Endophthalmitis Panorama in The Jerusalem Area

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Abstract

Purpose: The spectrum of microbial infections and the pattern of their susceptibility is variable among communities. Researching this data will lead to the establishment of the most appropriate national management strategies. The purpose of this study was to analyze the epidemiological, clinical, microbial spectrum and antibiotic susceptibility of endophthalmitis cases in a tertiary referral center in Jerusalem.

Methods: Retrospective review of medical charts of patients presenting with endophthalmitis over a 12-year-period.

Results: Included were 74 eyes of 70 patients (males 56%). Mean age±SD at presentation was 60±19.5 years. Exogenous endophthalmitis accounted for 78% of cases; of which, 62% followed an intraocular surgery, 21% occurred after intravitreal injections, 10% followed infectious keratitis and 7% were post-traumatic. Endogenous cases were predominantly observed in diabetic patients. Microbial isolates were identified in 44 samples. Of them, gram-positive bacteria were the predominant microorganisms detected in 33 samples (75%); Staphylococcus epidermidis and Enterococcus faecalis were the most commonly detected pathogens.

Mean presenting±SD LogMAR visual acuity (VA) was 2.38±1.21 and it improved at last follow-up to 1.7±1.37 (*p=0.004*, paired t-test). Cases secondary to gram-positive microbes were associated with improved VA during the follow-up while cases secondary to gram-negative microbes was correlated with poor final VA (*p=0.046*, r^2=0.4). There was no evidence of bacterial resistance in the antibiograms for either vancomycin, ceftazidime, ceftriaxone or amikacin.

Conclusions: Intraocular surgery remains the most common event preceding endophthalmitis with coagulase-negative staphylococci being the most frequently detected microorganisms. The microbial spectrum of endophthalmitis is similar to that in the western world.

Introduction

Endophthalmitis is one of the most dreadful entities in Ophthalmology. Whether of exogenous or endogenous origin, the consequences for the visual function and globe integrity could be poor. The infection involves the inner layers of the eye producing a vitreous exudate that characterizes the disease. The majority of cases are related to intraocular surgery. Exogenous cases especially those related to trauma and endogenous cases pose a challenge for the ophthalmologist who needs to institute prompt and effective treatment in order to obtain the best possible results [1-3].

Characterizing the epidemiological data is important in order to reveal the spectrum of the most common pathogens, their susceptibility/resistance profile, the predisposing conditions and to determine the best empirical antibiotic regimen to use. This data will lead to the establishment of the most appropriate management strategies. The spectrum of microbial infections and the pattern of their susceptibility is variable among communities [1-3]. To date, there are no publications that studied the microbial spectra and the antibiotic susceptibility in the Jerusalem area. The aim of the present study is to analyze the epidemiological, clinical, microbial spectra and antibiotic susceptibility of patients diagnosed with endophthalmitis in a tertiary referral center in Jerusalem.

Methods

This is a retrospective study in which the medical records of patients diagnosed with endophthalmitis between the years 2007- 2019 were reviewed. Data retrieved from the medical files included demographic features, year of presentation, type of endophthalmitis (exogenous, endogenous), the inciting event in exogenous cases and the underlying illnesses in exogenous and endogenous endophthalmitis, systemic and local therapy, surgical management including lapse of time between presentation and surgical intervention, specific microorganism isolated by cultures and susceptibility according to the antibiogram.

The ocular examination included collection of vitreous and/or aqueous humor samples either by pars plana vitrectomy or tap. The samples were inoculated onto blood agar, chocolate agar and thioglycolate broth and incubated at 37°C for bacterial isolation. Until 2012, bacterial isolates were identified by classical biochemical methods (sugar fermentation tests). From 2012 and on, isolates were identified mainly by matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDi TOF-MS, VITEK MS, bioMérieux, France).

Antibiotic susceptibility testing of the isolates was performed using disk diffusion method, E-test or VITEK MS. The antibiotic susceptibilities were determined according to the criteria of the Clinical and Laboratory Standards Institute (CLSI).

