Original Article

# *Enterobacter* endophthalmitis: Clinical settings, susceptibility profile, and management outcomes across two decades

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**Purpose:** To describe the clinical presentation and management of *Enterobacter* endophthalmitis and compare with previous in-house published literature. **Methods:** This was a retrospective interventional comparative case series involving 44 cases with culture proven *Enterobacter* endophthalmitis from April 2006 to August 2018 who underwent vitrectomy/vitreous biopsy, intravitreal antibiotics with or without additional procedures as appropriate. The current outcomes were compared to the outcomes previously reported a decade back from our center. The mean age at presentation, predisposing factor, number of interventions, interval between inciting event and presentation, type of intravitreal antibiotic used, anatomic, and the functional outcomes were analyzed and compared to the previous series. **Results:** There were 30 males. Mean age was 22.73 ± 21.35 years (median 14 years). Inciting event was open globe injury in 34 (77.27%) eyes, 4 (9.09%) eyes following cataract surgery, 3 (6.81%) eyes with endogenous endophthalmitis, 2 (4.54%) eyes following keratoplasty, and 1 eye (2.27%) following trabeculectomy. Presenting visual acuity was favorable (≥20/400) in 2 eyes (4.54%), at the final visit it was in 11 eyes (25%). The organisms were most sensitive to ciprofloxacin (95.12%), amikacin (90.47%), and ceftazidime (85.36%). A comparison of the current study with previous in-house study showed that number of eyes with presenting vision ≥20/400 as well as final vision ≥20/400 were comparable. Susceptibility was highest to ciprofloxacin 39 (95.12%) (previous series) and 33 (92%) (current series). **Conclusion:** *Enterobacter* organisms show susceptibility to ciprofloxacin, amikacin, and ceftazidime. Susceptibility profile, clinical presentations, and management remain largely similar over many years. Final outcome is unfavorable.

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*Enterobacter* constitutes gram-negative facultative anaerobic bacteria and is a commensal in the human and animal gut. It is a rod-shaped bacterium belonging to the family *Enterobacteriaceae*. *Enterobacter* is well known to cause systemic afflictions like upper respiratory tract infection, urinary tract infection, osteomyelitis, and septicemia.[1-3] The initial occurrence of *Enterobacter* endophthalmitis was reported in 1966 as a case of postcataract surgery endophthalmitis.[4] Since then various reports have demonstrated the occurrence of *Enterobacter* endophthalmitis in different ocular settings like open globe injury, cataract surgery, glaucoma filtering surgery, and as an endogenous infection.[5-9]

Though a handful of reports exist, literature on *Enterobacter* endophthalmitis is relatively sparse. A decade back, we reported the presentations and outcomes of a large series of cases of *Enterobacter* endophthalmitis was published in literature.[10] In the current communication, we report the clinical settings, microbiologic profile, and management outcomes of *Enterobacter* endophthalmitis managed at our institute in the current decade. We also compare the current results with those of the previous decade from our center.

## Methods

This was a retrospective interventional consecutive case series conducted at a tertiary eye care center in India. Case records of all cases with culture-proven *Enterobacter* endophthalmitis from April 2006 to August 2018 were identified by the institute medical record system and the microbiology laboratory records. The cases included in a publication from the same center in 2012 were excluded for this study. Institutional Review board approval for the study was taken as appropriate and the study conformed to all the tenets of the Declaration of Helsinki. Details of history, clinical examination, and clinical features at presentation, microbiological evaluation,

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antibiotic susceptibility, and clinical response to therapy were obtained from the chart review. *Enterobacter* was identified using API 20 NE (Bio- Meriux, Marcy l'Etoile, France). Antibiotic sensitivity was determined using the Kirby–Bauer disk diffusion technique. The essential clinical findings included presenting and final best corrected visual acuity, status of anterior segment, presence/absence of hypopyon, extent of fundal glow, and status of the retinal vessels, if visible. Whenever the fundus was not visible by the binocular indirect ophthalmoscope using the highest illumination, B-scan ultrasonography was done to determine the extent and location of vitreous involvement and other posterior segment diseases, such as retinal detachment, choroidal thickening, or choroidal detachment.

### Intervention

The surgical management of endophthalmitis consisted of pars plana vitrectomy, microscopy, and culture of undiluted vitreous, antimicrobial susceptibility testing of bacterial isolates, and intravitreal antibiotics (vancomycin, 1 mg/0.01 ml + ceftazidime, 2.25 mg/0.01 ml) with or without dexamethasone (400 µg/0.01 ml).[11] The medical treatment included intensive topical antibiotics (ciprofloxacin 0.3% one hourly) and corticosteroid (prednisolone acetate 1% one hourly) and oral ciprofloxacin (750 mg two times per day) for 7--10 days. Additional procedures such as repeat intravitreal antibiotics or repeat pars plana vitreous lavage depended on the response to treatment and were left to the decision of the treating physicians. In cases with hazy view due to corneal involvement, a vitreous biopsy was taken instead of a vitrectomy procedure.

