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Microbiological profile of cultureproven cases of exogenous and endogenous endophthalmitis: a 10-year retrospective study

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Abstract

Purpose To identify the microbial aetiology of infectious endophthalmitis and to determine the in vitro antibacterial susceptibilities of bacterial isolates. Methods A retrospective analysis was carried out of all patients presenting between January 1997 and December 2006 with clinically diagnosed infectious endophthalmitis who underwent microbiological evaluation. Intraocular specimens (aqueous and vitreous fluids) were collected from all cases of clinically suspected infectious endophthalmitis. In addition to intraocular aspirates, blood specimens from endogenous endophthalmitis, and corneal and scleral scrapes from relevant cases were also collected. The collected intraocular specimens, blood specimens, and corneal and scleral scrapes were subjected to microbiological evaluation.

Results Samples from 955 patients with endophthalmitis underwent microbiological analysis, of which 424 (44.4%) were found to be culture positive. Of 424, 364 (85.8%) had bacterial growth and the remaining 60 (14.2%) had fungal growth. Among post-surgical endophthalmitis, Gram-negative bacilli (75%) were found to be the predominant cause for developing fulminant onset, Staphylococcus spp. (68.6%) for acute, and Streptococcus spp. (75%) for chronic onset of infections, whereas in post-traumatic endophthalmitis, Gramnegative bacilli (65.2%) were found to be the predominant cause for fulminant onset, Gram-positive bacillus (28.4%) for acute onset, and fungi (52.3%) for chronic onset of

infections. Endophthalmitis associated with microbial keratitis was mainly caused by filamentous fungi (37.2%) and Gram-negative bacilli (37.2%). Overall, gatifloxacin (97.7%) showed highest activity against bacterial isolates followed by ciprofloxacin (95.9%) and ofloxacin (95.1%).

Conclusion Gram-negative bacilli cause predominantly fulminant onset, Staphylococci and Gram-positive bacilli acute, and Streptococci, Nocardia, and fungi chronic endophthalmitis. Gatifloxacin demonstrated greatest efficacy against these bacterial isolates. Eye (2009) 23, 945–956; doi:10.1038/eye.2008.197; published online 4 July 2008

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Introduction

Infectious endophthalmitis, a potentially blinding disorder, is a major public health concern. Infectious endophthalmitis is defined as an inflammation of intraocular tissues or fluids secondary to intraocular infection.1 Colonization of organisms inside the eye can occur either by the introduction of infectious agents into the eye following a breach in the ocular barriers or by dissemination through the systemic blood stream. When infectious agents reach the vitreous cavity across an opening in

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the globe, it is termed as exogenous endophthalmitis and when it occurs by hematogenous spread, it is termed as endogenous or metastatic endophthalmitis. Exogenous endophthalmitis occurs usually following surgical or traumatic alteration of the structural integrity of the globe. Occasionally, exogenous endophthalmitis results from contagious spread of infectious microbes from the ocular adnexa, especially following infections on the cornea or sclera.²

Post-operative infectious endophthalmitis can be encountered after any intraocular procedure, and its incidence is estimated as 0.05–0.37%. The incidence can vary with the surgical procedure and is most frequently seen with cataract surgery where coagulase-negative *staphylococci* (CoNS) are isolated in nearly 70% of cases.^{3,4} Exogenous endophthalmitis is more common following penetrating ocular injuries than following surgery, and the reported incidence among penetrating injury ranges between 3 and 17%.⁴ Endogenous endophthalmitis (EE) is less common than exogenous endophthalmitis and accounts for only 2–6% of all cases of endophthalmitis, usually in debilitated or immuno-compromised patients or in patients with a history of intravenous drug abuse.⁵

Literature reviews show a distinct pattern of variation in the microbial aetiology of infectious endophthalmitis according to the clinical settings.^{2–8} The microorganisms responsible for post-operative endophthalmitis (eg *staphylococci* and *streptococci*) generally reside on the eyelid margins and pre-ocular tear film, whereas in the case of post-traumatic infectious endophthalmitis (eg *Bacillus* spp. and fungi), the organisms are generally derived from the environment. The most common causes of EE are *Streptococcus* species, *Staphylococcus* species, and *Bacillus cereus*.^{9,10} Hence, documentation of the microbial pathogens causing endophthalmitis is of the highest priority and their antimicrobial susceptibilities are essential for better understanding and prompt management of this disease.

Several studies have investigated risk factors, microbial aetiology, visual outcomes, and the causative role of residential microbial flora in developing endophthalmitis. 11-13 However, none of the single centre series has described the comparison of the spectrum of microbial pathogens causing post-operative, posttraumatic, and post-corneal infective and EE. The purpose of this study was to determine specific microbial pathogens responsible for the development of the various forms of endophthalmitis presenting in a tertiary eye care referral centre in South India. An attempt was also made to compare the in vitro antibacterial susceptibility pattern of bacterial pathogens recovered from each type of endophthalmitis. This will help significantly in the implications on the treatment protocol practised in such patients.