Samples were concomitantly evaluated for fungal infections. They were stained by calcofluor white dye and were cultured on sabouraud dextrose agar and incubated at 25°C for up to 2 weeks. From 2007-2012, identification of Candida and filamentous fungi was based on microscopic appearance and the use of CHROMagar culture medium and API ID 32C (bioMérieux, France). From 2012 and on, isolates were identified mainly by Matrix-Assisted Laser Desorption Ionization Time-of-Flight mass spectrometry (MALDi TOF-MS, VITEK MS, bioMérieux, France). Susceptibility testing was performed using the E-test method according to manufacturer's instructions (bioMérieux, France).

Presenting visual acuity (VA) and VA at one month and at last follow-up, ophthalmic manifestations and ocular complications were recorded. LogMAR (log of the minimum angle of resolution) notation was used to compute the change in VA. VA of £ 6/60 was defined as severe visual loss, VA of > 6/60 - <6/12 was defined as moderate visual loss and VA of ³ 6/12 was defined as good VA.

The institutional review board of the hospital approved the study, including waiver of informed consent for this chart review study. The study was conducted adhering to the tenets of the Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using SPSS (version 26.0; IBM Corp., Armonk, NY). Measure of VA was summarized using means, standard deviation (SD), median and range. Test for normality of data was first performed using the Kolmogorov–Smirnov and Shapiro–Wilk analysis. As the data were normally distributed, the comparison of VA at baseline and during the follow-up was performed using paired student's t-test. Where appropriate, sensitivity analysis using nonparametric Wilcoxon-signed rank tests or chi-square were performed. A univariate regression analysis was used to assess the correlation between the final VA and the microbe type, positivity of blood and vitreous cultures, presenting signs and symptoms, source and etiology of the infection, immune system status and treatment modality. In case both variables appeared to be statistically significant, a multivariate regression analysis was carried out. P value <0.05 was considered as statistically significant.

Results

Demographic features

Included were 74 eyes of 70 patients (39 males (56%)) diagnosed with endophthalmitis based on the clinical presentation. Mean±SD age at presentation was 60±19.5 years (median 59, range 3-90). Endophthalmitis was of an exogenous etiology in the majority of eyes (58 eyes, 78%). Mean follow-up time was 24 months (median 24 months, range 1 month- 8 years).

Exogenous Endophthalmitis (ExE)

Of the 58 eyes with ExE, 36 eyes (62%) presented following an eye operation, 12 eyes (21%) presented after intravitreal anti-vascular endothelial growth factor (VEGF) injection, six eyes (10%) presented secondary to infectious keratitis and four eyes (7%) presented after a penetrating trauma of the globe (**Table 1**).

Of the 36 postoperative cases: Seventeen eyes (47%) were infected following cataract extraction and intraocular lens (IOL) implantation, 10 eyes (28%) after glaucoma procedures, four eyes (11%) after vitrectomy, four eyes (11%) after combined phacoemulsification and vitrectomy and one eye (3%) after penetrating keratoplasty (**Table 1**).

Positive vitreous cultures were obtained in 35 (60%) out of the 58 eyes (57 patients), all of which indicated bacterial infection. Eleven patients (19%) had diabetes mellitus type 2 (DM2) and two were on immunosuppressive medications because of lupus in one patient and after bone marrow transplantation in another patient.

Endogenous Endophthalmitis (EnE)

EnE was observed in 16 (22%) eyes of 13 patients. Ten of them (77%) were occultly or overtly immunocompromised **(Table 2)** (5 patients (38%) had DM2).

Positive vitreous cultures were obtained in nine eyes (56%), of them; fungal infection was detected in five eyes (56%) and bacterial infection in four eyes (44%). Fungal isolates included Candida in four samples and Pseudallescheria boydii in one sample (**Table 2, 3**). Bacterial infections included Streptococcus anginosus, Streptococcus salivarius, Staphylococcus aureus and Staphylococcus epidermidis.

Three patients had bilateral EnE **(Table 2)**: in patient #4, Candida albicans was isolated from the vitreous sample of one eye, in patient #9 it was presumed to be fungal because of the compatible clinical findings on funduscopy and in patient #10 it was secondary to Methicillin-resistant staphylococcus aureus (MRSA) isolated from blood sample.

