# Etiology and epidemiological analysis of glaucoma-filtering bleb infections in a tertiary eye care hospital in south India

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Purpose: To evaluate the microbial etiology and associated risk factors among patients with blebitis following trabeculectomy. Materials and Methods: A retrospective analysis of all culture-proven blebitis was performed in patients who underwent trabeculectomy between January 2004 and December 2008. A standardized form was filled out for each patient, documenting sociodemographic features and information pertaining to risk factors. Swabbing of the infected bleb surface was performed for all suspected cases and further subjected to microbiological analysis. Results: A total of 23 patients with culture-proven blebitis were treated during the study period, with a mean age of 59.2 years (59.2 ± SD: 12.8; range, 30-81 years). Duration of onset was early ( $\leq$  36 months) in six (26%) cases and late (> 36 months) in 17 (74%) cases with a range between 15 and 144 months (mean, 82.91 months; SD: 41.89). All 23 blebs were located superiorly and of which, 21 (91%) were microcystic avascular, 1 (4%) diffuse avascular, and 1 (4%) vascular flattened. The predominant risk factor identified was bleb leak (35%; 8 of 23) followed by thin bleb (22%; 5 of 23) and blepharitis (17%; 4 of 23). Bleb leaks (100%) were recorded only in patients with late onset ( $\geq$  9 years) of infection (P < 0.001), while the incidence of ocular surface disease (100%) occurred early ( $\leq 3$  years) (P < 0.001). Use of topical steroids was associated frequently with cases of thin blebs (80%; 4 of 5) (P < 0.001), while topical antibiotics showed bleb leaks (88%; 7 of 8) (P< 0.001). Coagulase-positive staphylococci were frequently recovered from blebitis with thin blebs (71%; 5 of 7) (P = 0.001), Coagulase-negative staphylococci (CoNS) with bleb leak (100%; 8 of 8) (P< 0.001), Corynebacterium with blepharitis (100%; 3 of 3) (P = 0.001), and Streptococci with releasable sutures (75%; 3 of 4) (P = 0.001). Conclusion: Bleb leak is the principal risk factor responsible for late-onset blebitis, while early-onset blebitis could be ascribed to ocular surface diseases. Streptococci were mainly responsible for early onset of infection, while the late onset was due to CoNS.

**Key words:** Blebitis, bleb leak, microbiology, ocular surface diseases, risk factors

Trabeculectomy is a partial thickness glaucoma filtering surgery commonly performed to control the intraocular pressure when medical therapy or laser fails. The surgery is associated with various bleb complications, most frequently under filtration due to bleb failure, over filtration with hypotony, bleb leaks, bleb encapsulation, and bleb infection.<sup>[1,2]</sup> Eyes with filtering blebs face a constant risk of infection which may occur after decades of the initial surgery. Blebitis is a microbial infection of the glaucoma filtering bleb, without any clinically apparent vitreous involvement. Blebitis after trabeculectomy is a wellknown potentially dangerous complication that can lead to endophthalmitis, as the normal barriers to intraocular infections by bacteria are weakened.[3,4] Variety of risk factors that are responsible for bleb infections include inferior location of the bleb site, thin-walled blebs, trauma, the use of contact lenses, bleb leaks, infectious ocular adnexal diseases, long-term

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use of topical steroids, systemic diseases such as diabetes, malnutrition, or compromised immune system, and the use of releasable sutures.<sup>[1,2]</sup> Bleb infections are mainly caused by resident and transient flora, of which *Streptococcus* species was found to be the commonest cause for bleb-associated infections.<sup>[5,6]</sup> Considering the importance of blebitis as a cause for intraocular infection, a proper understanding of the risk factors predisposing to blebitis and causative microbial agents are a must for early recognition and prevention of endophthalmitis. This study delineates the microbial etiology and risk factors in patients with blebitis who underwent incisional glaucoma surgery at a tertiary eye care referral center in South India.