Materials and methods

A retrospective analysis was performed of all case records with culture-proven endophthalmitis treated at Aravind Eye Hospital and Postgraduate Institute of Ophthalmology, Tirunelveli, Tamil Nadu, South India over 10 years from January 1997 to December 2006. As a standard protocol followed in our institute, the diagnosis of endophthalmitis was based on the presence of pain, inflammation including anterior chamber cellular reaction and flare and vitreous cells or exudates, decrease in visual acuity and loss of media clarity with or without the presence of hypopyon following intraocular surgery, penetrating injury and/or corneal or scleral infections. 1,14-16 All patients with endophthalmitis presenting to our referral centre undergo thorough evaluation that includes: (1) the documentation of the demographic features, duration of symptoms, interval between the event and presentation to this institution, and use of medications; (2) information pertaining to the predisposing factors: ocular surgery, history of trauma, associated ocular diseases, systemic conditions, and presence of systemic diseases; (3) ocular examination findings (presenting Snellen's visual acuity, presence of hypopyon, presence of vitreous cells, and optic disc visibility), ultrasonography (with attention to the presence of vitreous membranes and vitreous exudates); and (4) microbiological workup that includes direct microscopy and culture results with antibacterial susceptibilities. Endophthalmitis occurring within 4 days of surgery or trauma were categorized as fulminant onset endophthalmitis; infections that present less than 6 weeks after surgery or trauma were categorized as acute endophthalmitis, whereas infection that develop 6 weeks after the initial event were categorized as chronic endophthalmitis.2

The confirmatory diagnosis of infectious endophthalmitis was established by the demonstration of significant microbial growth in cultures of intraocular specimens and in cases of EE, along with intraocular specimen presence of the same infectious agents in cultures of blood. Endophthalmitis due to corneal and scleral infections was confirmed by obtaining the same microbial pathogens in both corneal or scleral scrape and intraocular aspirates. The microbiological diagnosis of endophthalmitis was confirmed by a systematic approach for procuring intraocular fluids. Using standard techniques, 14-16 0.1-0.2 ml of anterior chamber fluids were aspirated through the peripheral clear corneal paracentesis using a 26-gauge needle on a 1 ml plastic sterile disposable tuberculin syringe. Vitreous specimen (0.5-1.0 ml) was obtained using a 22-gauge needle introduced through the pars plana just before injecting the intra-vitreal antibiotics or performing core

vitrectomy. The aspirated intraocular fluids were immediately inoculated on blood agar, chocolate agar, Sabouraurd's dextrose agar, brain heart infusion broth, and thioglycollate broth medium for culture in the operating room. Smears were prepared for Gram's and Giemsa staining techniques and also for 10% potassium hydroxide wet mount preparation. All inoculated media were incubated aerobically. A positive culture was defined as a growth of the same organisms on more than two solid phase mediums or confluent growth on one solid medium. If In general, indications for vitrectomy were according to the Endophthalmitis Vitrectomy Study guidelines. As the population study consisted of patients and volunteers, an Institutional Review Board was not necessary.

Statistical analysis

Statistical software, STATA 8.1 (Stata Corporation, College Station, TX, USA) was used for statistical analysis. A statistical analysis was carried out to determine the association between microbial aetiology and clinical settings, and microbial aetiology and type of onset of endophthalmitis. Pearson's χ^2 test was used for analysis, and P-value <0.05 was considered to be statistically significant.

Results

Table 1 summarizes the culture positivity of the patients with endophthalmitis who underwent microbiological evaluation according to the clinical setting. During the study period of 10 years, a total of 955 patients with endophthalmitis underwent microbiological analysis and

a single eye was infected in all cases. Of 955, 424 (44.4%) were found to be culture positive for microbial growth, of which 413 (97.4%) had exogenous endophthalmitis and 11 (2.6%) had EE. The rate of culture positivity was found to be higher among aspirates from exogenous endophthalmitis (46.7%; 413 of 884) when compared with EE (15.5%; 11 of 71) (P < 0.0001). The rate of culture positivity of specimens from eyes with post-surgical endophthalmitis (36%; 225 of 625) was found to be significantly lower than those obtained from eyes with endophthalmitis due to trauma (65%; 141 of 217) (P < 0.001), microbial keratitis (100%; 43 of 43) (P < 0.001), and microbial scleral abscess (100%; 4 of 4) (P = 0.008). The rate of culture-proven endophthalmitis was found to be higher among acute onset than chronic onset both in post-surgical (66.2%; 149 of 225, including 28 fulminant onset) and post-traumatic endophthalmitis (68.8%; 97 of 141, including 23 fulminant onset). The growth patterns of microbes isolated from intraocular aspirates, corneal scrapes, scleral scrapes, and blood specimens collected from patients with culture-proven endophthalmitis, according to the duration of onset, are presented in Table 2.

Microbial pathogens recovered from eyes with infectious endophthalmitis are documented in Table 3. Of the total of 424 patients with culture-proven endophthalmitis, 364 (85.8%) had bacterial aetiology and the remaining 60 (14.2%) had fungal aetiology. Among bacteria, CoNS (30.5%; 111 of 364) were the predominant isolates followed by *Streptococcus pneumoniae* (22.3%; 81 of 364) and *Pseudomonas aeruginosa* (11.5%; 42 of 364), whereas among fungal isolates recovered, *Aspergillus* spp. (60%; 36 of 60) were the most common isolates followed by *Fusarium* spp. (33.3%; 20 of 60). Among

Table 1 Patients with endophthalmitis who underwent microbiological evaluation between January 1997 and December 2006 according to the clinical settings

Sl no	c. Categories of endophthalmitis	No. of patients/eyes that underwent microbiological evaluation	No. of patients whose intraocular aspirates, corneal scrapes, scleral scrapes and/or blood specimens were positive for microbial growth (%)
1	Total no. of patients/eyes with exogenous endophthalmitis	884	413 (46.7)
	(i). No. of patients/eyes with endophthalmitis after intraocular surgeries	625	225 (36)
	(ii). No. of patients/eyes with endophthalmitis after penetrating ocular injuries	217	141 (65)
	(iii). No. of patients/eyes with endophthalmitis associated with microbial keratitis	43	43 (100)
	(iv). No. of patients/eyes with endophthalmitis associated with microbial scleral abscess	4	4 (100)
2	Total no. of patients/eyes with endogenous endophthalmitis	71	11 (15.5)
	Total no. of patients/eyes (%)	955	424 (44.4)