Microbial Spectrum

Table 3 presents the microbial isolates from the 44 (59%) culture-positive samples. Gram-positive bacteria were the most commonly isolated microorganisms, detected in 33 samples (75%). Gram-negative bacteria were isolated in six (14%) and fungi were present in five samples (11%).

Among all the 44 isolates, Staphylococcus epidermidis was the most commonly isolated microbe present in 14 samples (32%). Enterococcus faecalis was the second most commonly detected microbe observed in four samples (9%).

Clinical Presentation

All patients were symptomatic. The majority of patients (41 patients, 59%) presented with a combination of symptoms. The most common presenting symptom was deterioration of vision reported by 50 patients (71%). Thirty-four patients (49%) presented with pain, 30 patients (43%) presented with eye redness and 14 patients (20%) presented with eye discharge.

Mean presenting LogMAR±SD VA was 2.38±1.21 and even though it remained poor throughout the entire study, it improved at one month of follow-up to 1.68±1.29 (*p=0.002*, paired t-test) and at the last visit to 1.7±1.37 (*p=0.004*, paired t-test, baseline VA compared to VA of last visit). At presentation, 56 eyes (76%) had severe visual loss and this significantly decreased to 42 eyes (57%) by the last follow-up (*p= 0.004*) (**Table 4**). On the other hand, only 7 eyes (9%) had good VA at presentation and this significantly increased to 17 eyes (23%) at the last follow-up (*p= 0.02*). Subgroup analysis by the microorganism type (**Figure 1**) demonstrated improvement in VA at one month and at the last visit in comparison to baseline VA in eyes with gram-positive endophthalmitis (2.17±1.24 at presentation vs. 1.35±1.18 and 1.34±1.34, respectively, *p=0.06*, *p=0.09*, paired t-test). VA in eyes with gram-negative endophthalmitis did not improve (2.75±1.19 at presentation vs. 2.41±1.16 and 2.55±1.21, respectively, *p= 0.45, p=0.62*, paired t-test). On first presentation, hypopyon was observed in 41 eyes (55%), dense vitritis obscuring the view of the fundus in 55 eyes (74%) and retinal infiltrates in 10 eyes (14%).

Univariate and multivariate analysis were used to assess the correlation between last VA and microbe type, positivity of blood and vitreous cultures, presenting signs and symptoms, source and etiology of the infection, immune system status and treatment modality. In those models, cases secondary to gram-positive microbes were associated with improved VA during the follow-up while cases secondary to gram-negative microbes were correlated with poor final VA ($p=0.046$, $r^2=0.4$). **Figure 1** shows the changes in VA throughout the study period per microorganism type.

Ocular Complications

The most common complication was rhegmatogenous retinal detachment, documented in 12 eyes (16%). Phthisis bulbi developed in 12 eyes (16%), five of which were eviscerated/enucleated (**Table 5**). The mean age± SD of patients who developed phthisis bulbi was 68± 20 years (median 72 years, females 58%). The preceding events were cataract operation in four eyes, infectious keratitis in three eyes, glaucoma filtering valve in two eyes, intravitreal injection in two eyes and endogenous fungal endophthalmitis after near-drowning in one eye. In six eyes (50%), no pathogen was isolated. The most commonly isolated microorganism was Enterococcus faecalis in two eyes. Mycobacterium chelonae, Streptococcus mitis, Streptococcus agalactiae, and

Pseudallescheria boydii were each isolated in one eye. Of the five eyes that were enucleated/eviscerated, no growth was documented in three eyes whereas Mycobacterium chelonae and Pseudallescheria boydii were detected in the remaining two eyes.

Treatment

Seventy-one eyes (96%) were treated empirically with a combination of intravitreal ceftazidime (2 mg/ 0.1 mL) and vancomycin (1 mg/0.1 mL). Of those 71 eyes, seven received voriconazole (100 mcg/0.05 mL) and two received amphotericin (5 mcg/0.1 mL) concomitantly.