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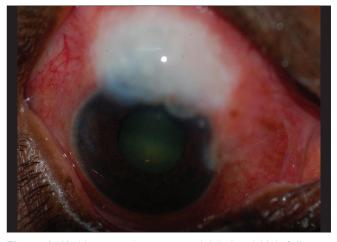
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## Materials and Methods

A retrospective analysis was conducted after approval of Institutional Review Board of Aravind Eye Hospital on all case records exhibiting culture-proven blebitis among patients who had undergone trabeculectomy surgery at a tertiary eye care referral center in south India from January 2004 to December 2008. Blebitis was clinically diagnosed in patients who represented with history of redness, photophobia, conjunctival discharge, intense peribleb-conjunctival congestion, opalescent bleb (white or red appearance), epithelial defects (a positive Seidel's test) with or without anterior chamber reaction, and the absence of vitritis [Fig. 1].<sup>[7]</sup> The diagnosis of infectious

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**Figure 1:** Highly avascular cystic multilobulated bleb following trabeculectomy with mitomycin-c, developed infection after three years, shows infected bleb with severe circumcorneal congestion

blebitis was confirmed by the significant microbial growth in swab cultures obtained from bleb surfaces. Cases of iritis, purulent conjunctivitis, or ulcerative blepharitis without bleb infiltration were excluded. Seidel's test was performed in all the clinically suspected cases before being subjected to microbiological evaluation. The data protocol followed for each patient with blebitis comprised of documentation of sociodemographic features, associated clinical features, duration of symptoms, duration of surgery, predisposing risk factors and associated ocular conditions, systemic diseases, and information pertaining to the history of medical therapy. After detailed ocular examinations, bleb cultures were collected from bleb surfaces using sterile swab pre-moistened with brain heart infusion broth and were subjected to microbiological analysis based on the standard protocols.<sup>[8]</sup> Swab cultures were made on blood agar (supplemented with 5% defibrinated sheep blood), chocolate agar, and Sabouraud dextrose agar, inoculated into thioglycolate medium and brain heart infusion broth. Smears were also made from swabs for direct microscopic identification by Gram's stain.

The inoculated blood agar, chocolate agar, thioglycolate broth, and brain heart infusion broth were incubated at 37°C under 5%  $CO_{\gamma}$  examined daily, and discarded at 7 days if growth was absent. The inoculated Sabouraud dextrose agar plates were incubated at 27°C under biochemical oxygen demand, examined daily, and were discarded at 3 weeks if there was no growth.<sup>[8]</sup> Microbial cultures were considered significant if growth of the same organism was demonstrated on more than one solid phase medium, and/or if growth of one medium was consistent with direct microscopy findings (that is, appropriate staining and morphology with Gram stain).<sup>[8]</sup> The isolated bacterial strains were identified up to species level by using standard biochemical tests.<sup>[9]</sup> The in vitro susceptibility testing was performed by Kirby-Bauer disc diffusion method and interpreted using Clinical and Laboratory Standards Institute serum standards.<sup>[10]</sup> The antibacterial agents used were constantly tested for their consistency in efficacy against standard ATCC (American Type Culture Collection) bacteria (Staphylococcus aureus ATCC 25923, Streptococcus pneumoniae ATCC 49619, Haemophilus influenzae ATCC 49241, Pseudomonas *aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922) as a general quality control laboratory procedure.

Statistical software STATA version 8.1 (Stata Corporation LP, College Station, Texas, USA) was used to carry out all analyses. Data are expressed in terms of mean  $\pm$  standard deviation for continuous variables; number (%) for categorical variables. Pearson's Chi-square test (Yates Corrected) was used to determine the association between the predisposing risk factors identified and the isolated microbial etiology found responsible for the development of blebitis, and also to determine the significance in the onset of infection and predisposing risk factors identified. *P*< 0.05 was considered statistically significant.