Table 2 Microbial growth pattern of intraocular aspirates, corneal scrapes, scleral scrapes, and blood specimens collected from patients with infectious endophthalmitis presenting at a tertiary eye care referral centre in South India between January 1997 and December 2006

Name of the specimens collected from patients with endophthalmitis	Total no. of eyes with endophthalmitis positive for microbial	No. of eyes with exogenous endophthalmitis positive for microbial growth													
	growth	Eyes with endophthalmitis after intraocular surgeries positive for microbial growth					Eyes with en penetrating ocu micro	Endophthalmitis associated with microbial keratitis positive for microbial growth		Endophthalmitis associated with scleral abscess positive for microbial growth		No. of eyes with endogenous endophthalmitis positive for microbial growth			
		Total no. (%)	No. of eyes with fulminant type of endo- phthalmitis: < 4 days	No. of eyes with acute type of endo- phthalmitis: 4 days-6 weeks	No. of eyes with chronic type of endo- phthalmitis: > 6 weeks	Total no. (%)	No. of eyes with fulminant type of endo- phthalmitis: <4 days	No. of eyes with acute type of endo- phthalmitis: 4 days–6 weeks	No. of eyes with chronic type of endo- phthalmitis: > 6 weeks	Total no. (%)	No. of eyes with chronic type of endo- phthalmitis: > 6 weeks		No. of eyes with chronic type of endo- phthalmitis: >6 weeks	Total no. (%)	No. of eyes with chronic type of endo- phthalmitis: > 6 weeks
1. Vitreous humour	40	19	0	6	13	21	0	7	14	NA	NA	NA	NA	NA	NA
alone collected 2. Anterior and vitreous humour	326	206	28	115	63	120	23	67	30	NA	NA	NA	NA	NA	NA
were collected 3. Anterior and vitreous humour, and corneal scrapes	31	NA	NA	NA	NA	NA	NA	NA	NA	31	31	NA	NA	NA	NA
were collected 4. Both vitreous humour and corneal scrapes	12	NA	NA	NA	NA	NA	NA	NA	NA	12	12	NA	NA	NA	NA
were collected 5. Both vitreous humour and scleral scrapes	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	4	4	NA	NA
were collected 6. Anterior and vitreous humour, and blood specimens were	3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	3	3
7. Both vitreous humour and blood specimens were collected	8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	8	8
Conceieu	424	225 (53.1)	28/225 (12.4)	121/225 (53.8)	76/225 (33.8)	141 (33.3)	23/141 (16.3	74/141 (52.5)	44/141 (31.2)	43 (10.1)	43/43 (100)	4 (0.94)	4/4 (100)	11 (2.6)	11/11 (100)

NA: not applicable.

Table 3 Microbial pathogens recovered from intraocular aspirates, corneal scrapes, scleral scrapes, and blood specimens collected from patients with infectious endophthalmitis presenting at a tertiary eye care referral centre in South India

no.	Microbial isolates ecovered from eyes vith infectious indophthalmitis	Total no. of isolates (%)	Microorganisms recovered from eyes with exogenous endophthalmitis													organisms ered from es with ogenous uthalmitis
			Eyes with endophthalmitis after intraocular surgeries				Е	penetrating ocular injuries					Endophthalmitis Eyes with associated with microbial keratitis associated with scleral abscess			Eyes with chronic type of endo- phthalmitis:
			Total no. (%)	Eyes with fulminant type of endo-phthalmitis: < 4 days	Eyes with acute type of endo- phthalmitis: 4 days-6 weeks	Eyes with chronic type of endo- phthalmitis: >6 weeks	Total no. (%)	Eyes with fulminant type of endo-phthalmitis:	Eyes with acute type of endo- phthalmitis: 4 days–6 weeks	Eyes with chronic type of endo- phthalmitis: >6 weeks	Total no. (%)	Eyes with chronic type of endo- ph thalmitis: >6 weeks	Total no. (%)	Eyes with chronic type of endo- phthalmitis: >6 weeks		>6 weeks
1	Total no. of bacterial isolates	364 (85.8)	213 (94.7)	28	118	67	109 (77.8)	23	65	21	27 (62.8)	27	4 (100)	4	11 (100)	7
	(i). No. of Gram-positive cocci	233 (55)	162 (72)	7	97	58	55 (39)	5	35	15	7 (16.3)	7	2 (50)	2	7 (63.6)	7
	Coagulase-positive staphylococci	111	83	6	76	1	27	1	13	13					1	1
	Staphylococcus aureus	14	7		7		3		3		1	1	1	1	2	2
	Streptococcus pneumoniae	81	62	1	13	48	9	2	7		6	6	1	1	3	3
	Streptococcus viridans	27	10		1	9	16	2	12	2					1	1
	(ii). No. of Gram-positive bacilli	30 (7.1)	6 (2.7)	0	3	3	23 (16.3)	2	21	0	1 (2.3)	1	0	0	0	0
	Corynebacterium spp.	15	6		3	3	9	1	8							
	Bacillus spp.	15	0				14	1	13		1	1				
	(iii). No. of actinomycetes	24 (5.7)	10 (4.4)	0	4	6	10 (7)	1	3	6	3 (7)	3	1 (25)	1	0	0
	Nocardia spp.	24	10		4	6	10	1	3	6	3	3	1	1		
	(iv). No. of Gram-negative bacilli	77 (18.2)	35 (15.6)	21	14	0	21 (14.9)	15	6	0	16 (37.3)	16	1 (25)	1	4 (36.4)	4
	Pseudomonas aeruginosa	42	20	12	8		8	6	2		11	11	1	1	2	2
	E. coli	12	6	4	2		3	2	1		2	2			1	1
	Klebsiella spp.	9	2	2			4	2	2		2	2			1	1
	Proteus mirabilis	3	1	1			1	1			1	1				
	Enterobacter spp.	8	5	2	3		3	2	1							
	Acinetobacter spp.	3	1		1		2	2								
2	Total no. of fungal isolates	60 (14.2)	12 (5.3)	0	3	9	32 (22.7)	0	9	23	16 (37.2)	16	0	0	0	0
	(i). Yeast-like organisms	2 (0.5)	1 (0.4)	0	0	1	1 (0.7)	0	0	1	0 (0)	0	0	0	0	0
	Candida albicans	2	1			1	1			1						
	(ii). Filamentous fungus	58 (13.7)	11 (4.9)		3	8	31 (22)		9	22	16 (37.2)	16	0	0	0	0
	Aspergillus spp.	36	8		2	6	18		5	13	10	10				
	Fusarium spp.	20	3		1	2	13		4	9	4	4				
	Bipolaris sp.	1	0								1	1				
	Curvularia sp.	1	0								1	1				
	Total no. of isolates (%)	424 (100)	225 (100)	28	121	76	141 (100)	23	74	44	43 (100)	43	4 (100)	4	11 (100)	11



