Original Article

Clinical profile and outcome of endogenous endophthalmitis at a quaternary referral centre in South India

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Purpose: The purpose of this study is to evaluate the clinical profile, visual, anatomical and survival outcome of patients with endogenous endophthalmitis. **Methods:** Retrospective chart review of consecutive cases with endogenous endophthalmitis presenting from 2009-2016. **Results:** In our study, 41 eyes of 34 patients were included. Most common co-morbidity associated with endogenous endophthalmitis was Diabetes Mellitus (70.7%) and most common infective foci was UTI (73.2%). Among the culture positive cases, fungi and bacteria were evenly distributed, 76.93% were Gram positive bacteria and 23.07% were Gram negative. Fungal endogenous endophthalmitis was more commonly seen in immunosuppressed state (72.7%) and bilateral cases (66.7%). The mean presenting vision (log MAR) of patients who died during the study were poor compared to those who survived (P = 0.014) Poor mean visual acuity at presentation was associated with more death (P = 0.014). Eyes with poor presenting vision, fungal isolates, culture positivity and immune suppression had poor visual and survival outcome. Poor visual outcome was observed more frequently in eyes with Aspergillus infection (85.7%) compared to Candida (75%) and bacteria (58.3%). Evisceration was done for 5 out of 41 eyes (12.2%). Vitrectomy rate was 53.7% in our study, with 40% of them showing overall improvement in vision. **Conclusion:** Endogenous endophthalmitis is a sight threatening condition associated with high mortality particularly when caused by *Aspergillus* spp. in immunocompromised patients. Contrary to the prior published reports of endogenous endophthalmitis outside India, we found an equal distribution of fungal and bacterial organisms among our cases, with predominance of Aspergillus among fungal isolates and Gram-positive organism among bacteria. Fungal infections, especially with *Aspergillus* spp., resulted in poor visual and survival outcome.

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Endophthalmitis is intraocular infection affecting inner coats of the eye with progressive vitreous inflammation.[1,2] Endogenous endophthalmitis [EE] accounts for approximately 2-8% of endophthalmitis.[1,3,4] EE results from hematogenous spread of pathogens from distant infective foci.[5,6] The most common risk factors associated with EE include diabetic mellitus, malignancy, lymphoproliferative disorders, gastro-intestinal tract infections, immunosuppression, parenteral alimentation, alcoholism, HIV, intravenous drug abuse, in-dwelling catheters, UTI, endocarditis, prolonged use of corticosteroids, joint infections, COPD, chronic liver disease, end stage renal disorders.[7,8]

Etiology of EE is multifactorial and causative agents show extensive geographical variation. Both bacteria and fungi have been reported as etiological agents for EE, fungi being most common in western world.[4,7,9] Studies done in Asia, however, shows fungal cause to be less common compared to bacterial in cases of EE.[10-12] In a study conducted in India by Sharma *et al*., bacteria (Gram-positive) was found to be more common than fungi.[10] Among bacterial EE, Gram-positive (Streptococci and Staphylococci) are more prevalent in North America and Europe, while Gram-negative in East Asian regions.[10] In East Asia, *Klebsiella pneumoniae* was seen in majority of cases with liver abscess frequently associated with it.[13]

Bacterial endophthalmitis usually presents acutely whereas fungal endophthalmitis typically has a subacute presentation. The common presenting complaint in EE is decreased vision (68%) followed by ocular discomfort (44%), red eye (20.8%) and ocular pain (17.4%).[11] Intraocular inflammation is typically diffused in bacterial endophthalmitis, while the intraocular inflammation in fungal endophthalmitis tends to occur in clumps within the aqueous and/or vitreous.[2] In addition to timing of presentation and intervention, visual outcome also depends on the virulence of organism.[14-16]

Etiology of EE is multifactorial, and the causative agents show extensive geographical variation. The knowledge

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of microbial profile in a geographical location will help in choosing appropriate empirical treatment while waiting for the microbial report. In India, studies focusing exclusively on EE are very few. Majority of these studies are concentrated on postoperative or exogenous endophthalmitis. The present study looked at the clinical profile, microbial profile, visual, anatomical and survival outcome of patients with endogenous endophthalmitis. This study will help to fill the lacunae in the existing literature.