#### Results

During the study period of five years, a total of 51 patients with clinical diagnosis of blebitis having a history of incisional glaucoma surgery were evaluated and underwent microbiological evaluation at our institute. Of the 51 patients, 23 eyes of 23 patients showed significant bacterial growth in microbial culture. All the trabeculectomies were performed by a senior glaucoma consultant of the institute using standard surgical procedures; 19 (83%) were males and four (17%) were females. Their ages ranged from 30 to 81 years, with a mean of 59.17 ± SD: 12.75. Most of them (91%) had trabeculectomy for primary open-angle glaucoma. The mean duration between the trabeculectomy performed and the onset of blebitis was 82.9 months (SD: 41.9; range: 15 to 144 months). Twelve (52%) patients had used topical steroids and eight (35%) had used topical antibiotics for more than 6 months beyond the postoperative period. Apart from patients with blebitis, ocular adnexal diseases were noted in seven (30%), nasolacrimal duct obstruction in three (13%), and systemic diseases in six (26%) patients. Most (91.3%) of the blebs were functioning as avascular [Table 1].

Factors predisposing to blebitis in all the 23 patients were classified into primary risk factors which directly influenced the infection and secondary risk factors that in one way or the other influenced blebitis. In all patients, more than one risk factor predisposed to blebitis [Table 2]. The most common primary and secondary risk factors encountered were bleb leak (35%; 8 of 23) and the use of topical steroids (12, 52%), respectively. Patients with blebitis-associated bleb leaks (100%; 8 of 8 bleb leaks) were recorded only in cases with late onset of infections  $(\geq 9 \text{ years})$  (89%; 8 of 9 late onset of infections) (P<0.001), while those with ocular adnexal diseases (blepharitis, conjunctivitis, and dacryocystitis) (86%; 6 of 7 ocular surface infections) were seen exclusively during the early onset of infection ( $\leq$  3 years) (100%; 6 of 6 early onset of infections) (P< 0.001). Blebitis associated with thin blebs were exhibited among patients using topical steroids continuously (80%; 4 of 5 thin blebs) (P < 0.001), while the use of topical antibiotics too was significantly noted among patients with blebitis associated with bleb leaks (88%; 7 of 8 bleb leaks) (*P*< 0.001).

All the 23 culture swabs obtained from bleb surfaces of patients showed bacterial growth. The predominant bacterial isolate recovered in this study was *Staphylococcus* species (65%; 15 of 23), of which *Staphylococcus aureus* (26%; 6 of 23) was frequently isolated. All three strains of *Corynebacterium xerosis* were recovered from blebitis associated with blepharitis (100%)

#### Table 1: Demographic and clinical characteristics of patients with culture-proven blebitis treated at tertiary eye care center in South India

Characteristics	No. of eyes (%)
Age	
Mean <u>+</u> SD	59.17 <u>+</u> 12.75
Range	30 - 81 years
30 - 35 years	2 (9)
36 - 40 years	1 (4)
41 - 45 years	1 (4)
46 - 50 years	1 (4)
51 - 55 years	3 (13)
56 - 60 years	2 (9)
61 - 65 years	5 (22)
66 - 70 years	5 (22)
71 - 75 years	2 (9)
76 - 80 years	0
81 - 85 years	1 (4)
Sex	
Male	19 (83)
Female	4 (17)
Eye	. ()
Right	10 (43)
Left	13 (57)
Glaucoma diagnosis	
Primary glaucoma	
Primary open angle	21 (91)
Primary angle closure glaucoma	2 (9)
Location of filter	2 (0)
Superior 12 'O clock	23 (100)
Duration between trabeculectomy per	
symptoms	
Mean ± SD	82.91 <u>+</u> 41.89
Range	15 to 144 months
<24 months	1 (4)
24 - 36 months	5 (22)
37 - 48 months	1 (4)
49 - 60 months	1 (4)
61 - 72 months	1 (4)
73 - 84 months	1 (4)
85 - 96 months	3 (13)
97 - 108 months	3 (13)
109 - 120 months	2 (9)
120 - 132 months	2 (9)
133 - 144 months	3 (13)
Conjunctival flap	0 (10)
Limbal based	2 (9)
Fornix based	21 (91)
Type of bleb	21 (01)
Functioning	
Microcystic avascular	21 (01)
Diffuse avascular	21 (91)
	1 (4)
Non-functioning Vascularized	1 (1)
vascularizeu	1 (4)

