• Clinical Research •

Clinical features and treatment outcomes of endogenous *Klebsiella* endophthalmitis: a 12-year review

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Abstract

● **AIM:** To identify the clinical features and treatment outcomes of endogenous *Klebsiella pneumoniae* endophthalmitis and investigate prognostic factors of poor visual outcome.

● **METHODS:** The clinical records of all patients diagnosed with endogenous *Klebsiella* endophthalmitis between January 2007 to December 2018 in Prince of Wales Hospital, Hong Kong, China were retrospectively reviewed. Thorough ophthalmological examination findings were recorded in the case note, including visual acuity testing, slit-lamp examination, indirect ophthalmoscopy and B-scan ultrasonography if media opacity precluded fundus viewing.

● **RESULTS:** A total of 18 eyes in 14 patients were identified. Bilateral involvement was noted in 4 patients (28.6%). Hepatobiliary sepsis was the source in 9 patients (64.3%). Culture of intraocular fluid was positive in 5 out of 18 eyes (27.8%). Mortality was noted in 2 patients (14.3%). Mean final visual acuity was 20/1500. Six out of 16 eyes had total loss of sight (37.5%) and 3 eyes required evisceration (18.8%). Multivariate linear regression revealed poor presenting visual acuity (P=0.031) and lack of fundus view due to vitritis (P=0.02) as prognostic factors of poor visual outcome.

● **CONCLUSION:** Visual outcome of endogenous *Klebsiella* endophthalmitis is poor. Poor presenting visual acuity and lack of fundus view predict poor visual outcome. High index of suspicion for endophthalmitis is important in *Klebsiella* sepsis patients with complaints of ocular symptoms. Ophthalmological screening is recommended in non-communicable patients with *Klebsiella* sepsis.

● **KEYWORDS:** *Klebsiella pneumoniae*; endogenous endophthalmitis; screening; liver abscess; sepsis
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INTRODUCTION

Endogenous endophthalmitis is a severe form of intraocular inflammation, results from haematogenous spread of pathogens from a primary site of infection into the normally sterile eye. The condition is sight-threatening with often poor visual outcome[1].

Endogenous *Klebsiella pneumoniae* endophthalmitis is a severe complication of systemic *Klebsiella* sepsis. Despite being a rarity, it is recognised as most prevalent in East Asia, where abundance of *Klebsiella* pyogenic liver abscess and invasive *Klebsiella* infection has been observed[2-3]. Even with increasing reports and awareness, together with improving intervention for endogenous *Klebsiella* endophthalmitis, visual outcomes reported by recent studies remain poor with high rates of total loss of vision and evisceration[4-8]. Ophthalmological screening has been advocated but benefits are uncertain.

This study aimed at identifying the clinical features and treatment outcomes of endogenous *Klebsiella* endophthalmitis. Prognostic factors associated with poor visual outcome were analysed. By further understanding the features of the disease entity, we sought to improve recognition of the condition among clinicians managing *Klebsiella* sepsis, and make recommendations on ophthalmological screening.

SUBJECTS AND METHODS

Ethical Approval An Institutional Review Board approval

was obtained from the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (CREC Ref. No.2019.133). This study was adherent to the tenets of the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study.

A retrospective review of all patients diagnosed with endogenous *Klebsiella pneumoniae* endophthalmitis between January 2007 to December 2018 by ophthalmologists in Prince of Wales Hospital, Hong Kong was performed.

Cases of endogenous *Klebsiella pneumoniae* endophthalmitis were retrieved from the Clinical Data Analysis and Reporting System (CDARS) of the Hospital Authority of Hong Kong with the diagnosis code of "endophthalmitis". Simultaneous review of our vitreoretinal clinic and inpatient consultation record was also performed to identify cases of endogenous *Klebsiella* endophthalmitis. A case was defined as an intraocular inflammation in the background of systemic sepsis caused by *Klebsiella pneumoniae*, where positive culture was obtained from blood or the primary source of infection. Alternatively, when there was no obvious primary source, a case was defined as intraocular inflammation with positive culture of *Klebsiella pneumoniae* from intraocular fluid (vitreous, aqueous or intraocular content of evisceration). Cases with exogenous cause of endophthalmitis, including recent corneal ulcer, ocular trauma or intraocular surgery in the past 6mo, and history of glaucoma filtration surgery were excluded. Cases with history of non-infective intermediate or posterior uveitis, and infectious uveitis caused by organisms other than *Klebsiella pneumoniae* were also excluded.