Methods

The medical records of all diagnosed cases of EE treated at quaternary referral centre in south India, from 2009-2016 were retrospectively reviewed and followed up for 2 years.

EE was diagnosed clinically in the presence of significant vitreous inflammation associated with sepsis and/or presence of other concomitant infection, having ruled out non-infectious causes of vitritis. Patients with history of ocular surgery or ocular trauma within one year of the onset of infection, corneal ulcer related endophthalmitis, glaucoma filtering surgery related endophthalmitis and uveitis were excluded. Age of the patients, sex, presenting complaints, underlying systemic infections, preexisting medical conditions, source of infection, laterality, microbial profiles, treatment methods, initial and final visual acuities (VA) were collected.

All cases were investigated with blood culture, urine culture and extensive work up including imaging where ever indicated aiming at finding the primary source of infection and general management of the patient. Vitreous biopsy, culture and sensitivity, intravitreal and systemic broad-spectrum antibiotics and/or antifungals where administered for all the patients. Intravitreal antibacterial used were vancomycin (1 mg in 0.1 ml) plus either of ceftazidime (2.25 in 0.1 ml) or amikacin (400 mg in 0.1 ml) whereas amphotericin B (5 microgram in 0.1 ml) was used in the suspected fungal cases. Patients were reviewed daily after intravitreal injections. If the vision deteriorated/vitritis increased after 48 hours of intravitreal injection Pars Plana Vitrectomy (PPV) was performed. PPV was also performed in patients with presenting visual acuity ≤ hand movement. None of the patients underwent repeat vitrectomy.

VA was recorded using Snellens visual acuity chart. VA pre-treatment and post-treatment were collected and categorized into three groups: (1) improved, (2) stable, and (3) deteriorated. An improvement was defined as either a gain of ≥ one line of Snellen VA, where subjects were within Snellen acuity range and for those presenting with very poor visual acuity, which couldn't be assessed with Snellen VA chart (Beyond Snellen), an improvement of one-measured step or more (for example, from HM to CF). Deterioration defined as either a loss of ≥ one line of Snellen VA, where subjects were within Snellen acuity range or for those in the 'beyond Snellen' a loss of one-measured step or more (for example, HM to PL).

'Culture positive' was defined as isolation of any microorganism from vitreous sample and 'culture negative' when no organisms grown from vitreous biopsy. Blood/urine culture was performed for all cases; in addition, samples were collected for culture from any other suspected foci of infection elsewhere. Based on the organism isolated from vitreous biopsy, EE was grouped into bacterial and fungal.

'Poor visual outcome' was defined as vision less than or equal to (≤) counting fingers (CF) at 3 feet (Snellen visual acuity) and 'good visual outcome' as vision more than or equal to ≥ 20/200 (Snellen visual acuity). Snellen visual acuity was converted to logMAR vision for statistical analysis.

Statistical analysis was done using IBM SPSS 20.0 (SPSS Inc, Chicago, USA). For all the continuous variables, the results are given in Mean ± SD and for categorical variables as number and percentage. To compare the mean difference of numerical variables between groups, independent two sample 't' test was applied for parametric data and Mann Whitney U test for non-parametric data. To obtain the association of categorical variables, Chi square with Fisher's exact test was applied. P value < 0.05 was considered statistically significant.

Results

Demographics and comorbidities

In our study, 34 patients (41 eyes) were included. There were 22 males and 12 females. The maximum number of patients belonged to the age group 51-60 years (age range 1 month to 73 years) including one neonate. Mean age was 49.47 ± 17.14 years. Unilateral EE was seen in 27 patients and 7 had bilateral EE.