post-surgical endophthalmitis, Gram-negative bacilli (75%; 21 of 28) were the predominant cause for developing fulminant infection, Staphylococcus spp. (68.6%; 83 of 121) for acute infection, and *Streptococcus* spp. (75%; 57 of 76) for chronic infection, whereas among cases of post-traumatic endophthalmitis, Gram-negative bacilli (65.2%; 15 of 23) were the most common cause for fulminant infection, Gram-positive bacilli (28.4%; 21 of 74), Streptococcus spp. (25.7%; 19 of 74), and Staphylococcus spp. (21.6%; 16 of 74) acute infection and fungi (52.3%; 23 of 44) chronic infection. The predominant microbial pathogen causing endophthalmitis associated with microbial keratitis was filamentous fungi (37.2%; 16 of 43) and Gram-negative bacilli (37.2%; 16 of 43), followed by S. pneumoniae (14%; 6 of 43). Gram-negative bacilli (36.4%; 4 of 11) and Streptococcus spp. (36.4%; 3 of 11) were predominant isolates from patients with EE.

A total of 111 CoNS were isolated; their prevalence was significantly higher in acute onset post-surgical endophthalmitis (73.9%; 82 of 111 total CoNS isolates) than the prevalence of CoNS in other forms of endophthalmitis (26.1%; 29 of 111) (P < 0.0001), whereas S. pneumoniae was more prevalent in chronic onset postsurgical endophthalmitis (59.3%; 48 of 81 total isolates) than in other forms of endophthalmitis (40.7%; 33 of 81) (P<0.0001). Gram-positive bacilli produced significantly higher numbers of acute onset post-traumatic endophthalmitis (70%; 21 of 30 total isolates) than other forms of endophthalmitis (30%; 9 of 30) (P<0.0001). Nocardia spp. were more frequently found in chronic onset post-surgical (25%, 6 of 24 total isolates, P = 0.073), post-traumatic (25%, 6 of 24, P = 0.041), and endophthalmitis associated with microbial keratitis (100%; 3 of 3). Gram-negative bacilli were frequently associated with fulminant onset than acute or chronic onset in both post-surgical (27.3%, 21 of 77 total Gramnegative bacilli, P < 0.001) and post-traumatic endophthalmitis (19.5%, 15 of 77, P < 0.001). Filamentous fungi were found predominantly among cases with posttraumatic endophthalmitis (53.5%; 31 of 58 total fungal isolates) compared to endophthalmitis associated with microbial keratitis (27.6%, 16 of 58, P = 0.058) and postsurgical endophthalmitis (19%, 11 of 58, P < 0.001). The prevalence of Gram-positive bacilli was found to be higher in causing post-traumatic endophthalmitis (76.7%; 23 of 30 total isolates) rather than other forms of endophthalmitis (23.3%; 7 of 30) (*P* < 0.001).

The antibacterial susceptibilities of bacterial isolates recovered from eyes with endophthalmitis are presented in Table 4. The highest percentage of Gram-positive cocci were susceptible to both cefazolin (100%) and moxifloxacin (100%) followed by chloramphenicol (98.3%), vancomycin (96.6%), and gatifloxacin (95.3%). The Gram-positive bacilli were susceptible in highest

percentage to amikacin (100%) and all four tested fluoroquinolones, ciprofloxacin (100%), ofloxacin (100%), gatifloxacin (100%), and moxifloxacin (100%). Amikacin (100%), gatifloxacin (100%), and moxifloxacin (100%) showed highest efficacy against Nocardia spp. of endophthalmitis isolates. The highest percentage of Gram-negative bacilli were susceptible to gatifloxacin (100%), amikacin (100%), ciprofloxacin (97.4%), and ofloxacin (97.4%). Overall, gatifloxacin (97.7%) showed the highest activity against bacterial endophthalmitis isolates followed by ciprofloxacin (95.9%) and ofloxacin (95.1%). A comparative analysis of the antibacterial susceptibilities of bacterial isolates, according to the clinical settings, is presented in Table 5.