Clinical records of all retrieved cases were reviewed. Thorough ophthalmological examination findings were recorded in the case note, including visual acuity testing (Snellen chart or hand-held Snellen chart), slit-lamp examination, indirect ophthalmoscopy and B-scan ultrasonography if media opacity precluded fundus viewing. Lack of fundus view was defined as a vitreous haze of National Institutes of Health (NIH) grade 3+ or above[9]. Intraocular fluid sample (vitreous or aqueous) was taken, while systemic antibiotics and intravitreal ceftazidime (2 mg/0.1 mL) with or without intravitreal vancomycin (1 mg/0.1 mL) were given upon suspicion of endogenous endophthalmitis. Decision to repeat intravitreal antibiotics and perform pars plana vitrectomy or evisceration was made at the discretion of the treating ophthalmologist with regard to patients' ocular and systemic condition. Data variables including demographics, clinical course, medical history, laboratory results and treatment were collected and recorded.

Statistical Analysis Statistical analysis was performed using IBM SPSS Statistics version 25.0 (Armonk, NY: IBM Corp., USA). Descriptive statistics were expressed as frequency and mean, with standard deviation. Multivariate linear regression was performed as appropriate. Regression was performed for all individual eyes, as well as single eye from bilateral cases (with right eye selected for bilateral cases by convention). Occasional missing values were replaced with mean during regression. $P<0.05$ was taken as significant. For statistical analysis, Snellen visual acuities were converted to the logarithm of the minimal angle of resolution (logMAR). Categorical acuities of low non-numerical vision were converted to logMAR scale based on previous works[10-12]. The following values were used: finger counting (CF)=1.7, hand movement (HM)=2.0, light perception (LP)=2.3 and no light perception (NLP)=3.0. Visual acuity post-evisceration was counted as no light perception during calculation.

RESULTS

Totally 18 eyes in 14 patients were identified as cases of endogenous *Klebsiella pneumoniae* endophthalmitis in the study period. Clinical summary of individual patients is presented in Table 1. Demographics, clinical features and outcomes are summarised in Table 2.

Demographics The mean age of the patients was 58.2±12.4y. Male predominance was noted (*n*=9, 64.3%). All patients were Chinese. The commonest underlying medical condition was diabetes mellitus (*n*=8, 57.1%). Background malignancy was noted in 3 patients (21.4%).

Ocular Symptoms and Signs The majority of cases were unilateral (*n*=10, 71.4%). The 16 out of 18 eyes (88.9%) were symptomatic before the time of diagnosis. Common presenting symptoms included blurring of vision (87.5%), eye redness (43.8%) and floaters (18.8%). Mean time from systemic symptom onset to ocular symptom onset was 6.1±10.7d, while mean time from ocular symptom onset to clinical diagnosis of endogenous *Klebsiella* endophthalmitis was 3.8±5.3d. Mean presenting visual acuity was poor at logMAR 1.48±0.86 (Snellen equivalent 20/600). Conjunctival injection was noted in 83.3% of eyes. Hypopyon was seen in 33.3%. No fundus view could be obtained from 61.1% of eyes due to severe vitritis. Subretinal abscesses were seen in 5 out of the 7 eyes with visualisable fundi.

Systemic Sources and Microbiological Profile Hepatobiliary system was the commonest source of infection (64.3%), followed by respiratory system (28.6%). Other non-ocular sites of infection accounted for 14.3% of patients. No clear source could be identified in 2 cases (14.3%). Blood culture was positive in 7 patients (50.0%). Positive intraocular fluid (aqueous or vitreous) culture was obtained in 5 eyes (27.8%). The majority of patients (85.7%) had infection caused by non-resistant strain of *Klebsiella pneumoniae*, which was sensitive to amoxicillin/clavulanate, cefuroxime, ciprofloxacin

Table 1 Clinical summary of patients with endogenous *Klebsiella* endophthalmitis