Left eye was involved in 53.7% and right eye in 46.3%. Most common co-morbidities associated with EE were diabetes mellitus (70.7%), hypertension, chronic liver disease, immunosuppressed state (which comprises patients with malignancies, post-transplant and on immunosuppressive drugs/chemotherapy) and chronic kidney disease [Table 1]. At least one comorbid condition were seen in 90.24% of the patients, diabetes mellitus was the most common comorbidity among bilateral cases. Immune statuses were suppressed in 17 out of 34 patients, 3 patients had bilateral EE. Concomitant infections elsewhere in the body were identified in 30 eyes (73.1%). Most common concomitant infection noted was urinary tract infection (32.3%) followed by sepsis (20.5%), abscess (14.7%) and infective endocarditis (5.8%).

Microbiological profile

Culture positive organisms were isolated from vitreous from 26 out of 41 eyes. Among the culture positive cases,

Table 1: Distribution of Systemic comorbidities among bacterial and fungal EE

COMORBIDITIES	Bacterial EE (*n*=13)	Fungal EE (*n*=13)
Diabetes Mellitus	7	11
Hypertension	7	9
Chronic kidney disease	0	1
Chronic liver disease	2	8
Transplant	1	4
Malignancy	1	3
Immunosuppressive drugs	1	1
Infective endocarditis	0	1
Dyslipidemia	3	2
Others	5	4

Twenty-two patients with culture positivity had more than one comorbidity. This table shows details of only the culture positive cases

fungi and bacteria were evenly distributed, *Aspergillus* spp. and *Staphylococcus aureus* being the most common organisms respectively [Table 2]. Among the bacteria 76.93% were Gram-positive and 23.07% were Gram-negative. *Aspergillus* spp. constituted 53.8% and *Candida albicans* 30.7% of the fungal infections in our study [Table 2]. Fungal EE were noted more commonly with immunosuppressed state, chronic liver disease and diabetes mellitus. Among immunosuppressed patients, 5/11 culture positive eyes were infected by *Aspergillus*. Out of the total eyes infected by Aspergillus, majority of them were in the immunosuppressed group (71.4%) [Table 3].

Bilateral involvement was twice more with fungal EE (4/6) than bacterial EE (2/6). Out of seven patients with bilateral involvement, most common organisms were *Aspergillus fumigatus* and *Staphylococcus aureus* [Table 3].

Blood cultures were positive in 7 (20.5%) patients and urine culture in 11 (32.3%). Most common organisms isolated were *E. coli* from urine and *Staphylococcus aureus* from blood.

Table 2: Microbial isolates from vitreous

Type of organism	Total	Organisms	Number
Fungal	13	*Aspergillus* species	7
		Candida albicans	4
		Unidentified filamentous fungi.	2
Bacterial	13	*Staphylococcus aureus*	7
		Streptococcus pneumoniae	2
		Nocardia species	1
		Hemophilus influenzae	1
		Klebsiella pneumoniae	1
		Pseudomonas aeruginosa	1

Visual outcome

At presentation, 28 eyes had VA <20/200 that was evenly distributed among fungal and bacterial groups. Initial vision could not be assessed in 3 eyes and final vision could not be assessed among 5 eyes, which included a neonate, 4-year-old child and patients with serious systemic illness who couldn't cooperate for assessment of vision (these patients had permanent neurological sequelae on follow up).

At initial visit, 10 out of 41 eyes had vision ≥20/200 (good vision). Out of these 10 eyes with good vision at presentation, 70% eyes maintained vision ≥20/200 (good visual outcome), 30% had vision ≤ CF at 3 feet (poor visual outcome) and 9.1% eyes developed no light perception (NLP). Whereas out of 23 eyes (61.0%) with vision less than or equal to counting finger 3 feet at presentation (poor vision) only 30.4% eyes had good visual outcome, 69.6% had poor visual outcome and 36.0% had NLP [Table 4]. At the last follow-up, 9/14 eyes with bilateral infection had poor visual outcome compared to 12/22 eyes with unilateral involvement ($P = 0.51$).

Even though initial VA were comparable in immunosuppressed group and others, poor visual outcome was noted more in immunosuppressed eyes (70.0%) compared to others (43.8%). The mean logMAR vision of immunosuppressed (1.45) were poor compared to other patients (1.0) ($P = 0.09$) [Table 4].