Antimetabolites	
Mitomycin-C (0.02% for 2 minutes)	23 (100)
5-FU	0
Type of surgery	
Trabeculectomy alone	21 (91)
Trabeculectomy with phacoemulsification	2 (9)
and posterior capsular IOL implantation	
Systemic diseases	
Hypertension	2 (9)
Diabetic mellitus	2 (9)
Asmatic	2 (9)
Use of topical steroids	
Intermittent use	8 (35)
Continuous and chronic use	4 (17)
Use antibiotics	
Intermittent use	7 (30)
Continuous and chronic use	1 (4)
Nasolacrimal duct potency	
Free	20 (87)
Not free with clear fluid	2 (9)
Not free with pus and mucus	1 (4)
Early postoperative complication if any	
Flat anterior chamber	1 (4)
Early wound leak	0
Bleb leak	
Early onset of bleb leak (<9 years)	0
Late onset of bleb leak ( $\geq$ 9 years)	8 (35)
Status of the bleb walls on presentation	
Thin wall	5 (22%)
Type of sutures	
Releasable sutures	3 (13)
Fixed scleral flap	20 (87)
Ocular surface diseases	
Blepharitis	4 (17)
Conjunctivitis	2 (9)
Dacryocystitis	1 (4)

(P = 0.001). More number of *Streptococcus* species were isolated from blebitis associated with releasable sutures (75%; 3 of 4 total Streptococcus isolates) than any other ocular conditions (25%; 1 of 4) (P = 0.001). Coagulase-positive staphylococci (CoPS) were recovered significantly from blebitis associated with thin bleb (71%; 5 of 7 total CoPS) than in cases with any other ocular conditions (29%; 2 of 7) (P = 0.001). All the coagulasenegative staphylococci (CoNS) were recovered only from blebitis associated with bleb leak (100%; 8 of 8) (P< 0.001). All the three Streptococcus pneumoniae (100%) were recovered only from blebitis associated with obstruction of nasolacrimal duct (P = 0.001) [Table 3]. All the CoNS recovered were from blebitis that occurred during the late postoperative period, > 8 year (P < 0.001), whereas the bacterial isolates that were recovered from blebitis associated with eye lid infections represented C. xerosis to be significantly associated with early postoperative period (*P*< 0.001) [Table 4].

Viewing the antibacterial susceptibility nature, it was extrapolated that the large percentage of bacterial isolates were

Name of risk factors Total Direction between	Total					ration b	hetween	the tra		Dirration hetween the trahecidectomy nerformed	arforme	o pue p	nset of	and onset of the infection in months	ction in	month	U			
identified	number of cases (%)	15	24	26	30	36	40	56	72	80	86	96	100	108	110	115	122	130	133	144
Primary risk factors						ĝ					;	ģ		Q						í.
l otal number of cases (%)	23 (100)	1 (4) 1 (4)		1 (4)	1 (4)	2 (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)	1 (4)	Z (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)
Blepharitis	4 (17)	1 (25)	1 (25)	0	1 (25)	1 (25)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivitis	2 (9)	0	0	1 (50)	0	0	0	0	0	0	0	0	0	1 (50)	0	0	0	0	0	0
Bleb leak	8 (35)	0	0	0	0	0	0	0	0	0	0	0	0	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	2 (25)
Thin bleb	5 (22)	0	0	0	0	0	0	0	1 (20)	0	1 (20)	2 (40)	1 (20)	0	0	0	0	0	0	0
Releasable sutures	3 (13)	0	0	0	0	0	1 (33)	1 (33)	0	1 (33)	0	0	0	0	0	0	0	0	0	0
Dacryocystitis	1 (4)	0	0	0	0	1 (100)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secondary possible risk factors																				
Total number of cases (%)	23 (100)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)	1 (4)	2 (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)
Nasolacrimal duct obstruction	3 (13)	0	0	0	0	1 (33)	1 (33)	1 (33)	0	0	0	0	0	0	0	0	0	0	0	0
Continuous and chronic use of topical antibiotics	1 (4)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (100)
Intermittent use of topical antibiotics	7 (30)	0	0	0	0	0	0	0	0	0	0	0	1 (14)	1 (14)	1 (14)	1 (14)	1 (14)	0	1 (14)	1 (14)
Continuous and chronic use of topical steroids	4 (17)	1 (25)	1 (25)	1 (25)	1 (25)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Intermittent use of topical	8 (35)	0	0	0	0	-	0	0	-	-	-	2 (25)	0	-	0	0	0	-	0	0