Amikacin monotherapy (0. 4 mg/0.1 ml) was injected to one eye (1.3%) based on a positive vitreous culture result of amikacin-sensitive Pseudomonas aeruginosa from another hospital. Voriconazole monotherapy was injected to one eye (1.3%) of a patient with candidemia. One eye (1.3%) did not receive intravitreal therapy given the late presentation and the lack of potential vision that necessitated evisceration (**Table 2, pt #13**). Intravitreal dexamethasone (0.4 mg/0.1 mL) was administered to 22 eyes (31%) in combination with intravitreal antimicrobial therapy. The median number of intravitreal antimicrobial injections was two (mean 1.77, range 1-5).

Systemic intravenous antibiotics were part of the treatment regimen in 44 patients (63%) (All patients with EnE received systemic antibiotics). Vancomycin was the most commonly used systemic antibiotic treatment, administered to 25 patients; Ceftazidime was used in 16 and ceftriaxone in 11 patients. Oral prednisone was administered in 13 patients (19%). Pars plana vitrectomy was performed in 57 eyes (77%) at a median of 1 day after presentation.

Antibiograms did not reveal resistance to the used antimicrobial agents (**Table 6**).

Discussion

The present study is the first study in Israel that aimed to portray the microbial spectra of endophthalmitis cases and their susceptibilities to antimicrobial agents. It is also the first study that aimed to study the demographic, clinical and microbiological characteristics of patients presenting with endophthalmitis in the Jerusalem area. Jerusalem has currently a population of 927,000 inhabitants making it the biggest city in Israel (https://www.cbs.gov.il/he/mediarelease/DocLib/2019/156/11_19_156b.pdf).

The present study highlights the following points: First, ExE post cataract operation was the leading cause of endophthalmitis. All ExE cases were caused by bacterial microorganisms mainly gram-positive bacteria of which, Staphylococcus epidermidis was the most common pathogen. Second, of all the isolates, gram-positive bacteria accounted for 75% of them whereas gram-negative bacteria and fungi accounted for 14% and 11% of them, respectively. Third, EnE was mainly caused by fungal infection in immunocompromised patients, of which candida was the predominant pathogen. Fourth, all gram-positive bacteria were susceptible to vancomycin. Fifth, treatment resulted in a significant drop in the percentage of eyes with poor VA and evisceration/enucleation were performed in five eyes only. Finally, there was no evidence of bacterial resistance in the antibiograms for either vancomycin, ceftazidime, ceftriaxone or amikacin.

Similar to our study, Gentile et al reported [3] that gram-positive bacteria were the most common isolates followed by gram-negative bacteria in 10.3% and fungi in 4.6% (**Table 7**). Schimel et al [4] and Liu et al [2] found that gram-positive bacteria were the predominantly isolated pathogens in 72.9% and 65% respectively, however, fungi were the second most prevalent pathogens in 15.8% and 18.4% respectively and gram-negative bacteria ranked third in 10.7% and 16.6% respectively. On the other hand, Lin et al [6] and Satpathy et al [5] reported a higher percentage of gram-negative bacteria in their studies, 27.8% and 38% respectively. Lin et al [6] reported that gram- negative bacteria accounted for 26% and 30% of the microbial isolates that caused posttraumatic and keratitis –related endophthalmitis respectively. In the present study, infectious keratitis and trauma were the least common predisposing causes of endophthalmitis accounting only for 10% and 7% of the cases respectively. This could explain the much lower isolation of gram- negative bacteria in our study. Cases secondary to gram-negative microbes were correlated with poor final VA, similar to the results of the endophthalmitis vitrectomy study group [7].

Fungal endophthalmitis was the least frequent microbial cause of endophthalmitis in the present study (11%), typically affecting immunocompromised patients. The most common infection was candida while aspergillus was not detected in the present study. Lin et al [6] reported on fungal endophthalmitis as the cause of 24.3% of endophthalmitis cases. Filamentous fungi accounted for 57.6% of isolates causing keratitis- related endophthalmitis. Fusarium and aspergillus species caused 24.24% and 21.21% respectively of all cases of keratitis- related endophthalmitis. [6] The low rate of keratitis is the most likely explanation to the absence of these pathogens in our case series.