Infective organisms were isolated in 26 out of 41 eyes. Poor visual results were noted more among culture positive eyes (69.6%) [Mean logMAR 1.43] compared to culture negative eyes (38.5%) [Mean logMAR 0.94] ($P = 0.06$) [Table 4].

At last follow-up, 15 eyes showed visual improvement, eight eyes maintained stable vision and 13 eyes showed deterioration in vision from the initial visit despite treatment.

Table 3: Laterality, immune status and microorganisms

	Bacteria *n* (%)	Fungal *n* (%)	*P*	Fungal		
				Aspergillus spp.	Candida albicans	Others
Single eye *n*=14	9 (64.3)	5 (35.7)	0.238	3	2	0
BL *n*=12	4 (33.3)	8 (66.7)		4	2	2
Immunosuppressed *n*=11	3 (27.3)	8 (72.7)	0.23	5	3	0
No immunosuppression=15	10 (66.7)	5 (33.3)		2	1	2

BL- bilateral, *6 patients=12 eyes

Table 4: Visual, anatomical and survival outcomes

	Poor vision at last follow up (*n*=21)	*P*	Evisceration (*n*=5)	*P*	Patient who died (*n*=7)	*P*	NLP (*n*=12)	*P*
Good vision at initial visit *n*=11 (%)	3 (30)*	0.08	1 (9.1)	0.97	0	0.19	1 (9.1)*	0.20
Poor vision at initial visit *n*=25 (%)	16 (69.6)*		4 (16)		6 (24)*		9 (36.0)*	
Fungal** *n*=13 (%)	10 (83.3)*	0.19	1 (7.7)	1.0	5 (38.5)	0.16	3 (23.1)	0.67
Bacteria** *n*=13 (%)	6 (54.5)		2 (15.4)		1 (7.7)		5 (38.5)	
Culture positive *n*=26 (%)	16 (69.6)*	0.06	3 (11.5)	1.0	6 (23.1)	0.36	8 (30.8)	1.0
Culture negative *n*=15(%)	5 (38.5)*		2 (13.3)		1 (6.7)		4 (26.7)	
Immuno-suppressed *n*=20(%)	14 (70.0)*	0.11	4 (20.0)	0.31	4 (20.0)	0.94	6 (30.0)	0.92
No Immunosuppression *n*=21(%)	7 (43.8)*		1 (4.8)		3 (14.3)		6 (28.6)	

NLP- no light perception, *missing data- Initial vision could not be assessed among 3 eyes and final vision could not be assessed among 5 eyes. ** included only culture positive cases

Among the 13 eyes with visual deterioration, 3 were culture negative, 4 had bacterial EE and 6 had fungal EE. Out of the culture positive cases, half of the eyes with visual deterioration were caused by *Aspergillus fumigatus* among fungal group and *Staphylococcus aureus* in bacterial group [Table 5].

At presentation, 75% of bacterial and 63.6% of fungal EE had poor vision. Poor visual outcome was noted more among fungi compared to bacteria (83.3% Vs 54.5%). *Aspergillus* spp. (85.7%) showed worst visual outcome. At the last follow-up, 15 eyes (36.6%) of eyes had vision more than or equal to ≥20/200 and 12 eyes had no NLP.

Anatomical outcome

Evisceration was done for 5 out of 41 eyes. Eyes presented with poor BCVA at presentation underwent evisceration more (16%) compared to those with good BCVA (9.1%). In the immunosuppressed group, 20% of eyes needed evisceration compared to other patients in the study (14.3%). Evisceration performed was twice in eyes with bacterial infection compared to fungi (15.5% Vs 7.7%). Among culture positive cases, evisceration was seen in eyes infected with Nocardia, Klebsiella and Candida (one eye each) [Table 4].