Patient No.	Age/ gender	Eye(s) involved	Presenting ocular symptoms	Ocular signs	Presenting VA	Medical comorbidities	Systemic source of infection	Time from systemic symptom onset to EKE symptoms	Time from ocular symptom to EKE diagnosis	Blood culture	Culture of intraocular fluid	Ocular treatment	Final VA/ outcome	Remarks
1	60/M	RE	BOV, redness, pain	Injection, vitritis, lack of fundus view, EOM limitation, proptosis	LP	GPH	Liver abscess	5	0	-	+	IVI×1; PPV×1	Eviscerated	Eviscerated eye had NLP VA before operation
		LE	BOV, redness, pain	Injection, vitritis, lack of fundus view	10/200			5	0		+	IVI×1; PPV×1	NLP	
2	47/M	RE	BOV	Injection, AC fibrin, vitritis, lack of fundus view, EOM limitation	NLP	DM	Perianal abscess, liver abscess	1	17	+	-	IVI×1	Eviscerated	Eviscerated eye had NLP VA before operation
		LE	BOV	Injection, AC fibrin, vitritis, lack of fundus view, EOM limitation	LP			1	17		-	IVI×1; PPV×2	NLP	
3	58/M	RE	BOV	Injection, hypopyon, vitritis, lack of fundus view	HM	CA lung	Pneumonia	2	2	-	+	IVI×1; PPV×1	NLP	
4	43/M	LE	BOV, floaters	Injection, subretinal abscess	20/20	DM	Liver abscess	7	1	+	-	IVI×1; PPV×1	20/200	
5	55/M	LE	Asymptomatic	Injection, vitritis, subretinal abscess, exudative RD	N/A	DM	Lung abscess, liver abscess	N/A	N/A	+	-	IVI×5; PPV×1	20/200	Asymptomatic consult, ICU patient; Non-communicable at presentation
6	48/M	LE	BOV, redness, floaters	Injection, hypopyon, vitritis, lack of fundus view	20/100	HT HL	Liver abscess	-4	4	-	-	IVI×1	LP	Ocular symptoms preceded systemic symptom of infection
7	67/M	LE	BOV, pain	Injection, hypopyon, vitritis, lack of fundus view	HM	HT, DM, CA rectum	No source identified	N/A	1	-	+	IVI×1; PPV×2	LP	No other site of sepsis identified; Rectal cancer discovered by PET-CT
8	76/M	LE	BOV	Injection, hypopyon, vitritis, lack of fundus view	20/400	HT DM CVA	Liver abscess	2	2	+	-	IVI×1; PPV×2	HM	
9	42/M	RE	BOV	Vitritis	20/100	DM	Lung abscess	6	3	+	-	IVI×1	20/16	LE index examination normal; Found LE vitritis on the next day; No injection noted at first examination
		LE	BOV, floaters	Vitritis	20/60			4	4		-	IVI×1	20/13	
10	43/F	RE	Asymptomatic	Subretinal abscess	N/A	DM	Lung abscess, liver abscess	N/A	N/A	+	-	IVI×1	Death	Asymptomatic consult, ICU patient. Non-communicable at presentation; No injection noted at first few examinations
11	74/F	RE	BOV	Injection, hypopyon, vitritis, lack of fundus view	CF	HT	Liver abscess, brain abscess	7	1	-	-	IVI×1	Eviscerated	Eviscerated eye had NLP VA before operation
12	65/F	RE	BOV, redness	Injection, vitritis, subretinal abscess	5/200	GPH	Liver abscess	4	2	+	-	IVI×2; PPV×1	20/200	
		LE	BOV, redness	Injection, hypopyon, vitritis, lack of fundus view	LP			4	2		-	IVI×3	HM	
13	77/F	RE	Redness, periocular swelling	Injection, AC fibrin, vitritis, lack of fundus view	N/A	DM, HT, CVA, recurrent IO	No source identified	N/A	1	-	+	IVI×1	Death	Non-communicable institutionalised patient presented with eye redness; Resistant to amoxicillin/clavulanate.
14	60/F	LE	Redness	Injection, subretinal abscess	20/60	ALL with neutropenic fever	Persistent bacteremia	42	4	+	-	IVI×4	20/80	Multidrug resistant Klebisella with ESBL; Normal ocular exam screened by ophthalmologist 6wk prior to presentation

AC: Anterior chamber; ALL: Acute lymphoblastic leukemia; BOV: Blurring of vision; CA: Carcinoma; CVA: Cerebrovascular accident; DM: Diabetes mellitus; EKE: Endogenous *Klebsiella* endophthalmitis; EOM: Extra-ocular movement; ESBL: Extended-spectrum beta-lactamases; GPH: Good past health; HL: Hyperlipidemia; HT: Hypertension; ICU: Intensive care unit; IO: Intestinal obstruction; IVI: Intravitreal injection; LE: Left eye; PET-CT: Positron emission tomography-computed tomography; PPV: Pars plana vitrectomy; RD: Retinal detachment; RE: Right eye; VA: Visual acuity.