Discussion

A wide range of microorganisms that enter the eye from the external environment or by haematogenous spread cause endophthalmitis. Recovery of these causative organisms is an important step in the management of infective endophthalmitis. The rate of recovery depends on the clinical settings, method of specimen collection and inoculation, load of viable microbes in the inoculum, previous medical therapy, and the environment in which the inoculated plates are incubated. 17-19 In this study, 100% recovery rate achieved in endophthalmitis following corneal and scleral infections, whereas it accounted for 65% in post-traumatic (141 of 217), 36% in post-surgical (225 of 625), and 15.5% in EE (11 of 71). In comparison, higher recovery rates are documented in many studies from postoperative endophthalmitis (67% in EVS, 9,16 53% in South India, 20 60% in Canada, 21 67% in Australia,²² and 75% in Sweden²³). Many factors may have contributed to this, the most likely factor being that the patients were treated for infections before they were referred to tertiary care. On the other hand, the high rates in corneal and scleral infections could have been due to a large load of virulent organisms.

We found that bacteria (85.8%; 364 of 424) were followed by fungi (14.2%; 60 of 424) as the most common causative organisms, supported by Puliafito et al⁸ study. The most frequently isolated bacterial species were CoNS (26.2%; 111 of 424) followed by S. pneumoniae (19.1%; 81 of 424), similar to the findings in various other studies.^{2,8} We found that CoNS (62.8%; 76 of 121) were the principal cause for acute post-surgical endophthalmitis along with S. pneumoniae (10.7%; 13 of 121), compared to the Gramnegative bacilli (75%; 21 of 28), especially P. aeruginosa (43%; 12 of 28), for fulminant onset. These findings are similar to those in various studies. 6,24,25 In comparison, the predominant cause for chronic post-surgical endophthalmitis was Streptococcus species (75%; 57 of 76) followed by fungi (11.8%; 9 of 76). This, however, is in

Table 4 *In vitro* antibacterial susceptibilities of bacterial isolates recovered from intraocular aspirates, corneal scrapes, scleral scrapes, and blood specimens collected from patients with infectious endophthalmitis presenting at a tertiary eye care referral centre in South India between January 1997 and December 2006

Microbial isolates recovered from eyes with infectious endophthalmitis	No. of the susceptible bacterial isolates/no. of the tested isolates (% of the susceptible isolates) against common antibacterial agents by Kirby–Bauer disc diffusion methods												
	Cz	Ce	Ca	Ak	Tb	G	Nx	Cf	Of	Gf	Мо	Ch	Va
(i). Total no. of Gram-positive cocci	233/233 (100)	208/233 (89.3)	216/233 (92.7)	134/233 (57.5)	128/233 (54.9)	128/233 (54.9)	214/233 (91.9)	222/233 (95.3) 2	219/233 (94)	55/57 (96.5)	57/57 (100)	229/233 (98.3)	225/233 (96.6)
Coagulasepositive staphylococci	111/111 (100)	94/111 (84.7)	99/111 (89.2)	109/111 (98.2)	94/111 (84.7)	94/111 (84.7)	103/111 (92.8)	103/111 (92.8)	103/111 (92.8)	26/28 (92.9)	28/28 (100)	109/111 (98.2)	111/111 (100)
Staphylococcus aureus	14/14 (100)	10/14 (71.4)	12/14 (85.7)	14/14 (100)	12/14 (85.7)	12/14 (85.7)	12/14 (85.7)	12/14 (85.7)	12/14 (85.7)	5/5 (100)	4/4 (100)	14/14 (100)	14/14 (100)
Streptococcus oneumoniae	81/81 (100)	80/81 (98.8)	80/81 (98.8)	5/81 (6.2)	16/81 (19.8)	16/81 (19.8)	78/81 (96.3)	81/81 (100)	81/81 (100)	18/18 (100)	18/18 (100)	81/81 (100)	76/81 (93.8)
Streptococcus viridans	27/27 (100)	24/27 (88.9)	25/27 (92.6)	6/27 (22.2)	6/27 (22.2)	6/27 (22.2)	21/27 (77.8)	23/27 (85.2)	26/27 (96.3)	6/6 (100)	6/6 (100)	25/27 (92.6)	24/27 (88.9)
(ii). Total no. of Gram-positive bacilli	29/30 (96.7)	25/30 (83.3)	27/30 (90)	30/30 (100)	27/30 (90)	27/30 (90)	27/30 (90)	30/30 (100)	30/30 (100)	8/8 (100)	8/8 (100)	26/30 (86.7)	26/30 (86.7)
Corynebacterium spp.	15/15 (100)	13/15 (86.7)	15/15 (100)	15/15 (100)	13/15 (86.7)	13/15 (86.7)	13/15 (86.7)	15/15 (100)	15/15 (100)	3/3 (100)	3/3 (100)	13/15 (86.7)	13/15 (86.7)
Bacillus spp.	14/15 (86.7)	12/15 (80)	12/15 (80)	15/15 (100)	14/15 (86.7)	14/15 (86.7)	14/15 (86.7)	15/15 (100)	15/15 (100)	5/5 (100)	5/5 (100)	13/15 (86.7)	13/15 (86.7)
(iii). Total no. of aerobic actinomycetes	0/24 (0)	10/24 (41.7)	11/24 (45.3)	24/24 (100)	12/12 (50)	12/12 (50)	12/12 (50)	22/24 (91.7)	22/24 (91.7)	6/6 (100)	6/6 (100)	10/24 (41.7)	12/24 (50)
Nocardia spp.	0/24 (0)	10/24 (41.7)	11/24 (45.8)	24/24 (100)	12/12 (50)	12/12 (50)	12/12 (50)	22/24 (91.7)	22/24 (91.7)	6/6 (100)	6/6 (100)	10/24 (41.7)	12/24 (50)
(iv). Total no. of Gram-negative bacilli	2/77 (2.6)	43/77 (55.8)	59/77 (76.6)	74/77 (96.1)	69/77 (89.6)	69/77 (89.6)	72/77 (93.5)	75/77 (97.4)	75/77 (97.4)	16/16 (100)	4/16 (25)	35/77 (45.5)	6/77 (7.8)
Pseudomonas veruginosa	2/42 (4.8)	24/42 (57.1)	38/42 (90.5)	40/42 (95.2)	38/42 (90.5)	38/42 (90.5)	39/42 (92.9)	41/42 (97.6)	41/42 (97.6)	8/8 (100)	3/8 (37.5)	19/42 (45.2)	5/42 (11.9)
E. coli	0/12 (0)	8/12 (66.7)	8/12 (66.7)	11/12 (91.7)	10/12 (83.3)	10/12 (83.3)	11/12 (91.7)	11/12 (91.7)	11/12 (91.7)	3/3 (100)	0/3 (0)	6/12 (50)	0/12 (0)
Klebsiella spp.	0/9 (0)	3/9 (33.3)	3/9 (33.3)	9/9 (100)	8/9 (88.9)	8/9 (88.9)	8/9 (88.9)	9/9 (100)	9/9 (100)	2/2 (100)	0/2 (0)	3/9 (33.3)	0/9 (0)
Proteus mirabilis	0/3 (0)	2/3 (66.7)	2/3 (66.7)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	_	_	1/3 (33.3)	0/3 (0)
Enterobacter spp.	0/8 (0)	4/8 (50)	6/8 (75)	8/8 (100)	7/8 (87.5)	7/8 (87.5)	8/8 (100)	8/8 (100)	8/8 (100)	2/2 (100)	1/2 (50)	4/8 (50)	1/8 (12.5
Acinetobacter spp.	0/3 (0)	2/3 (66.7)	2/3 (66.7)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	1/1 (100)	0/1 (0)	2/3 (66.7)	0/3 (0)
Total no. of susceptible isolates/no. of tested isolates (% of the susceptible isolates)	264/364 (72.5)	286/364 (78.6)	313/364 (86.0)	262/364 (72.0)	236/364 (64.8)	236/364 (64.8)	325/364 (89.3)	349/364 (95.9)	346/364 (95.1)	85/87 (97.7)	75/87 (86.2)	300/364 (82.4)	269/364 (73.9