In the present study, one patient sustained *Pseudallescheria boydii* EnE after near-drowning in a pond that necessitated evisceration. Endophthalmitis caused by *P. boydii* complex is a rare and devastating condition with poor visual outcomes. It is a condition that is difficult to treat because of its variable antifungal agent resistance. Moloney et al [8] reported on four patients with P.boydii- associated EnE where enucleation was required in two patients and the remaining two patients had final BCVA of perception of light and no perception of light, respectively. Currently, *P. boydii* is recognized as the fungus most commonly implicated in invasive disease after near-drowning. These fungi are ubiquitous and are present in soil, manure, sewage, polluted water and decaying vegetation [9-11]. Fungal infection caused by the presence of generally harmless saprophytes in victims of near-drowning is increasingly being reported to cause serious or lethal infections, even in immunocompetent individuals [12].

Evisceration/enucleation was performed in five eyes only (7%). This is lower than what has been reported in large series. Lin et al [6] reported that 10.42% of endophthalmitis cases underwent evisceration/ enucleation with much higher incidence of evisceration/enucleation in cases of keratitis-related endophthalmitis compared to the total endophthalmitis population [6]. All pathogens detected in those cases were either gram-negative bacilli or fungi, while Pseudomonas aeruginosa was the most commonly detected pathogen [6].

Abulafia et al [13] reported on 812,112 cataract surgical procedures performed over a 25 year-study period (between 1990 and 2014) in Israel and indicated that the incidence of postoperative endophthalmitis after cataract operations dropped from 0.25% in 2002 to 0.028% in 2014.This was mostly attributed to the widespread use of intracameral cefuroxime recommended by the European Society of Cataract & Refractive Surgeons study [14] that demonstrated a 5-fold decrease in the endophthalmitis rate with the intracameral cefuroxime injection. Despite the marked drop in the incidence of post cataract operation endophthalmitis, it was the leading cause of endophthalmitis in the present study, accounting for 23% of all cases of endophthalmitis and for 47% of exogenous endophthalmitis cases. This could be attributed to the fact that acute postoperative endophthalmitis in Israel is always managed as an in-patient emergency in tertiary referral centers of university-affiliated hospitals (even if the cataract surgery was performed at an ambulatory center). As the study center is the biggest tertiary referral center in Jerusalem, it possibly treated endophthalmitis cases referred from the private practice in the city and its suburbs.

Sixty-three percent of patients in our cohort were treated with systemic antibiotics reflecting the debatable efficacy of intravenous antibiotics in cases of ExE. Systemic antibiotic penetration to the globe is low especially in phakic patients and is variable among the different antibiotics even in the same class (for example ceftriaxone vs ceftazidime) [15]. Arguably, it would be preferable to administer the same medication intravitreally and systemically thus reducing the elimination of the antibiotic from the vitreous [16]. But unfortunately the data of intravitreal toxicity of many antibiotics is scarce and in some medications, it originated only from animal models [17, 18], which is not completely applicable to humans.

Vancomycin and ceftazidime were the most commonly used intravitreal treatment in our cohort. This regimen potentially covers 100% of the bacterial infections documented but the microbiology efficacy of ceftazidime is reduced in streptococcal cases in comparison to ceftriaxone [19]. Seven isolates of different streptococci species in the present study would have been treated more efficiently had ceftriaxone been used instead of ceftazidime. As the prognosis of streptococcal endophthalmitis is poor [20], systematic evaluation of intravitreal ceftriaxone (1-2mg/0.1 ml) [21] combined with vancomycin may be considered.

The main limitation of this study is the retrospective nature of the design and the sample size not enabling further analysis on whether there was a changing trend in pathogens or their sensitivity to antibiotics over the study period. However, this study is the first panoramic report on the epidemiological, clinical and microbial profiles and antibiotic susceptibility in the Jerusalem area and the biggest study of its kind in Israel. Strategies for treatment of endophthalmitis include characterizing the epidemiologic features of patients and groups at risk, identification of the etiologic organisms and prompt initiation of broad-spectrum antimicrobial therapy. Evaluation of the microbial profile and susceptibility to the frequently used antibiotics is imperative in tertiary referral settings in order to best select the empiric intravitreal antimicrobial therapy. Continuous monitoring of epidemiological data of endophthalmitis is essential for early identification of changes in the microbial ecology and susceptibility profile. The present study emphasizes the importance of adhering to the already established protocol of using vancomycin empirically as it maintained excellent effectivity and its microbial sensitivity in the present study was 100%.