Name of the bacterial	<b>Total number</b>	Primary ri	isk factors	associate	d with bl	Primary risk factors associated with blebitis Number (%)	oer (%)	Sec	ondary fact	Secondary factors associated with blebitis. Number (%)	d with blebitis.	. Number ('	(%
species isolated	of isolates (%)	Blepharitis	Conjun- ctivitis	Bleb leak	Thin bleb	Relesable sutures	Dacryo- cystitis	Total number of isolates (%)	Nasola- crimal duct obstruct- ion	Continuous and chronic use of topical antibiotics	Intermittent use of topical antibiotics	Conti- nuous and chronic use of topical steroids	Inter- mittent use of topical steroids
Haemophilus influenzae	1 (4)	0	1(100)	0	0	0	0	1 (4)	0	0	0	1 (100)	0
Corynebacterium xerosis	3 (13)	3 (100)	0	0	0	0	0	3 (13)	0	0	0	2 (67)	1 (33)
Streptococcus species	4 (17)	0	0	0	0	3 (75)	1 (25)	4 (170)	3 (75)	0	0	0	1 (25)
S. pneumoniae	3 (13)	0	0	0	0	2 (67)	1 (33)	3 (13)	3 (100)	0	0	0	0
S. viridans group	1 (4)	0	0	0	0	1 (100)	0	1 (4)	0	0	0	0	1 (100)
Staphylococcus species	15 (65)	1 (7)	1 (7)	8 (53)	5 (33)	0	0	15 (65)	0	1 (7)	7 (47)	1 (7)	6 (40)
Coagulase positive	7 (30)	1 (17)	1 (15)	0	5 (71)	0	0	7 (30)	0	0	÷	-	4
S. aureus	6 (26)	1 (17)	1 (17)	0	4 (67)	0	0	6 (26)	0	0	۲	-	4
S. intermedius	1 (4)	0	0	0	1 (100)	0	0	1 (4)	0	0	0	0	-
Coagulase negative	8 (35)	0	0	8 (100)	0	0	0	8 (35)	0	-	9	0	-
S. epidermidis	2 (9)	0	0	2 (100)	0	0	0	2 (9)	0	0	2 (100)	0	0
S. hominis	3 (13)	0	0	3 (100)	0	0	0	3 (13)	0	1 (33)	1 (33)	0	1 (33)
S. caprae	2 (9)	0	0	2 (100)	0	0	0	2 (9)	0	0	2 (100)	0	0
S. saccharolyticus	1 (4)	0	0	1 (100)	0	0	0	1 (4)	0	0	1 (100)	0	0
Total no. of isolates (%)	23 (100)	4 (17)	2 (9)	8 (35)	5 (22)	3 (13)	1 (4)	23 (100)	3 (13)	1 (4)	7 (30)	4 (17)	8 (35)