### Surgical technique

Undiluted vitreous samples were collected via a vitreous biopsy at the beginning of the surgery in all cases. Further handling and processing of the samples and final interpretation was done as per institute protocol. In cases undergoing a vitrectomy, it was done within 24 h of presentation, either using a 20 G or 23/25 G system. In the former cases, the conjunctiva and scleral incisions were sutured with 7--0 polyglactin sutures. Topical 5% povidone iodine was instilled in the cul-de-sac in all cases at the end of surgery.

### Outcome definition

The outcome at the last visit was considered for final analysis. Anatomic success was defined as preservation of the globe, absence of hypotony (intraocular pressure ≥5 mm Hg), attached retina and absence of active inflammation. A functional success was defined as an attached retina with a best- corrected vision of ≥20/400.

### Statistical analysis

The data were arranged on an Excel spread sheet and analyzed using the statistical software MedCalc ver 12.2.1.0 (Ostend, Belgium). Percentage confidence intervals were calculated using online statistical calculators (https://www.allto.co.uk/tools/statistic-calculators). Odds ratio with appropriate confidence intervals was computed for possible risk variables. A $P$ value < 0.05 was considered statistically significant. Comparison of continuous nondependent variable with a categorical dependent variable was done using logistic regression.

## Results

The study included 44 eyes of 44 patients. There were more males (30, 68.2%) than females ($P$ = 0.04). The mean age at presentation was 22.73 ± 21.35 years (median 14 years). History of decreased vision was noted to be since 4 ± 3.51 days (median 3 days). Open globe injury was the commonest etiology of infection accounting for 34 eyes (77.27%). This was followed by 4 (9.09%) eyes following cataract surgery, 3 (6.81%) eyes with endogenous endophthalmitis, 2 (4.54%) eyes following keratoplasty, and 1 eye (2.27%) following trabeculectomy [Table 1]. In the postsurgical cases, the interval between surgery and the start of symptoms was 15.33 ± 29.79 (median = 4) days. Visual acuity at presentation was no perception of light in 6 eyes (13.6%), perception of light to hand motions close to face in 34 eyes (77.27%), from counting fingers close to face to <20/400 in 2 eye (4.54%), and ≥20/400 in 2 eyes (4.54%) [Fig. 1].

Five eyes (11.36%) showed a corneal infiltrate at presentation. Six cases underwent a vitreous tap, whereas 38 cases underwent a pars plana vitrectomy. The mean repeat injections done were 2.72 ± 1.56 (median = 2). Mean follow-up was 9.99 ± 12.98 months (median = 4). At the last visit, visual acuity was noted as no perception of light in 19 eyes (43.2%), perception of light to hand motions close to face in 11 eyes (25%), from counting fingers close to face to <20/400 in 3 eyes (6.81%) and ≥20/400 in 11 eyes (25%). Anatomic success was seen in 19 eyes (44.2%), whereas functional success was seen in 11 eyes (25%). Six cases had mixed infection. All cases with mixed infection were those following open globe injuries. The species isolated was *Enterobacter cloacae*

**Table 1: Table showing summary of demographic factors in the current case series**

| Total eyes included | *n*=44 |
|---|---|
| Age | 22.73±21.35 years<br>Median 14 years |
| Etiology of infection | 4 (9.09%) postcataract surgery<br>34 (77.27%) postopen globe injury<br>3 (6.81%) endogenous<br>2 (4.54%) postkeratoplasty<br>1 (2.27%) posttrabeculectomy |
| Interval between inciting event and start of symptoms | 15.33±29.79 days<br>median 4 days |
| Cases with concurrent corneal infiltrates | 5 (11.36%) |
| Favorable vision at presentation | *n*=2 (4.54%) |
| Favorable vision at last follow-up | *n*=11 (25%) |
| Anatomic success at last follow-up | 19 (44.2%) |
| Species isolated | |
| *E. cloaceae* | 29 (65.9%) |
| *E. aerogenes* | 1 (2.27%) |
| *E. sakzakii* | 1 (2.27%) |
| *E. faecium* | 1 (2.27%) |
| Unidentified *Enterobacter* species | 5 (11.36%) |

in 29 cases, unidentified *Enterobacter* species in 12 cases, and one case each of *Enterobacter sakzakii, Enterobacter faecium, and Enterobacter aerogenes*. Antimicrobial susceptibility was the best for ciprofloxacin and ofloxacin followed by amikacin, gatifloxacin, and moxifloxacin [Table 2]. (Add data of comparison with previous report. Antibiotic susceptibility data is important to compare since gram negative organisms are known to develop resistance over a period of time. Your purpose claims comparison of clinical data including outcome).