Cz: cefazolin; Ce: cephotaxime; Ca: Ceftazidime; Ak: amikacin; Tb: tobramycin; G: gentamicin; Nx: norfloxacin; Cf: ciprofloxacin; Of: ofloxacin; Gf: gatifloxacin; Mo: moxifloxacin; Ch: chloraphenicol; Va: vancomycin.

bacilli

 Table 5
 Comparative in vitro antibacterial susceptibilities of bacterial isolates recovered from eyes with endophthalmitis according to the clinical settings

Microbial isolates recovered from eyes with infectious	No. of bacterial isolates recovered	No. of the susceptible bacterial isolates/no. of the tested isolates (% of the susceptible isolates) against common antibacterial agents by Kirby–Bauer disc diffusion methods												
endophthalmitis		Cz	Се	Са	Ak	Tb	G	Nx	Cf	Of	Gf	Мо	Ch	Va
Post-surgical		168/213 (79)	186/213 (87)	201/213 (94)	159/213 (75)	154/213 (72)	154/213 (72)	207/213 (97)	211/213 (99)	211/213 (99)	48/50 (96)	44/50 (88)	185/213 (87)	176/213 (82)
endophthalmitis Gram-positive cocci		162/162 (100)	154/162 (95.1)	159/162 (98.2)	108/162 (66.7)	107/162 (66.1)	107/162 (66.1)	160/162 (98.8))160/162 (98.8)	160/162 (98.8)	34/36 (94.4)	36/36 (100)	161/162 (99.4)	162/162 (100)
Gram-positive bacilli	6	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	3/3 (100)	3/3 (100)	6/6 (100)	6/6 (100)
Aerobic actinomycetes	10	0/10 (0)	4/10 (40)	4/10 (60)	10/10 (100)	6/10 (60)	6/10 (60)	6/10 (60)	10/10 (100)	10/10 (100)	2/2 (100)	2/2 (100)	4/10 (40)	6/10 (60)
Gram-negative bacilli	35	0/35 (0)	22/35 (62.9)	32/35 (91.4)	35/35 (100)	35/35 (100)	35/35 (100)	35/35 (100)	35/35 (100)	35/35 (100)	9/9 (100)	3/9 (33.3)	14/35 (40)	2/35 (5.7)
Post-traumatic	109	80/109 (73)	94/109 (86)	102/109 (94)	80/109 (73)	68/109 (62)	68/109 (62)	101/109 (93)	107/109 (98)	107/109 (98)	26/26 (100)	23/26 (89)	94/109 (86)	85/109 (78)
endophthalmitis Gram-positive cocci		55/55 (100)	50/55 (90.9)	53/55 (96.4)	26/55 (47.3)	21/55 (38.2)	21/55 (38.2)	54/55 (98.2)) 53/55 (96.4)	53/55 (96.4)	15/15 (100)	15/15 (100)	54/55 (98.2)	55/55 (100)
Gram-positive bacilli	23	23/23 (100)	19/23 (82.6)	21/23 (91.3)	23/23 (100)	21/23 (91.3)	21/23 (91.3)	21/23 (91.3)	23/23 (100)	23/23 (100)	5/5 (100)	5/5 (100)	20/23 (87)	20/23 (87)
Aerobic actinomycetes	10	0/10 (0)	6/10 (60)	7/10 (70)	10/10 (100)	5/10 (50)	5/10 (50)	5/10 (50)	10/10 (100)	10/10 (100)	2/2 (100)	2/2 (100)	6/10 (60)	6/10 (60)
Gram-negative bacilli	21	2/21 (9.5)	19/21 (90.5)	21/21 (100)	21/21 (100)	21/21 (100)	21/21 (100)	21/21 (100)	21/21 (100)	21/21 (100)	4/4 (100)	1/4 (25)	14/21 (66.7)	4/21 (19)
Associated with microbial keratitis	27	7/27 (26)	4/27 (15)	6/27 (22)	17/27 (63)	9/27 (33)	9/27 (33)	12/27 (44)	22/27 (82)	19/27 (70)	5/27 (19)	3/27 (11)	10/27 (37)	4/27 (15)
Gram-positive cocci	7	7/7 (100)	2/7 (28.6)	2/7 (28.6)	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)	6/7 (85.7)	3/7 (42.9)	2/3 (66.7)	2/3 (66.7)	6/7 (85.7)	4/7 (57.1)
Gram-positive bacilli	1	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	NA	NA	01/(0)	0/1 (0)
Aerobic	3	0/3 (0)	0/3 (0)	0/3 (0)	3/3 (100)	1/3 (33.3)	1/3 (33.3)	1/3 (33.3)	1/3 (33.3)	1/3 (33.3)	1/1 (100)	1/1 (100)	0/3 (0)	0/3 (0)
actinomycetes Gram-negative bacilli	16	0/16 (0)	2/16 (12.5)	4/16 (25)	13/16 (81.2)	8/16 (50)	8/16 (100)	11/16 (68.8)) 14/16 (87.5)	14/16 (87.5)	2/2 (100)	0/2 (0)	4/16 (25)	0/16 (0)
Associated with scleral	4	2/4 (50)	0/4 (0)	0/4 (0)	2/4 (50)	1/4 (25)	1/4 (25)	1/4 (25)	3/4 (75)	3/4 (75)	3/4 (75)	3/4 (75)	2/4 (50)	0/4 (0)
abscess Gram-postive cocci	2	2/2 (100)	0/2 (0)	02/(0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)	1/2 (50)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)
Gram-positive bacilli	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Aerobic actinomycetes	1	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)
Gram-negative	1	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	NA	NA	1/1 (100)	0/1 (0)

