	1	20	2	40	3	75	-	-	1	25	6	60	1	10	2	20
Gentamycin	1	20	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	3	30	1	10	3	30
Piperacillin	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	7	70	-	-	3	30
Colistin	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	10	100	-	-	-	-
Imipenem	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	4	40	2	20	4	40

S - sensitive, I- Intermediate, R- Resistant, GPC- Gram positive cocci, GPB- Gram negative bacilli, GNB- Gram negative Bacilli, NA- Not available

Supplementary Table 2: Summary of Studies on Pediatric Endogenous Endophthalmitis in India

Author/ Year	Number of study eyes	Mean age in years	Predisposing medical conditions	Presenting features	Culture Positivity	Organism isolated in order of predominance	Intervention	Unfavourable Outcome
Maitray *et al.*[11] 2016	30	6.8±3.8	Febrile illness (13%) > broncho pneumonia and diarrhoea (3.3%)	Reduced vision – 90% Vitritis=AC cells with flare – 100% Hypopyon- 26.7% Vitreous exudates- 23% Cataract- 13.3%	Vitreous (76.7%) > Urine (6.7%) Blood culture nil positivity	GPC (36.66%) > Parasite (30%) > GNB (20%) > Fungi (10%) > GNC (3.33%) (GPB not isolated)	IOAB=PPV (77%)	Phthisis- 16.7%
Murugan *et al.*[11] 2016	13	1.44±1.34	Febrile illness (Respiratory tract infection - 27.2%)	Pain, redness and swelling in the eyes- 91% Rest details not mentioned	Vitreous (45.45%) > Blood (9%) Urine culture results not available	GNB=Fungi (15.38%) > GPC=GNC (7.6%) (GPB not isolated)	IOAB - 100% PPV - 76.9%	Phthisis - 38.4% Death- 1 subject
Basu *et al.*[13] 2018	6	29.5±2.6 weeks	Sepsis/ Premature low birth weight babies (100%)	Loss of red reflex- 66.6% Corneal haziness -83.3% Hypopyon – 33.3%	Vitreous (66.6%) > Blood (33.3%) Urine culture results not available	GNB (66.7%) > GPC=Fungi (16.7%) (GPB not isolated)	IOAB - 33.3% PPV - 16.6%	Phthisis - 16.6%
Our study	48	5.28±4.96	systemic illness (68.6%)	Reduced vision-20.8% Vitritis -89.58% Hypopyon-47.91% AC reaction- 31.25% Cataract- 35.41%	Vitreous (54.05%) > Urine (16.21%) > Blood (5.4%)	GNB (18.91%) > GPC (13.51%) > GPB=Fungi (10.81%)	IOAB - 68.62% PPV - 54.90%	Phthisis - 45.83%

IOAB- Intraocular antibiotics; PPV- Pars plana Vitrectomy