Survival outcome

During the study period, a total of 7 patients died. Among those who presented with poor BCVA, 6 patients died compared to none with good vision at presentation. The mean presenting vision of people who died during the study were poor (mean logMAR 1.71) compared to those who survived (mean logMAR 1.42) (P = 0.014). Among the patients with fungal EE, 38.5% died compared to 7.7% with bacterial. Among the fungal EE who died 4/5 (80%) of them had *Aspergillus* spp. Even before the initiation of treatment 3 patients had died, all of them had *Aspergillus* spp isolated from vitreous. Number of patients died were more among those who were immunosuppressed (20%) and culture positive eyes (23.1%) [Table 4]. The most common systemic comorbidity associated with patient who died were diabetes mellitus (71.4%) and hypertension (71.4%) followed by chronic liver disease (57.1%). Among the etiology of the patients who died sepsis (secondary to UTI and liver abscess) was most frequent followed by infective endocarditis [Table 6].

Treatment

PPV with intravitreal antibiotics was performed for 22 eyes and 14 needed only vitreous tap and intravitreal antibiotics. Out of 34 patients, 28 were already receiving systemic antibiotics even before diagnosing EE. Among culture positive cases, PPV rate was 80% and 50% in fungal and bacterial EE respectively. 40% of eyes showed improvement and 20% maintained stable vision with combined PPV and intravitreal injection whereas 58.3% of eyes showed improvement with injection alone [Table 5].

Table 5: Visual status among organisms and procedure

ORGANISMS	Visual status		
	Improved	Stable	Deteriorated
Bacterial EE			
Staphylococcus aureus	3	1	2
Klebsiella pneumoniae	0	0	1
Nocardia spp.	0	0	1
Haemophilus influenzae	1	0	0
Streptococcus pneumoniae	1	0	0
Pseudomonas aeruginosa	0	1	0
Fungal EE			
Aspergillus spp.	2	2	3
Candida albicans	1	1	2
Unidentified filamentous fungi.	0	0	1
Procedure			
Vitrectomy + Intra vitreal injection	2	7	8
Intra vitreal injection	3	2	7

Table 6: Etiology of the patients who died

Etiology of the patients who died	Numbers (n=7)
Sepsis [from UTI (2), liver abscess (1)]	3
Infective endocarditis	2
Liver transplant rejection, Cholangitic abscess	1
Lymphoblastic leukemia	1

Discussion

This study looked at the cause, etiological organisms, site of infection, risk factors, visual, anatomical and survival outcomes in EE. Most common co-morbidity associated with endogenous endophthalmitis was diabetes mellitus and most common infective foci was UTI. Among the culture positive cases, fungi and bacteria were evenly distributed. Fungal endogenous endophthalmitis was more commonly seen in immunosuppressed state and bilateral cases. Poor mean visual acuity at presentation was associated with more death (P = 0.014). Eyes with poor presenting vision, fungal isolates, culture positivity and immune suppression had poor visual and survival outcome. Poor visual outcome was observed more frequently in eyes with Aspergillus infection. Vitrectomy rate was 53.7% in our study, with 40% of them showing overall improvement in vision.

Bilateral eye involvement was seen in 20.6% of our patients, predominantly fungal and *Aspergillus* spp. constituting half of it. Series published by Essman *et al.*, Okada *et al.* and Schiedler *et al.* have reported that bilateral cases are more common among fungi than bacteria.[3,4,17] There are reports of bilateral cases of EE demonstrated with bacteria such as Clostridium.[18,19]

In our study, 90.24% of the patients had at least one systemic co-morbid condition, most common being diabetes mellitus. In a review by Jackson *et al.* among bacterial EE, 56% of patients had an underlying condition that increased the risk of infections.[20] Connell *et al.* found an identifiable risk factor in 78.1% and Schiedller *et al.* in all his cases of EE.[4,7] Twenty patients were in immunosuppressed state and fungal EE was more common in immunosuppressed group than bacteria. Majority of immunosuppressed in our study yielded Aspergilli which is in concurrence with the earlier reports by Ness *et al.* and Riddel *et al.* that EE caused by molds were frequently associated with history of use of chemotherapy, organ transplantation, immunosuppressive therapy and systemic corticosteroids.[9,21]