Declarations

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The authors report no conflict of interest

The corresponding author has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis as well as the decision to submit for publication.

Code availability: none

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Tables

Table 1: Etiology of exogenous endophthalmitis.

Etiology (n= 58 eyes)	**Number of Eyes (%)**
Postoperative	36 (62%)
· *Post Cataract Extraction*	· 17 (47%)
· *Post Glaucoma Procedures*	· 10 (28%)
· *Post Pars Plana Vitrectomy*	· 4 (11%)
· *Post Combined Cataract Extraction and Pars Plana Vitrectomy*	· 4 (11%)
· *Post Penetrating Keratoplasty*	· 1 (3%)
Post Intravitreal anti-vascular endothelial growth factor injections	12 (21%)
Infectious Keratitis	6 (10%)
Penetrating globe trauma	4 (7%)

- The percentage is the number of cases out of the 36 eyes that suffered from postoperative endophthalmitis.

Table 2: Demographic characteristics of patients with endogenous endophthalmitis, comorbidities, preceding invasive procedure or triggering event and microbial isolates.

Pt. #	Age/ Gender	Eye	Comorbidities	Invasive Procedure or Triggering Event	Ocular Microbial Isolates	Blood Cultures
1	64/ F	LE	DM2	Infection of foot ulcer with osteomyelitis	Staphylococcus aureus	Staphylococcus aureus
2	67/ F	LE	DM2, Pancreatic Adenocarcinoma	Pancreaticoduodenect-omy	Candida tropicalis	Klebsiella pneumoniae, Enterococcus faecium, Pseudomonas aeruginosa
3	60/ M	RE	DM2	Indwelling vesical catheter	Streptococcus salivarius	Klebsiella pneumoniae
4	63/ F	BE	DM2	Lithotripsy	Candida albicans	No isolation
5	65/ F	LE	DM2	Ileocolic resection after motor vehicle accident	Candida albicans	Candida albicans
6	65/ M	LE	AML	Bone marrow transplantation	No isolation	No isolation
7	57/ M	LE	Hepatic cirrhosis associated with Hepatitis C	Endoscopy and Colonoscopy	Staphylococcus epidermidis	No isolation
8	30/ M	RE	Chronic oral steroid therapy for corneal graft rejection	Topical and oral steroids	Candida glabrata	No isolation
9	28/ F	BE	Acute IBD	Colonoscopy and spontaneous abortion	No isolation	No isolation
10	23/ M	BE	MRSA carrier and recurrent soft tissue abscesses	Pelvic abscess that developed 3 months after stitch abscess	No isolation	MRSA
11	46/ M	LE	None	None	Streptococcus anginosus	No isolation
12	86/ F	LE	Urinary tract infection	Indwelling vesical catheter	No isolation	No isolation
13	24/ M	LE	None	Near-drowning	Pseudallescheria boydii	No isolation

F: female, M: male, RE: right eye, LE: left eye, BE: both eyes, DM2: diabetes mellitus type 2, AML: acute myelogenic leukemia, IBD: inflammatory bowel disease, MRSA: methicillin- resistant staphylococcus aureus

Table 3: Microbial spectrum of the endophthalmitis positive isolates.

Microorganism	N=44	% Total
Gram Positive		
Staphyloccocus epidermidis	14	32%
Enterococcus faecalis	4	9%
Streptococcus pneumoniae	2	5%
Streptococcus agalactiae	2	5%
Streptococcus mitis	1	2%
Streptococcus anginosus	1	2%
Streptococcus gordoni	1	2%
Streptococcus salivarius	2	5%
Staphylococcus coagulase negative	1	2%
Staphylococcus aureus	1	2%
Staphylococcus sanguinis/anginosus	1	2%
Granulicatella adiacens	1	2%
Mycobacterium chelonae	1	2%
Mycobacterium fortuitum	1	2%
Gram Negative		
Haemophilus influenza	2	5%
Proteus mirabilis	1	2%
Pseudomonas aeruginosa	1	2%
Moraxella nonliquefancies	1	2%
Neisseria subflava	1	2%
Fungi		
Candida albicans	2	5%
Candidada glabrata	1	2%
Candida tropicalis	1	2%
Pseudallescheria boydii	1	2%
Total	44	100%

Table 4: Visual acuity at presentation and at last follow-up visit.