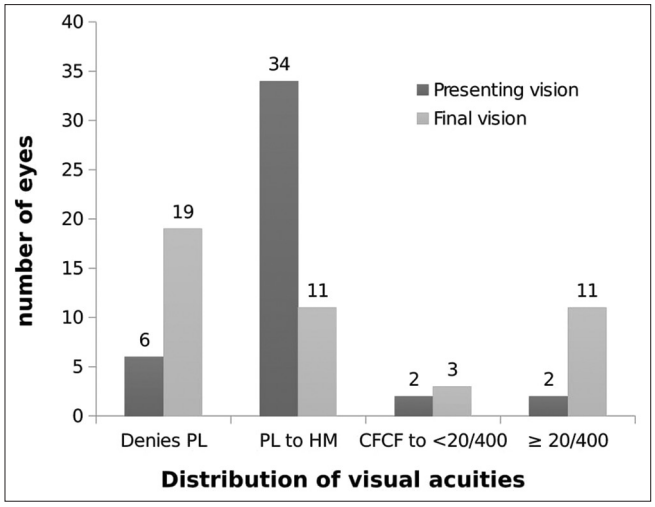


**Figure 1:** Comparative visual acuities at presentation and at the last follow-up

## Discussion

In the current communication, we report the largest series on *Enterobacter* endophthalmitis till date. The commonly known gram-negative organisms causing endophthalmitis include *Pseudomonas, Hemophilus,* and *Klebsiella*. Cases of *Enterobacter* endophthalmitis, though not very common, are increasing. Most major studies including the endophthalmitis vitrectomy study, reported a very low incidence of *Enterobacter* as a causative agent for endophthalmitis.[12,13] The largest study till date on *Enterobacter* was published in 2012[10] [Table 3]. In that study, the incidence of *Enterobacter* endophthalmitis was found to be 3.24%. In the current study, we reported 1091 cases of culture-proven endophthalmitis from April 2006 to August 2018 of which 44 cases had *Enterobacter* endophthalmitis, leading to an incidence of 4.03% which is marginally more than the previous decade. Previous studies done at our center and in southern India noted the incidence of *Enterobacter* endophthalmitis to be around 1.5%.[14,15] A further increase in the incidence of *Enterobacter* endophthalmitis could be attributed to increase in cases of endophthalmitis postopen globe injury in our subset. The open globe injuries can get contaminated with soil. Literature suggests a higher occurrence of *Enterobacter* as resident fauna of soil around the world.[16,17] In the present series, all cases but one had an acute presentation with a median time period between start of symptoms and presentation to the clinic being 4 days. This is consistent with previous literature on *Enterobacter* endophthalmitis and on gram-negative endophthalmitis.[13-15] Recently, Sachdeva, *et al*. reported a series of endophthalmitis postintravitreal anti-VEGF (Vascular endothelial growth factor) injections.[18] This included

**Table 2: Antimicrobial susceptibilities for the antibiotics tested**

| Antibiotic | Current study | | Pathengay *et al.* | | *P* |
|---|---|---|---|---|---|
| | Susceptibility | Samples tested | Susceptibility | Samples tested | |
| Amikacin | 38 (90.47%) | 42 | 27 (86%) | 31 | 0.55 |
| Imipenem | 18 (81.81%) | 22 | No data | | |
| Ofloxacin | 39 (95.12%) | 41 | No data | | |
| Gentamicin | 35 (85.36%) | 41 | 19 (72%) | 26 | 0.18 |
| Ceftazidime | 35 (85.36%) | 41 | 22 (78%) | 28 | 0.43 |
| Gatifloxacin | 38 (90.47%) | 42 | No data | | |
| Moxifloxacin | 38 (90.47%) | 42 | No data | | |
| Ciprofloxacin | 39 (95.12%) | 41 | 30 (92%) | 33 | 0.58 |
| Chloramphenicol | 37 (90.24%) | 41 | No data | | |

**Table 3: Comparison of the current series with a series, a decade back from the same center**

| | Pathengay, *et al.*[10] (1995-2006) | Current study (2006-2018) | *P* |
|---|---|---|---|
| Total eyes | 36 | 44 | |
| Incidence of *Enterobacter* endophthalmitis | 3.24% | 4.03% | 0.85 |
| Mean age (years) | 31.5±23.47 | 22.73±21.35 | 0.08 |
| % Males | 75 | 68.18 | 0.5 |
| Number of cases following open globe injury | 25 (69.44%) | 34 (77.27%) | 0.43 |
| Eyes with presenting vision ≥20/400 | 2 (4.54%) | 2 (4.54%) | 1 |
| Eyes with final vision ≥20/400 | 12 (33.33%) | 20 (45.45%) | 0.27 |
| People with final vision of NLP/phthisis | 16 (44.44%) | 19 (43.18%) | 0.91 |

the first report of *Enterobacter* endophthalmitis following anti-VEGF injections which occurred following injection of intravitreal bevacizumab. In our series no case was noted to be following anti-VEGF injections.