Table 5 (Continued)

,	No. of bacterial isolates recovered		No. of the susceptible bacterial isolates/no. of the tested isolates (% of the susceptible isolates) against common antibacterial agents by Kirby–Bauer disc diffusion methods													
endophthalmitis	•	Cz	Се	Ca	Ak	Tb	G	Nx	Cf	Of	Gf	Мо	Ch	Va		
Endogenous endophthalmitis	11	7/11 (64)	2/11 (18)	4/11 (36)	4/11 (36)	4/11 (36)	4/11 (36)	4/11 (36)	6/11 (55)	6/11 (55)	3/3 (100)	2/3 (67)	9/11 (82)	4/11 (36)		
Gram-positive cocci	7	7/7 (100)	2/7 (28.6)	2/7 (28.6)	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)	2/7 (28.6)	2/2 (100)	2/2 (100)	7/7 (100)	4/7 (57.1)		
Gram-positive bacilli	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		
Aerobic actinomycetes	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		
Gram-negative bacilli		0/4 (0)	0/4 (0)	2/4 (50)	4/4 (100)	4/4 (100)	4/4 (100)	4/4 (100)	4/4 (100)	4/4 (100)	1/1 (100)	0/1 (0)	2/4 (50)	0/4 (0)		
Total no. of susceptible isolates/no. of tested isolates (% of susceptible isolates)	364	264/364 (72.5)2	86/364 (78.6)3	13/364 (86.0)2	62/364 (72.0)2	36/364 (64.8)2	36/364 (64.8)3	25/364 (89.3)3	49/364 (95.9)3	46/364 (95.1)8	35/87 (97.7):	75/87 (86.2)3	00/364 (82.4)2	69/364 (73.9)		

Cz: cefazolin; Ce: cephotaxime; Ca: Ceftazidime; Ak: amikacin; Tb: tobramycin; G: gentamicin; Nx: norfloxacin; Cf: ciprofloxacin; Of: ofloxacin; Gf: gatifloxacin; Mo: moxifloxacin; Ch: chloraphenicol; Va: vancomycin; NA: not applicable.



contrast with the findings by Anand et al (4.8% of Streptococcus spp.) who showed a higher rate of fungal infection (35.7%).24 In our study, the most common fungal isolates were Aspergillus spp. (7.9%; 6 of 76), in contrast with studies from the Western countries.²⁶⁻²⁸

In post-traumatic endophthalmitis, the predominant organisms identified were filamentous fungi (22%; 31 of 141), followed by CoNS (19%; 27 of 141), and Grampositive bacilli (16.3%; 23 of 141). In fulminant cases, Gram-negative bacilli were predominant (65.2%; 15 of 23), whereas in acute onset, Bacillus sp. (17.6%; 13 of 74) and CoNS (17.6%; 13 of 74) followed by Streptococcus viridans (16.2%; 12 of 74) were frequently isolated. Filamentous fungi (50%; 22 of 44) were the major cause of chronic onset post-traumatic endophthalmitis in our study. A study review of the literature shows that posttraumatic endophthalmitis is associated with a wide variety of micro-organisms derived from the environment,^{2–4} and *Bacillus* spp. and fungi, respectively, have been reported as the second and third most common organisms after staphylococci.^{2,4,6} Bacillus endophthalmitis develops particularly in the setting of retained intraocular foreign bodies,²⁹ whereas fungal endophthalmitis is mainly associated with intraocular injuries with vegetable matter or soil contamination.^{2,30}

In cases of endophthalmitis associated with microbial keratitis, the most common isolates were Gram-negative bacteria (37.2%; 16 of 43) and fungi (37.2%; 16 of 43), comparable to the findings of Scott et al.7 Patients with microbial keratitis caused by unusually virulent organisms or the ones not responding to medical therapy are more likely to develop endophthalmitis. In vitro susceptibility testing of the organism recovered from cases with microbial keratitis showed high virulent and multi-drug resistance due to topical antimicrobial therapy. Scleral abscess was caused by Pseudomonas aeruginosa, S. pneumoniae, S. aureus, Proteus, and Nocardia spp. as well as atypical mycobacteria infection.³¹ Such virulent organisms causing diffuse scleral infection may spread to infect intraocular tissue leading to endophthalmitis. In the current series, endophthalmitis associated with scleral abscess is encountered in a few cases owing to Nocardia sp., Pseudomonas aeruginosa, S. aureus, and S. pneumoniae, and these isolates are resistant to most of the commonly used antibacterials.