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Name of risk factors	Total				Dur	<b>Duration between</b>	tween t	the trat	eculect	the trabeculectomy performed	rformed	and	onset of t	he infe	of the infection in months	month	S			
identified	number of cases (%)	15	24	26	30	36	40	56	72	80	86	96	100	108	110	115	122	130	133	144
Haemophilus influenzae	1 (4)	0	0	0	0	0	0	0	0	0	0	0	0	1 100)	0	0	0	0	0	0
Corynebacterium xerosis	3 (13)	1 (33)	1 (33)	0	0	1 (33)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Streptococcus species	4 (17)	0	0	0	0	1 (25)	1 (25)	1 (25)	0	1 (25)	0	0	0	0	0	0	0	0	0	0
S. pneumoniae	3 (13)	0	0	0	0	1 (33)	1 (33)	1 (33)	0	0	0	0	0	0	0	0	0	0	0	0
S. viridans group	1 (4)	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0	0	0	0	0
										(100)										
Staphylococcus species	15 (65)	0	0	1 (7)	1 (7)	0	0	0	1 (7)	0	1 (7)	2 (13)	1 (7)	1 (7)	1 (7)	1 (7)	1 (7)	1 (7)	1 (7)	2 (13)
Coagulase positive	7 (30)	0	0	1 (14)	1 (14)	0	0	0	1 (14)	0	(14)	-	(14)	0	0	0	0	0	0	0
S. aureus	6 (26)	0	0	1 (17)	1 (17)				1 (17)	0	(17)	1 (17) 1	(17)	0	0	0	0	0	0	0
S. intermedius	1 (4%)	0	0	0	0	0	0	0	0	0	0	100)	0	0	0	0	0	0	0	0
Coagulase negative	8 (35)	0	0	0	0	0	0	0	0	0	0	0	0	. (13)	(13)	1 (13)	1 (13)	1 (13)	1 (13)	2 (25)
S. epidermidis	2 (9)	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0	1 (50)	0	0	1 (50)	0
S. hominis	3 (13)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (33)	1 (33)	0	1 (33)
S. caprae	2 (9)	0	0	0	0	0	0	0	0	0	0	0	0	0	l (50)	0	0	0	0	1 (50)
S. saccharolyticus	1 (4)	0	0	0	0	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0
Total number (%)	23 (100)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)	1 (4)	(100) 2 (9)	1 (4)	1 (4)	1 (4)	1 (4)	1 (4)	2 (9)

susceptible to chloramphenicol (100%) followed by vancomycin (97%) and cefazolin (96%) [Table 5]. *Staphylococcus* spp. showed 100% susceptibility against chloramphenicol, vancomycin, cefazolin, amikacin, tobramycin, and gentamicin, whereas Streptococci portrayed 100% susceptibility against cefazolin, cefotaxime, chloramphenicol, and vancomycin. *Corynebacterium* spp. exhibited a higher susceptibility against chloramphenicol, vancomycin, vancomycin, cefazolin, and ofloxacin.

#### Discussion

Blebitis is infrequent, but if left untreated, may lead on to endophthalmitis after glaucoma filtering surgery. Blebitis is a mucopurulent infiltrate that is seen within the bleb along with or without anterior segment inflammation, whereas endophthalmitis is associated with the evidence of inflammation of the vitreous.[11] Literature reviews indicate that the normal flora of eyelids and conjunctiva are responsible for the development of blebitis. The present study demonstrates the role of resident or transient ocular bacterial flora with the predominance of Staphylococcus species (65%) in causing blebitis in trabeculectomized eyes. Several studies have reported Staphylococcus species to be the most common organism responsible for blebitis.<sup>[12-14]</sup> In addition, Staphylococcus species, especially CoNS, have been framed to be the common cause for the early onset of bleb-associated endophthalmitis which are similar to that of acute-onset endophthalmitis after cataract surgery.<sup>[15,16]</sup>

The analysis on the association between bacterial etiology isolated and the duration of the onset of disease revealed the significant association of CoNS with the late onset of blebitis (> 3 years) due to bleb leaks. Staphylococci neither produce exotoxins nor do they have the ability to penetrate intact conjunctiva.<sup>[17]</sup> However, it is possible that higher incidences of Staphylococcus species among blebitis with bleb leaks may allow less virulent bacteria to easily enter bleb and intraocular spaces.<sup>[12]</sup> Bacterial isolates recovered from blebitis associated with ocular surface diseases such as C. xerosis, S. aureus, and S. pneumoniae were recovered significantly during the early onset of infection ( $\leq$  3 years). Blepharitis, conjunctivitis, and dacryocystitis are the most important sources for infection of blebs and the association of *C. xerosis* in blepharitis cases, S. aureus in conjunctivitis, and S. pneumoniae in dacryocystitis demonstrates the source from ocular surfaces. It has been suggested that blebs associated with ocular surface infectious diseases become more susceptible to infection with the etiology of surface infection registering greater microbial load from infected sites. Higher prevalence of Streptococcus species during the late onset of bleb-associated endophthalmitis have also been reported.<sup>[5,6,18,19]</sup> Whereas, in the present study, the prevalence of Streptococcus species accounting to 75% in the early onset group of blebitis were associated with dacryocystitis and releasable sutures in those nasolacrimal ducts were obstructed. Thus, it seems that the higher prevalence of Streptococcus species in the early onset of blebitis is due to the presence of nasolacrimal duct obstruction in these cases.