In the current study, ciprofloxacin and ofloxacin demonstrated the highest antimicrobial susceptibility followed by amikacin and chloramphenicol. In our previous study also ciprofloxacin and amikacin showed a relatively high comparable susceptibility pattern.[10] Multidrug resistance is increasingly being seen in gram-negative infections around the world and is becoming a matter of concern.[19,20] This is also a similar concern in treatment of *Enterobacter* endophthalmitis. Singh *et al*.[21] described a case report of *Enterobacter* endophthalmitis following open globe injury. *Enterobacter* spp. isolated in the report was resistant to vancomycin, amikacin, ceftazidime, ciprofloxacin, gatifloxacin, chloramphenicol, and cefazolin by Kirby Bauer disc diffusion method. Due to the identified multidrug resistance pattern, this patient was treated with intravitreal piperacillin and tazobactam combination with a good final visual outcome of 20/40. Bhat *et al*.[22] reported a series of seven eyes with multidrug resistant *Enterobacter* endophthalmitis. In their series, the cases were resistant to vancomycin, amikacin, ceftazidime, ciprofloxacin, gatifloxacin, chloramphenicol, and cefazolin but sensitive to imipenem and piperacillin-tazobactam. Three eyes in their series had useful vision at the last follow-up, while two eyes underwent evisceration for panophthalmitis. In our series three cases were multidrug resistant, demonstrating resistance to aminoglycosides, cephalosporins, fluoroquinolones, penicillins, and chloramphenicol. All of them were postsurgical endophthalmitis with one each following cataract surgery, trabeculectomy, and penetrating keratoplasty. None of the cases were polymicrobial by culture. They were treated with intravitreal colistin with dexamethasone. All of the cases underwent pars plana vitrectomy as a primary treatment intervention within 24 h of presentation. Two of those cases ended with no perception of light vision and phthisis bulbi, whereas one eye could be salvaged with a final visual acuity of 20/60. In our previous series too, multidrug resistance was seen as a feature with one patient showing multidrug resistance. The patient however did well clinically to achieve a final vision of 20/40 on being treated with intravitreal tazobactam and piperacillin.

The number of eyes that achieved a favorable functional outcome was 11/44 (25%). This was comparable to the previous series from our center, 8/36 (22%). The overall unfavorable functional outcome can be attributed to the inherent virulence of these organisms as seen commonly in most gram-negative infections.[13,23] In our series, anatomic success was seen in 19/44 eyes (44.2%) only. Of the remaining 25 eyes, 19 (76%) underwent phthisis, 2 (8%) developed intractable hypotony and 4 (16%) had recurrent inoperable rhegmatogenous retinal detachment. In our previous study, 14 eyes (39%) became phthisical whereas in another case series reported by Mirza *et al*., 2/6 eyes (33%) developed phthisis.[6]

The current study has some inherent limitations. The majority of cases of endophthalmitis in this series were post trauma. Trauma itself is a confounding factor for a final poor visual outcome. Thus, it would be difficult to clearly delineate in the posttraumatic subset, whether the poor visual outcome is due to trauma or due to the subsequent endophthalmitis. The effect of various confounding factors could not be independently assessed due to the retrospective nature of the study. The limited sample size did not allow us to reach a statistical significance of the impact of certain factors such as the presence of unimicrobial infection, intravitreal dexamethasone, and presence of corneal infiltrates. Though these factors could potentially impact the outcome, the current study could not conclusively draw any such conclusions for the possible lack of an adequate sample size. There was a lack of a uniform treatment protocol and management decisions made by individual treating physicians were varied.

An important observation was that the comparative antibiotic susceptibility profile between our previous data[10] and the current data show ciprofloxacin, amikacin, and ceftazidime to be the antibiotic of choice for these infections. Over the last 2 decades, our previous study and the current study were comparable on most clinical parameters.

## Conclusion

Based on our observations, we suggest that the clinical settings, antimicrobial susceptibilities, and management outcomes of *Enterobacter* endophthalmitis have been largely similar over the last two decades in our set up. The limited sample size though, does not allow generalization of the results across different set ups and different treatment protocols. Due to high virulence of the organisms, final management outcomes stay poor in spite of early and appropriate management.

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### Conflicts of interest

There are no conflicts of interest.

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