Norhayaty S[1,3], Sangeetha T[1,3], Evelyn-Tai LM[1,3], Wan-Hazabbah WH[1,3], Zaidah AR[2,3], Azhany Y[1,3,*]

[1]Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.

[2]Department of Microbiology and Parasitology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia,16150, Kubang Kerian, Kelantan, Malaysia

[3]Hospital Universiti Sains Malaysia,16150 Kubang Kerian, Kelantan, Malaysia

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*Corresponding author:
Azhany Yaakub
E-mail: azhany@usm.my

Microbial Profile of Culture-Proven Cases of Endophthalmitis in Hospital Universiti Sains Malaysia: A 7-year Retrospective Study

Abstract— Infectious endophthalmitis is a devastating and potentially sight-threatening condition. The objective is to analyse the microbiological profile and visual outcome of culture positive endophthalmitis seen in Hospital Universiti Sains Malaysia. All patients with endophthalmitis admitted to Hospital Universiti Sains Malaysia over a 7-year period from January 2007 until December 2013 were recruited into this study. Retrospective review of medical and microbiology records was conducted among patients clinically diagnosed with endophthalmitis in Hospital Universiti Sains Malaysia from January 2007 until December 2013. Sixteen patients were admitted with endophthalmitis during this study period. Seven (43%) were culture-positive, in which five (71%) cases were from vitreous culture and two (29%) from blood specimens. The mean age for culture positive patients of presentation was 44 years. The most common bacterial isolate was *Pseudomonas* spp., while the most common fungus was *Candida* spp. Other organisms isolated were *Fusarium* sp., *Aspergillus* sp*., Staphylococcus* sp*.* and *Enterococcus* sp. The risk factors for culture-positive cases were ocular trauma, corneal keratitis, ocular chemical injury, severe urinary tract infection and retropharyngeal abscess. Only three of the affected eyes could be salvaged. The final visual acuity was poor in all the culture-positive eyes. Two cases underwent evisceration while one case underwent enucleation. As a conclusion, Culture-positive endophthalmitis in this study were mainly attributed to *Pseudomonas* spp. and *Candida* spp. The visual outcome of culture-positive endophthalmitis was poor.

Keywords: **endogenous endophthalmitis, exogenous endophthalmitis, culture positive, pseudomonas sp., candida sp.**

1 INTRODUCTION

Infectious endophthalmitis is a devastating condition that is potentially sight-threatening and can lead to blindness [1]. It is characterised by an inflammatory reaction of intraocular fluids or tissues [2]. Endophthalmitis can occur endogenously or exogenously. Exogenous infective endophthalmitis can occur most commonly after intraocular surgery or trauma whereas endogenous endophthalmitis is the result of hematogenous spread [2].

The incidence of endopthalmitis differs based on geographical variation. Krause et al [3] analysed 120 cases of endopthalmitis in Britain out of which 59% were exogenous and 41% were endogenous. In other study conducted in India by Ramakrishnan et al [4] found a high percentage of exogenous endopthalmitis amounting to 92.6%. Meanwhile, Bhoomibunchoo et al [5] conducted retrospective 420 cases of infectious endophthalmitis in Thailand, the result showed most common were exogenous endophthalmitis associated with trauma (43.1%) and postoperative intraocular surgery (32.2%).

Most studies have reported that Gram positive organisms are the most common causative cause of endophthalmitis [6, 7]. However, Malaysia is a developing country that is still largely agricultural based; hence, risk factors and causative organisms might differ [8]. Studies on endopthalmitis show considerable differences between developed and developing countries in relation to the causative microorganisms [9, 10, 11]. The visual prognosis of endophthalmitis depends on the virulence of the pathogen [12]. Culture-negative or coagulase-negative staphylococci usually yield better outcomes, while poorer outcomes are typically caused by streptococci, *Bacillus* species and moulds [12, 13].

To the best of our knowledge, there is no published data on culture-positive endophthalmitis in Malaysia. We conducted a

retrospective study in Universiti Sains Malaysia, a tertiary hospital in the northeast of Malaysia. Our aim was to analyse the microbial profile and outcome of culture positive endophthalmitis seen in our hospital. Based on the findings, we hope to identify the common causative organisms and treatment trends in this part of the country.