The most common risk factor identified was bleb leaks (35%) and its association was found to be highly significant with the late onset of blebitis ( $\geq$  9 years). Higher incidence of bleb leak among eyes with bleb-related infection have been documented.<sup>[2]</sup> It has been outlined that in bleb infections

associated with bleb leaks, the bacterial pathogens itself create a hole in the bleb first before entering the eye and causing infection, while the other school of thought stresses that once a hole is created, the pathogenic bacteria in the tear film invades and causes infection.<sup>[20,21]</sup> It needs to be emphasized that the tear film directly has an access to the anterior chamber through leaking filtering bleb and hence, it provides an uninterrupted passage way into the anterior chamber for infectious organisms.<sup>[22]</sup> In addition, most of the bleb leak cases had used topical antibiotics beyond the prescribed period following trabeculectomy. The use of prophylactic topical antibiotics beyond the prescribed postoperative periods have been reported and their strong association with an increased risk of bleb-related infections have been lucidly portrayed.<sup>[20,21,23]</sup> Next to bleb leaks, thin blebs too were frequently encountered, especially among blebitis after 6 to 8 years of the postoperative period from which CoPS were isolated, whose association was highly significant. In addition, 80% of the cases examined had used topical corticosteroids. Probably, the chronic use of topical corticosteroids in eyes that have undergone trabeculectomy can lead to the thinning of conjunctiva, and later become susceptible to highly virulent bacterial strains like S. aureus. The indiscriminate use of topical corticosteroids can damage the ocular tissues and lead to the increased risk of infection.<sup>[24]</sup>

All cases of blebitis associated with releasable sutures were caused by *Streptococcus* sp. and the association was highly significant. In addition, 67% of the releasable suture cases had nasolacrimal duct obstruction as secondary risk factors, with the association of Streptococcal infection in blebs further confirming the source of infection and Streptococci as the most common etiological agent. Since most bacterial isolates recovered in this study were the normal flora of conjunctiva and eyelids, it is important for an ophthalmologist to be aware the risk of infection of blebs by normal bacterial flora in post of trabeculectomy eyes.

In the present study, chloramphenicol is appeared to be 100% effective against the bacterial isolates recovered from blebitis. Chloramphenicol is a broad-spectrum bacteriostatic antibiotic widely used against Gram-positive and Gram-negative bacterial ocular infections.<sup>[25]</sup> Although chloramphenicol is an effective antibiotic, its use has been implicated in systemic hemotoxicity<sup>[26]</sup> and fatal aplastic anemia.<sup>[27]</sup> Vancomycin is a glycopeptide exhibiting greatest potency against blebitis pathogens, except *H. influenzae*. Similarly, the first-generation cephalosporin and cefazolin also revealed greatest activity here against the Gram-positive bacteria. However, vancomycin and cefazolin are not available as topical formulations and must be prepared for topical usage.

Aminoglycosides, especially amikacin and tobramycin, also depicted good activity against *Staphylococcus, Corynebacterium*, and *Haemophilus* species, whereas it was inactive against Streptococci. Among fluoroquinolones, gatifloxacin alone portrayed inhibition, with 74% of bacterial isolates showing good activity. One possible explanation for this could be attributed to the frequent and routine use of fluoroquinolones in ophthalmological preoperative preparations and postoperative management leading to antibiotic resistance among bacterial pathogens. It is of prime significance to note that fluoroquinolones resistance among streptococci and CoNS are common in ocular surface infections.<sup>[28]</sup>The current analysis