Endogenous endophthalmitis occurs when organisms reach the eye through the bloodstream. A review of the literature shows that EE comprises 2–17% of the cases of infectious endophthalmitis.⁵ In the current series, it is estimated at 2.6% (11 of 424) of all culture-proven endophthalmitis. The most common cause for EE identified in this study is Gram-positive cocci (63.6%; 7 of 11), of which S. pneumoniae (27.3%; 3 of 11) and S. aureus (18.2%; 2 of 11) are predominantly isolated.

Gram-negative bacilli are responsible for 36.4% (4 of 11) of the EE; including, Pseudomonas aeruginosa (18.2%; 2 of 11), E. coli (9%; 1 of 11) and Klebsiella pneumoniae (9%; 1 of 11). Unlike postoperative endophthalmitis, EE is rarely caused by CoNS. Similarly, Streptococcus species and S. aureus have been reported to be the predominant bacterial pathogens causing EE. 9,10 Conversely, a higher incidence of enteric Gram-negative microorganisms causing EE has been reported in many series with predominance of Klebsiella spp. and E. coli.2 Wong et al reported the increased incidence of Klebsiella spp. EE in the East Asian region.³² Another trend is the increasing incidence of Pseudomonas EE among patients with cystic fibrosis, immunosuppression, and endocarditis.³³

In this study, the fourth-generation fluoroquinolone, gatifloxacin (97.7%; 85 of 87) demonstrated greatest activities against endophthalmitis bacterial isolates followed by second-generation fluoroquinolones, ciprofloxacin (95.9%; 349/364), and ofloxacin (95.1%; 346 of 364). The other fourth-generation fluoroquinolone, moxifloxacin revealed a higher rate of efficacy against Gram-positive cocci (100%; 57/57), Gram-positive bacilli (100%; 8 of 8), and *Nocardia* spp. (100%; 6/6). The firstgeneration cephalosporin, cefazolin, shows higher effectiveness against Gram-positive cocci (100%; 233 of 233), compared to third-generation drugs (cefotaxime (89%; 208 of 233) and ceftazidime (92.7%; 216 of 233)). Among aminoglycosides, amikacin revealed higher efficacy against gram-positive bacilli (100%; 30 of 30), Nocardia spp. (100%; 24 of 24), and Gram-negative bacilli (96%; 74 of 77). Similarly, Anand et al²⁴ reported a higher activity of cefazolin (92.6%) against Gram-positive isolates and ciprofloxacin (73.2%) against Gram-negative isolates. Chloramphenicol, a broad-spectrum antibiotic, showed a higher rate of efficacy against Gram-positive cocci (98.3%; 229 of 233); however, chloramphenicol is not routinely used because of its toxicity.

The analysis on the *in vitro* susceptibility pattern shows variation among the susceptibility of isolates from different clinical settings. It is thought that with frequent and persistent long-term use of a given antibiotic, there is a greater chance of bacterial strains developing resistance to that drug.34,35 High antibiotic resistance strains of bacteria recovered from endophthalmitis associated with scleral abscess, with microbial keratitis, and with EE suggest the same. The percentage of susceptibility was less in these cases compared to post-surgical and posttraumatic endophthalmitis (Table 5 and Figure 1). The indiscriminate use or misuse and prolonged antibiotic use appear to be a major factor in the development of drug resistance, as also the transformation of drugresistant plasmid or DNA molecule among normal flora of extra-ocular surface.35 It must be noted that the conventional Kirby-Bauer disc diffusion method of

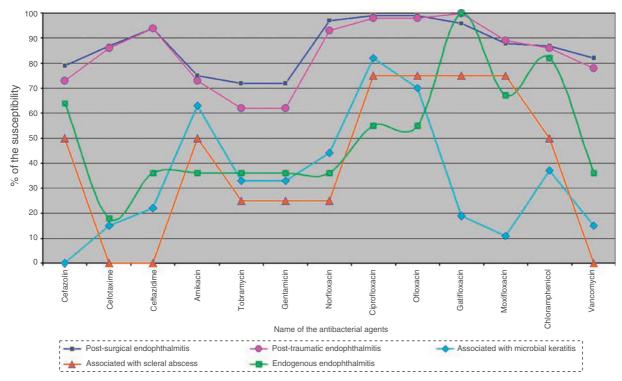


Figure 1 Diagrammatic representation of the comparative *in vitro* antibacterial susceptibilities of bacterial isolates recovered from eyes with endophthalmitis according to the clinical settings.

in vitro antibacterial susceptibility testing may not directly apply to ocular pathogens, as the results of disc diffusion susceptibility tests relate to the level of drug achievable in serum and do not relate directly to the concentration of drug produced in the pre-ocular tear film and ocular tissues by standard routes of administration.¹⁵ With this current study, we document the microbiological profile of infectious endophthalmitis; this will help in evidence-based management of endophthalmitis.

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