2 METHODS

A retrospective review was conducted involving medical records of all patients diagnosed with endophthalmitis from 1 January 2007 until 31 December 2013 in Hospital Universiti Sains Malaysia. An analysis was performed to study the demographic features, microbiological results, therapy received and final visual outcomes post treatment. Patients were divided based on categories of endophthalmitis; exogenous or endogenous. Exogenous endophthalmitis was further divided into post traumatic, post intraocular surgery and associated with microbial keratits.

The diagnostic code assigned to the patient was based on the clinical diagnosis determined by the attending ophthalmologist. Information collected from the patients' medical records included demographics, systemic comorbidities, presenting symptoms, microbiologic culture results, sources of infection, treatment modalities and visual outcomes.

Inclusion criteria included patients with complete eye examination under slit lamp biomicroscopy. Relevant microbial investigations were carried out. Investigations include corneal scrapings from the base and edges of the ulcer were taken for patients with corneal ulcer and vitreous samples of endophthalmitis patients were taken via pars plana prior to antibiotic injection. For patients treated as endogenous endophthalmitis, specimens were taken both from blood and vitreous samples via pars plana, prior to the antibiotic injection. The collected samples were inoculated directly on nutrient agar, blood agar, Sabouraud and McConkey agar. In microbiology laboratory, the samples were processed according to standard protocols. Antibiotics susceptibility testing was performed and interpreted according to Clinical Laboratory and Standard Institute guidelines. Cases with incomplete laboratory data were excluded.

Table I Demographic profile of recruited endophthalmitis patients.

Patient Profile	**Number of Total Patients (%) N=16**	**Number of Culture positive Patients (%) N=7**
Gender (n, %)		
Males	11 (69)	4 (57)
Females	5 (31)	3 (43)
Mean age (years)	47.9	44.0
Categories of endophthalmitis (n, %)		
Exogenous	12 (75)	5 (71)
a) Endophthalmitis after intraocular surgeries	3 (25)	1 (20)
b) Endophthalmitis after intraocular injuries	6 (50)	2 (40)
c) Endophthalmitis associated with microbial keratitis	3 (25)	2 (40)
Endogenous	4 (25)	2 (29)

3 RESULTS

Sixteen patients were diagnosed with endopthalmitis during the study period of 7 years. The demographic profiles of the patients are summarized in Table I. Seven (43%) of these had positive culture; of which five patients had exogenous endophthalmitis. Five positive cultures (71%) were obtained from vitreous specimens while two (29%) were from blood specimens. The mean age of presentation for culture positive patients was 44 years.

Table II summarises the microbiological profile, risk factors, treatment and visual outcomes of the patients. Three patients (42.8%) had bacterial isolates, another three patients (42.8%) had fungal growth and one patient (14.4%) was mixed growth of *Staphylococcus* sp. and *Aspergillus* sp. Bacteria isolated in our study include *Pseudomonas* sp., *Staphylococcus* sp. and *Enterococcus* sp. Isolated fungi were *Aspergillus* sp., *Candida* sp. and *Fusarium*

Table II Microbiologic profile, risk factors, treatment modalities and visual outcome among culture positive endophthalmitis patients

No	Microbiological profile	Risk factors	Initial visual acuity	Antibiotic treatment	Ocular surgery	Final visual acuity
	Exogenous					
1	*Pseudomonas* sp.	Microbial keratitis	NPL	IVIT: Vancomycin, Ceftazidime Topical: Ceftazidime, Gentamycin Systemic: Ceftazidime	Evisceration	NPL
2	*Staphylococcus* sp.* *Aspergillus* sp.*	Chemical injury	HM	IVIT: Vancomycin, Ceftazidime, Amphotericin B Topical: Moxifloxacin, Gentamycin, Amphotericin B Systemic: Ciprofloxacin, Itraconazole	Enucleation	NPL
3	*Candida* sp.	Penetrating injury	HM	IVIT: Vancomycin, Ceftazidime, Amphotericin B Topical: Amphotericin B Systemic: Fluconazole, Ceftazidime	Vitrectomy	HM
4	*Fusarium* sp.	Microbial keratitis	HM	IVIT: Amphotericin B, Ceftazidime Topical: Natamycin, Amphotericin B, Ciprofloxacin Systemic: Fluconazole, Ciprofloxacin	Evisceration	NPL
5	*Candida* sp.	Diabetis Mellitus Post penetrating keratoplasty surgery	PL	IVIT : Amphotericin B Topical :Amphotericin B, Moxifloxacin Systemic : Amphotericin B , Ciprofloxacin	No surgical intervention	NPL
	Endogenous					
6	*Pseudomonas* sp.	Severe urinary tract infection	PL	IVIT: Amikacin, Ceftazidime Topical: Ciprofloxacin, Gentamycin, Ceftazidime Systemic: Ceftazidime	No surgical intervention	NPL
7	*Enterococcus* sp.	Retropharyngeal abscess Post chemotheraphy Nasopharyngeal carcinoma	CF	Topical: Moxifloxacin, Cefuroxime Systemic: Ceftazidime, Ampicillin /Sulbactam, Polymyxin	No surgical intervention	CF