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	No. of		Number o	Number of bacterial i	isolates susceptible / number of bacterial isolates tested (percentage of bacterial isolates susceptible)	ceptible / n	umber of	bacterial is	olates test	ed (percei	ntage of ba	acterial isol	ates susco	eptible)	
bacterial isolates	tested iso- lates	Amikacin	Tobra- mycin	Genta- micin	Cefazolin	Cefota- xime	Ceftazi- dime	Norflo- xacin	Cipro- floxacin	Oflo- xacin	Levoflo- xacin	Gatiflo- xacin	Moxiflo- xacin	Chloram- phenicol	Vanco- mycin
<i>Staphylococcus</i> species	15	15/15 (100)	15/15 (100)	15/15 (100)	15/15 (100) 12/15 (80)	12/15 (80)	11/15 (37)	7/15 (47)	9/15 (60)	7/15 (47) 7/15 (47)		13/15 (87)	10/15 (67)	15/15 (100)	15/15 (100)
Coagulase-positive	7	7/7 (100)	7/7 (100)	7/7 (100)	7/7 (100)	4/7 (57)	4/7 (57)	3/7 (43)	4/7 (57)	3/7 (43)	4/7 (57)	6/7 (86)	4/7 (57)	7/7 (100)	7/7 (100)
S. aureus	9	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)	4/6 (67)	4/6 (67)	3/6 (50)	4/6 (67)	3/6 (50)	4/6 (67)	5/6 (83)	4/6 (67)	6/6 (100)	6/6 (100)
S. intermedius	-	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)
Coagulase-negative	8	8/8 (100)	8/8 (100)	8/8 (100)	8/8 (100)	8/8 (100)	7/8 (88)	4/8 (50)	5/8 (63)	4/8 (50)	4/8 (50)	7/8 (88)	6/8 (75)	8/8 (100)	8/8 (100)
S. epidermidis	2	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	1/2 (50)	1/2 (50)	1/2 (50)	1/2 (50)	2/2 (100)	1/2 (100)	2/2 (100)	2/2 (100)
S. hominis	ю	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	2/3 (67)	1/3 (33)	2/3 (67)	1/3 (33)	1/3 (33)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)
S. caprae	0	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)	2/2 (100)
S. saccharolyticus	-	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
<i>Streptococcus</i> species	4	0/4 (0)	0/4 (0)	0/4 (0)	4/4 (100)	4/4 (100)	3/4 (75)	3/4 (75)	3/4 (75)	3/4 (75)	3/4 (75)	3/4 (75)	3/4 (75)	4/4 (100)	4/4 (100)
S. pneumoniae	ო	0/3 (0)	0/3 (0)	0/3 (0)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3(100)	3/3 (100)
S. viridans group	-	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Corynebacterium xerosis	ო	3/3 (100)	1/3 (33)	0/3 (0)	3/3 (100)	1/3 (33)	0/3 (0)	1/3 (33)	0/3 (0)	3/3 (100)	0/3 (0)	0/3 (0)	0/38 (0)	3/3 (100)	3/3 (100)
Haemophilus influenzae	-	1/1 (100)	1/1 (100) 1/1 (100) 1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	1/1(100)	1/1 (100)	1/1 (100) 1/1 (100) 1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (100)	1/1 (100)	0/1 (100)
Total no. of susceptible/total number tested (%)	23	19/23 (83)	19/23 (83) 17/23 (74) 16/23 (70)	16/23 (70)	22/23 (96)	18/23 (78)	15/23 (65)	12/23 (52)	12/23 (52) 13/23 (57)	14/23 (61)	11/23 (48)	16/23 (74)	13/23 (57)	23/23 (100)	22/23 (97)

on the *in vitro* antibacterial susceptibilities lucidly reveal and emphasize that the predominant etiology of blebitis being Gram-positive bacteria, chloramphenicol, vancomycin, and cefazolin are proven choices for treating post-trabeculectomy infections and could be advocated. In conclusion, bleb leak is the principal risk factor for blebitis of late onset, while the early-onset blebitis could be associated with ocular surface diseases. *Staphylococcus* species are the predominant bacterial pathogen recovered in this study, and are mainly associated with late onset, especially CoNS, while the early onset was due to *Streptococcus* species. Since Gram-positive bacteria (96%) are found to be the predominant cause for blebitis in this study; chloramphenicol, vancomycin, and cefazolin are proven choices of antibiotic for treating post-trabeculectomy infections.

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