The most common concomitant infection noted was urinary tract infection followed by sepsis. In a series by Zenith *et al*., an infective focus was identified in most of the patients with EE and urinary tract was the commonest source. Chung *et al.* reported that 22.2% had pneumonia and 16.7% had liver abscess as the infective foci.[22] Wong *et al*. reported hepatobiliary tract as the commonest foci of infection in 48% of cases, whereas intravenous drug use was the commonest in the West.[6,7,15]

In our study, culture positive organism was isolated from vitreous among 63.4% of eyes. Many other authors have reported varied culture positivity rate from intra ocular specimens. Jackson *et al.* reported that the detection of microorganisms from ocular specimens was possible in only 56%, whereas other authors reported high rates of positive culture from intraocular specimens such as 87% by Ness *et al.* and 86% by Okada *et al*.[8,9,20] Majority of the patients in our study were already receiving systemic antibiotics even before diagnosing EE, this could probably be the reason for lower culture positivity in our study. The most common organisms isolated were *E. coli* from urine and *Staphylococcus aureus* from blood. Jackson *et al*. and Ness *et al*. reported blood culture positivity rate of 56% and 33% respectively.[9,20] Polymerase chain reaction testing can be used to identify organisms from intraocular specimens in endophthalmitis cases and could be a valuable tool especially in culture negative cases.[2] However, in the present study, we did not perform PCR in any of our cases.

There are extensive geographical variations among the microbials that cause EE. Both bacteria and fungi are reported in literature. However, fungi are the commonest.[4,7,9] Fungi are predominant especially in western world, whereas in East Asia, it is Gram-negative bacteria.[11] However, in our study, fungi and bacteria were evenly distributed, *Aspergillus fumigatus* and *Staphylococcus aureus* being the most commonly isolated organisms respectively. The number of fungal isolates in our study was lower compared to studies in western world, whereas it is in accordance with studies done in Asia, where they reported fungal cause to be less common compared to bacterial in cases of EE.[10-12]

Among bacterial EE, Gram-positive organisms were more prevalent in North America and Europe, while Gram-negative organisms were more common in East Asia.[10] In East Asia, *Klebsiella pneumoniae* has been attributed to majority of cases and hepatobiliary infections has been frequently associated with it.[13] In our study, among the bacteria majority were Gram-positive organism which is in contrast to other studies from East Asia probably because of a smaller number of hepatobiliary infections in our study unlike in East Asian studies. There are similar results noted in studies conducted in India by Sharma *et al.* and Ramakrishnan *et al*., where bacteria (Gram positive) was more common than fungi.[10,23] Another Indian study by Tulsi *et al.* found even distribution of fungi and bacteria similar to our study. They found candida more common among fungal, equal number of Gram positive and negative organisms among bacteria.[24] However there are also reports of predominant Gram-negative bacterial EE in studies conducted in India by Dhanashree *et al*.[25] and Jalali *et al*.[25,26] Majority of the studies in Asia have been done in East Asian regions and they reported predominantly gram-negative organisms. However, both gram-positive and negative organisms have been reported by the few available Indian studies in the literature.[10,13,23-26]

Aspergillus constituted majority of the fungal infections in our study whereas Candida is the commonest isolate in other reports especially from Western part of the world and East Asian regions. However in a report from India by Chakrabarti *et al.* among fungal endophthalmitis, they found equal number of Aspergillus and Candida among fungal EE.[27] Immunosuppressed state is a reported risk factor for Aspergillus EE.[9,14,28] In our series nearly half of the patients were in immunosuppressed condition and 71.4% of eyes infected by Aspergillus had immunosuppression. More number of immunosuppressed eyes in our study could be the reason for predominance of Aspergillus infection.