* Isolates from same patient
NPL - No perception to light, PL – Perception to light, HM – Hand movement, CF – Counting finger
IVIT - Intravitreal

sp. All fungal positive cultures were seen in exogenous endophthalmits.

All cases received intravitreal (IVIT) antibiotics except one (14.4%) that refused the procedure. Choice of IVIT antibiotics given were combination of vancomycin and ceftazidime or combination of amikacin and ceftazidime. All fungal endophthalmitis patients received IVIT amphotericin B. Systemic antifungals were started in all patients with fungal positive isolates consisting of either amphotericin B or fluconazole.

The visual acuity at presentation was poor in all patients. Vitrectomy was performed in one patient. Evisceration was performed in two patients due to poor treatment response. One patient underwent enucleation due to extensive

chemical injury associated with endophthalmits. No surgical intervention was performed in two patients whom showed clinical improvement. There was one patient refused for any surgical procedure. Final visual outcome was poor in all cases.

4 DISCUSSION

Our study showed culture positive results in 43% of endophthalmitis cases. This was consistent with previous studies [2, 4, 11, 14]. Duan et al [14] found a rate of 31.8% of culture positive isolates in their study of endogenous and exogenous etiologies. Our study showed that in exogenous endophthalmitis associated with microbial keratitis, the micro-organisms isolated were Pseudomonas sp. and Fusarium sp. In a study by Gonzales et al [15], in predominantly agricultural regions; vegetative material-induced corneal trauma was the major cause of microbial keratitis. In Malaysia, however, a study by Norina et al [7] found that bacterial-related microbial keratitis contributed 79.3% of cases, in spite of vegetative-related trauma. Post-traumatic culture-positive endophthalmitis constituted 40% of exogenous endophthalmitis culture positive cases in our study. The organisms isolated were Staphylococcus sp., Candida sp. and Aspergillus sp. Our finding was comparable to previous studies, which documented a prevalence of 28.3% - 32.1% [2, 11]. In our study, the most common organism isolated among bacterial endophthalmitis was Pseudomonas aeruginosa, a Gram-negative bacteria. In other studies, the most common organism was Staphylococcus sp. [9, 11, 16]. The isolation of Pseudomonas sp. has been found to be higher in hot and humid climates [17]. Endophthalmitis leading to poor visual prognosis clinically correlates with high organism virulence and rapid progression of the condition [18, 19].

Fungal isolates were found in four of our patients (42%). All of the patients had exogenous endophthalmitis. The most common fungal organism isolated was Candida sp. Kunimoto et al [20] proposed that the risk of fungal endophthalmitis was due more to the climate than the mechanism of injury; thus, warmer tropical environments have a higher incidence of fungal organisms. Wykoff et al [21] found that 44% of fungal endophthalmitis was associated with keratitis. This finding mirrored our study, as 25% of our exogenous fungal endophthalmits was associated with microbial keratitis.