Visual Acuity	At presentation		At last follow-up		P-Value
	n	**%**	**n**	**%**	
Severe visual loss £6/60	56	76%	42	57%	*0.03*
Moderate visual loss > 6/60 - <6/12	11	15%	15	20%	*0.21*
Good visual acuity ^{3}6/12	7	9%	17	23%	*0.02*

Table 5: Demographic features of patients who developed phthisis bulbi, the inciting event, presenting visual acuity and the microbial isolates.

Patient #	Age/ Gender	Inciting event	Visual Acuity at presentation	Ocular Microbial Isolates
1	73/ F	Intravitreal Injection (Ranibizumab)	LP	Enterococcus faecalis
2	50/ F	Cataract operation	FC	Streptococcus mitis
3	65/ M	Ahmed valve + conjunctival graft	NLP	Mycobacterium chelonae
4	24/ M	Near-drowning	NLP	Pseudallescheria boydii
5	88/ F	Cataract operation	NLP	Streptococcus agalactiae
6	72/ M	Infectious Keratitis	LP	No isolation
7	78/ M	Infectious Keratitis	HM	No isolation
8	60/ M	Cataract operation	LP	No isolation
9	53/ F	Intravitreal Injection (Bevacizumab)	LP	No isolation
10	93/ F	Express valve	NLP	No isolation
11	71/ F	Infectious Keratitis	HM	No isolation
12	90/ F	Cataract operation	NLP	Enterococcus faecalis

F: female, M: male, LP: light perception, FC: counting fingers, NLP: no light perception, HM: hand motion.

Table 6: Antibiotic susceptibility of the isolated microorganisms.

Antibiotics	Number of susceptible/ Number of total tested	% Susceptibility
Vancomycin	31/31	100%
Penicillins/Beta Lactams		
Penicillin G	10/21	48%
Ampicillin	13/16	81%
Amoxicillin + Clavulanic Acid	2/2	100%
Methicillin	16/17	94%
Ticarcillin & Clavulanic Acid	2/2	100%
Piperacilin	2/2	100%
Piperacillin & Tazobactam	2/2	100%
Cephalosporins		
Cefuroxime	2/3	67%
Ceftazidime	2/2	100%
Ceftriaxone	13/13	100%
Macrolides		
Clarithromycin	1/1	100%
Erythromycin	15/31	48%
Aminoglycosides		
Gentamicin	18/19	95%
Amikacin	6/6	100%
Fluoroquinolones		
Levofloxacin	1/1	100%
Ofloxacin	1/1	100%
Ciprofloxacin	21/26	81%
Others		
Clindamycin	22/28	79%
Doxycycline	3/3	100%
Chloramphenicol	6/7	86%
Ertapenem	1/1	100%
Colistin	1/2	50%
Imipenem	3/3	100%

Clotrimoxazole	21/26	81%
Rifampicin	17/18	94%
Antifungals		
Voriconazole	5/5	100%
Itraconazole	1/1	100%
Caspofungin	2/2	100%
Amphotericin	1/1	100%
Fluconazole	3/3	100%
Flurocystosine	2/2	100%

Table 7: Comparison of the frequencies of the different microbial spectra between the present study and other studies from China, India and USA.