Poor visual outcome at last follow up visit was seen more among eyes that had poor vision at presentation, culture positivity, fungal etiology, eyes with bilateral involvement and immunosuppressed group. Overall visual results in EE have been reported to be poor and similar results were noted in our study.[6,20] Previous studies reported poor visual outcome in bacterial EE compared to fungal EE. Contrary to previous studies, our study reported poor visual outcome more among fungal EE compared to bacterial EE. Poor visual results were observed predominantly among Aspergillus infection compared to Candida and bacterial infection in our study. Poor visual results in fungal EE in our study could be attributed to the greater number of Aspergillus infection among the culture positive cases. Aspergillus causing poor visual outcomes has already been reported in various series. Schiedler *et al.* also reported high mortality rate among patients with fungal EE, majority of them were due to *Aspergillus* spp.[4,9,14,17,28] Visual outcome was poor among immunosuppressed and bilateral cases. This may be due to larger proportion of Aspergillus infection among both these groups as well. Culture negative cases resulted in better visual outcome and better survival outcome in our study compared to culture positive, similar to the report by Connell *et al.* attributing it to the altered virulence of unidentified organisms.[7]

Poor presenting visual acuity has already been reported as a poor prognostic factor by Sallam *et al*.[29] Among those who presented with poor BCVA, 24% died compared to none with good vision at presentation but the association was not statistically significant. However, the mean presenting vision (log MAR) of people who died during the study were poor compared to those who survived (P = 0.014) and it is statistically significant. Fungal infection especially with Aspergillus has already been reported to be associated with high mortality rate and we also observed more death in patients with Aspergillus EE.[4] More patients died in the immunosuppressed group and culture positive EE.

All the patients in our study were started on broad spectrum intravenous antibiotics once the EE diagnosis was established based on culture and sensitivity report of probable source of infection. The ocular penetrance of systemically administered antibiotics is variable. Meropenum, linezolid and moxifloxacin are the agents achieving best therapeutic levels.[30] The rationale for continued empiric use of vancomycin in endophthalmitis despite limited intraocular penetration, is its microbiological spectrum, covering almost 100% of the Gram-positive organisms causing endophthalmitis. For fungal EE, anti-fungal

agents recommended are fluconazole for *Candida*, voriconazole for fluconazole-resistant, but voriconazole-susceptible isolates, and liposomal amphotericin, with or without 5-flucytosine, for azole-resistant strains.[31]

Vitrectomy rate was 53.7% in our study, Connell *et al.* and Han Woong Lim *et al.* reported vitrectomy rate of 57% and 43.1%, respectively, in their study.[7,11] Among culture positive cases, pars plana vitrectomy rate was more among fungal compared to bacterial. Eyes with poor presenting vision, fungal EE and those which did not show any improvement with injection underwent vitrectomy, this could be the reason for less improvement in vitrectomy group compared to injection only group. Overall visual improvement with vitrectomy in the study reported by Connell at al and Lim *et al.* was 52% and 47.8% respectively.[7,11] Yoon *et al.* reported final visual outcome of CF or better or more among half of their patients who underwent vitrectomy.[32] In our study, at the last follow up visit, 45.0% of eyes that underwent vitrectomy had vision ≥20/200. Most of the studies reported poor visual results in spite of treatment, Zhang *et al.* and Chen *et al.* reported final visual outcome of 20/200 or more among 40% of their patients, whereas in our study, 36.6% of eyes had vision more than or equal to ≥20/200.[33,34]

Causative organisms for EE show a lot of geographical variation as discussed earlier.[20] Most of the Indian and other Asian studies have reported bacteria as the most common cause for EE in Asia contrary to studies done in Western world.[10,13,23-26] Majority of the studies in Asia have been done in East Asian regions and they have reported predominantly gram-negative organisms. However, both gram-positive and negative organisms have been reported by the few available Indian studies in the literature.[10,13,23-26] There are only very few Indian studies that has focused exclusively on EE, even though there are lot of reports available regarding post-operative and exogenous endophthalmitis. Our study focuses exclusively on EE and contributes to the limited information available regarding EE and factors influencing it in India.

Conclusion

EE is a sight threatening condition associated with high mortality particularly when caused by very virulent organism such as Aspergillus. Contrary to the prior published reports of EE outside India, we found an equal distribution of fungal and bacterial organisms among our cases, with predominance of Aspergillus infection among fungal infections and Gram-positive organism among bacteria. Fungal infections especially with Aspergillus resulted in poor visual and survival outcome, early detection and aggressive treatment is warranted in cases with virulent organisms to reduce the visual morbidity and general mortality.

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Conflicts of interest

There are no conflicts of interest.

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