Our study found that the organisms isolated in endogenous endophthalmitis were Enteroccocus sp. and Pseudomonas sp. Ramakrishnan et al [4] observed in his study of 424 culture-positive patients that 63.6% of isolates were Gram positive cocci. In our study, the risk factors for developing endogenous endophthalmitis were urinary tract infection and retropharyngeal abscess. One patient was diagnosed via blood culture while the other through a vitreous sample. Risk factors in our study include ocular trauma, microbial keratitis, ocular surgery, ocular chemical injury, diabetes mellitus, severe urinary tract infection and retropharyngeal abscess. In addition, other risk factors that have been attributed to the development of endophthalmitis are orbital cellulitis, liver abscess, pneumonia, endocarditis, meningitis and brain abscess [22, 23, 24].

Intravitreal antibiotics with or without vitrectomy is the current standard of care in bacterial endophthalmitis [2]. In our study, six cases of endophthalmitis were treated with intravitreal antibiotics. The antibiotics given were ceftazidime, amikacin and vancomycin. A study in India [10] found 54.5% and 55.37% of bacterial colonies showed moderate to high sensitivity to amikacin and ceftazidime respectively. Sharma et al [2] found that 100% of Gram-positive bacteria were sensitive to vancomycin. Data on common organisms cultured and their antibiotic sensitivity may help clinicians in choice of empirical antibiotics prior to isolation of a definite organism.

Cases of fungal endophthalmitis in our study were treated mainly with intravitreal amphotericin B and systemic flucanozole. Malaysian's Clinical Practice Guidelines on management of post-operative infectious endopthalmitis recommends intravitreal amphotericin B in suspected fungal along with systemic antifungal if it is indicated [25]. The Infectious Disease Society of America recommends systemic flucanozole or amphotericin B for the treatment of Candida sp. endophthalmitis [26].

According to the Endopthalmitis Vitrectomy Study which was carried out on post-operative endopthamitis, routine immediate vitrectomy is not necessary in patients with better than light perception vision at presentation but is of substantial benefit for those who have light perception-only vision [16]. However, the

limitation of this study leaves this conclusion to future modification. In our study, vitrectomy was performed in one indicated case while another two patients needed evisceration due to poor response to the treatment. Enucleation is not the standard procedure for endophthalmitis. However in our study, one patient underwent enucleation due to extensive chemical injury associated with mixed growth endophthalmits.

5 CONCLUSION

Culture-positive endophthalmitis in this study was mainly attributed to Pseudomonas spp. and Candida spp. The visual outcome of culture-positive endophthalmitis was poor despite of intensive treatment.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

[1] Greenwald MJ, Wohl LG, Sell CH. Metastatic bacterial endophthalmitis: a contemporary reappraisal. Surv Ophthalmol. 1986; 31(2):pp.81-101.

[2] Sharma S, Padhi TR, Basu S, Kar S, Roy A et al. Endophthalmitis patients seen in a tertiary eye centre in Odisha: A clinic-microbiological analysis. Indian J. Med. Res. 2014; 139:pp.91-98.

[3] Krause L, Bechrakis NE, Heimann H, Kildal D, Foerster MH. Incidence and outcome of endophthalmitis over a 13 year period. Can J Ophthalmol. 2009; 44:pp.88-94.

[4] Ramakrishnan R, Bharathi M, Shivkumar C, Mittal S, Meenakshi R et al. Microbiological profile of culture proven cases of exogenous and endogenous endophthalmitis; a 10 year retrospective study. Eye. 2008; 23:pp.945-956.

[5] Bhoomibunchoo C, Ratanapakorn T, Sinawat S, Sanguansak T, Moontawee K et al. Infectious endophthalmitis: review of 420 cases. Clin Ophthalmol. 2013; 7:pp.247-252.

[6] Keynan Y, Finkelman Y, Lagace-Wiens P. The microbiology of endophthalmitis: Global trends and a local perspective. Eur J Clin Microbiol Infect Dis. 2012; 31:pp.2879-2886.

[7] Han DP, Wisniewski SR, Wilson LA, Barza M, Vine AK et al. Spectrum and suceptibility of microbiologic isolates in the endophthalmitis vitresctomy study. Am J Ophthal. 1996; 122:pp.1-17.

[8] Norina T, Raihan S, Bakiah S, Ezanee M, Liza-Sharmini A et al. Microbial keratitis: aetiological diagnosis and clinical features in patients admitted to Hospital Universiti Sains Malaysia. Singapore Med J. 2008; 49:pp.67-71.