	Present Study, 2020 **%**	**Gentile et al.** [3] **USA** **2014**	**Liu C et al.**[2] **East China 2016**	**Lin L et al.** [6] **South China** **2020**	**Satpathy et al.** [5] **India 2017**	**Schimel et al.** [4] **USA 2013**
Gram Positive Bacteria	75%	85.1%	65%	47.9%	56%	72.9%
Gram Negative Bacteria	14%	10.3%	16.6%	27.8%	38%	10.7%
Fungal Infection	11%	4.6%	18.4%	24.3%	6%	15.8%
Viral Infection	ND	ND	ND	ND	ND	0.4%

ND: not detected

Figures

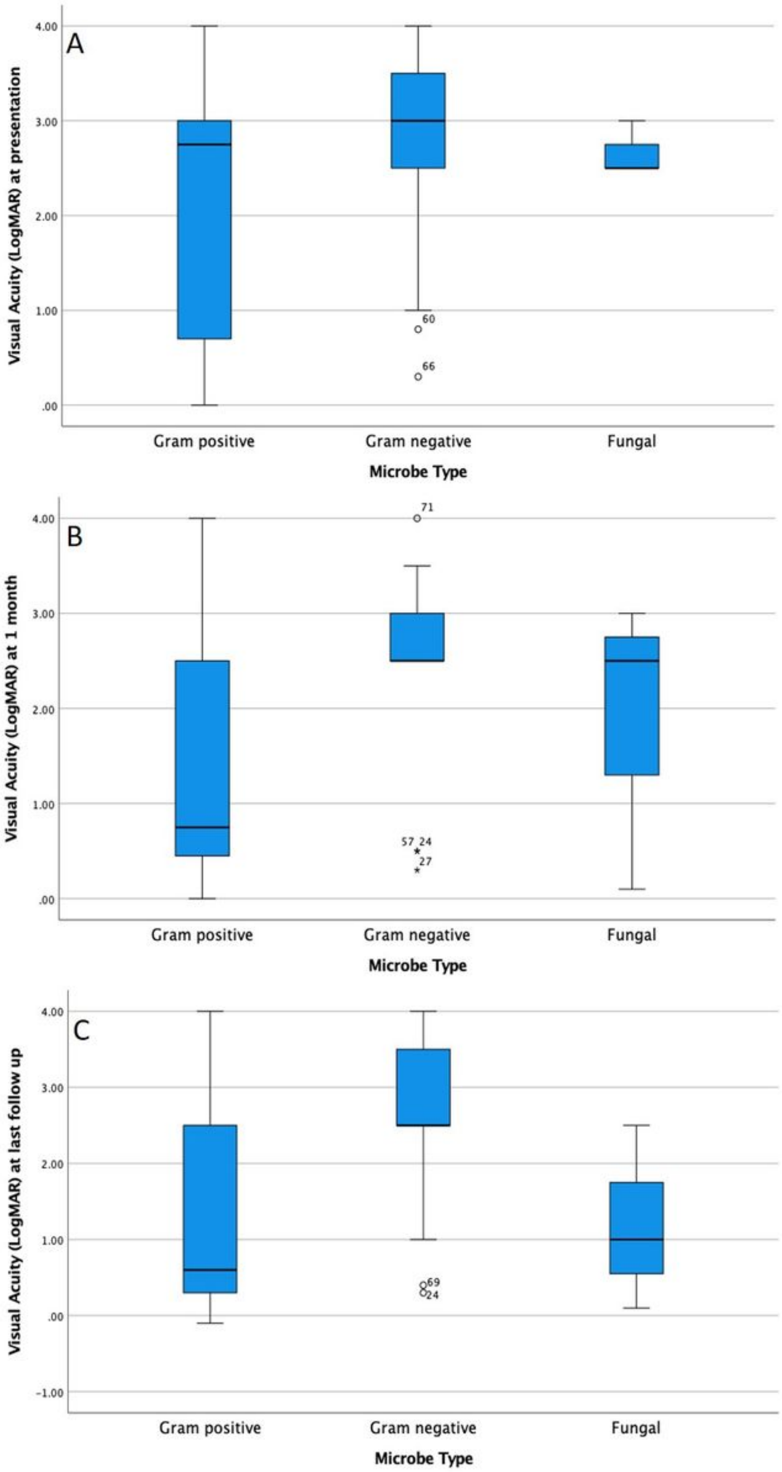

Figure 1

Box plot graphs show the median visual acuity at presentation (A), during the follow up at 1 month (B), and at the last visit (C). While the vision of patients with gram-positive bacteria improved during the study period, the visual acuity of eyes with gram-negative bacteria remained poor.