[9] Gupta A, Orlans HO, Hornby SJ, Bowler ICJW. Microbiology and visual outcomes of cultire positive bacterial endophthalmitis in Oxford,UK. Graefes Arch Clin Exp Ophthalmology. 2014; 252:pp.1825-1830.

[10] Melo G, Bispo PJM, Yu MCZ, Pignatari A, Höfling-Lima A. Microbial profile and antibiotic susceptibility of culture positive bacterial endophthalmitis. Eye. 2011; 25:pp.382-388.

[11] Bhattacharjee H, Bhattacharjee K, Gogoi K, Singh M, Singla B et al. Microbial profile of the vitreous aspirates in culture proven exogenous endophthalmitis; A 10 year retrospective study. Indian J Med Microbiol . 2016; 34:pp.153-158.

[12] Group EVS. Microbiologic factors and visual outcome in the Endophthalmitis Vitrectomy Study. Am J Ophthalmol. 1996;122(6):pp.830-846

[13] Durand ML. Endophthalmitis. Clin Microbiol Infect. 2013;19(3):pp.227-234

[14] Duan F, Wu K, Liao J, Zheng Y, Yuan Z et al. Causative Microorganisms of Infectious Endophthalmitis: A 5-Year Retrospective Study. Am J Ophthalmol. 2016; 2016:pp.1-7.

[15] Gonzales CA, Srinivasan M, Whitcher JP, Smolin G. Incidence of corneal ulceration in Madurai district, South India. Ophthalmic Epidemiol. 1996; 3:pp.159-166.

[16] Endophthalmitis Vitrectomy Study Group Results of the Endopthalmitis Vitrectomy Study Group. A randomized trial of immediate vitrectomy and if intravenous antbiotics for the treatment of postoperative bacterial endophthalmitis. Arch Opthalmol. 1995; 113:pp. 1479-1496.

[17] Jambulingam M, Parameswaran SK, Lysa S, Selvaraj M, Madhavan HN. A study on the incidence, microbiological analysis and investigations on the source of infection of postoperative endophthalmitis in a tertiary care ophthalmic hospital: A 8 year study. Indian J Ophthalmol. 2009; 58:pp.297-302.

[18] Eifrig CW, Scott IU, Flynn HW, Miller D. Endophthalmitis caused by Pseudomonas aeruginosa. Ophthalmology. 2003; 110(9):pp.1714-1717.

[19] Priya JL, Prajna L, Mohankumar V. Genotypic and phenotypic characterization of Pseudomonas aeruginosa isolates from post-cataract endophthalmitis patients. Microb Pathog. 2015; 78:pp.67-73.

[20] Kunimoto DY, Das T, Sharma S, Jalali S, Majji AB et al. Endophthalmitis Research Group Microbioloc spectrum and suceptibility of isolates:part II. Post traumatic endophthalmitis. Am J ophthalmol. 1999; 128:pp.242-244.

[21] Wykoff CC, Flynn HW, Miller D, Scott IU, Alfonso EC. Exogenous Fungal Endophthalmitis: Microbiology and Clinical Outcomes. Ophthalmology. 2008; 115:pp. 1501-1507.

[22] Jackson TL, Eykyn SJ, Graham EM, Stanford MR. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. Surv Ophthalmol. 2003;48(4):pp.403-23.

[23] Schiedler V, Scott IU, Flynn HW, Davis JL, Benz MS et al. Culture-proven endogenous endophthalmitis: clinical features and visual acuity outcomes. Am J Ophthalmol. 2004; 137 (4):pp.725-731.

[24] Sheu SJ, Kung YH, Wu TT, Chang FP, Horng YH. Risk factors for endogenous endophthalmitis secondary to Klebsiella pneumoniae liver abscess: 20-year experience in Southern Taiwan. Retina. 2011; 31 (10):pp.2026-2031.

[25] Clinical Practice Guidelines, Management of post-operative infectious endopthalmitis. MOH/P/PAK/116.06 (GU), August 2006. http://www.moh.gov.my/penerbitan/CPG2017/3909.pdf

[26] Pappas PG, Kauffman CA, Andes D, Benjamin DK, Calandra TF et al. Clinical practice guidelines for the management of candidiasis; 2009 update by the Infectious Society of America. Clin infect Dis. 2009; 48:pp. 503-505.