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Table 2 Demographics, clinical features and outcomes of patients with endogenous *Klebsiella* endophthalmitis

Demographics	Data
No. of patients (eyes)	14 (18)
Unilateral, *n* (%)	10 (71.4)
Bilateral, *n* (%)	4 (28.6)
Age, y (mean±SD)	58.2±12.4
Gender, *n* (%)	
Male	9 (64.3)
Female	5 (35.7)
Ocular features, *n* (%)	
Symptomatic eyes (*n*=18)	16 (88.9)
Presenting symptoms (*n*=16)	
Blurring of vision	14 (87.5)
Redness	7 (43.8)
Floaters	3 (18.8)
Ocular signs, *n* (%)	
Injection	15 (83.3)
Hypopyon	6 (33.3)
No fundus view from vitritis	11 (61.1)
Positive intraocular fluid culture, *n* (%)	5 (27.8)
Time from systemic symptom to ocular symptom, d (mean±SD)	6.1±10.7
Time from ocular symptom to EKE diagnosis, d (mean±SD)	3.8±5.3
Systemic features, *n* (%)	
Diabetes mellitus	8 (57.1)
Background malignancy	3 (21.4)
Bacteremia	7 (50.0)
Systemic non-ocular site of sepsis, *n* (%)	
Hepatobiliary system	9 (64.3)
Respiratory system	4 (28.6)
Others (brain abcess, perianal abscess)	2 (14.3)
No clear source identified	2 (14.3)
Clinical outcomes	
Final VA	
logMAR, mean±SD (Snellen equivalent)	1.87±1.16 (20/1500)
20/200 or worse, *n* (%)	13/16 (81.3)
Hand movement or worse, *n* (%)	10/16 (62.5)
No light perception or evisceration, *n* (%)	6/16 (37.5)
Evisceration, *n* (%)	3/16 (18.8)
Mortality, *n* (%)	2 (14.3)

EKE: Endogenous *Klebsiella* endophthalmitis; SD: Standard deviation; VA: Visual acuity.

and gentamicin. Two patients (14.3%) had infection caused by resistant strains, one of them was resistant to amoxicillin/clavulanate and the other one was extended spectrum beta-lactamases producing.

Treatment and Clinical Outcomes All patients received intravenous broad-spectrum antibiotics before or at the diagnosis of endophthalmitis. Intraocular fluid was sampled (vitreous or aqueous if dry vitreous tap) and intravitreal ceftazidime with or without vancomycin was injected in all affected eyes at clinical diagnosis of endophthalmitis. Four eyes (22.2%) received more than one intravitreal injections and 9 eyes (50%) underwent pars plana vitrectomy as indicated. Mortality occurred in 2 patients (14.3%). Mean final visual acuity was logMAR 1.87±1.16 (Snellen equivalent 20/1500). Visual outcome was unfavourable with 13 eyes (81.3%) having vision of 20/200 or worse. Six out of 16 eyes (37.5%) had complete loss of vision with no light perception and 3 eyes (18.8%) required evisceration. All eviscerated eye had visual acuity of no light perception before the procedure.

Table 3 Multivariate linear regression using final visual acuity in logMAR scale as dependent variable

Factors	Unstandardised coefficients beta	95%CI	Standardised coefficients beta	*P*
Using individual eyes as unit of analysis				
Constant	1.35	-1.145 to 3.846	-	0.241
Age	-0.028	-0.073 to 0.017	-0.306	0.189
Gender (male)	0.185	-0.693 to 1.062	0.082	0.634
Background DM	-0.609	-1.413 to 0.195	-0.286	0.116
Positive blood culture	0.012	-1.448 to 1.473	0.006	0.985
Positive intraocular fluid culture	-0.501	-1.972 to 0.971	-0.212	0.448
Unilateral involvement	0.991	0.094 to 1.888	0.466	0.035[a]
Time lapsed from ocular symptom to EKE diagnosis	-0.052	-0.19 to 0.086	-0.237	0.405
Presenting VA in logMAR	0.771	0.092 to 1.449	0.552	0.031[a]
Hypopyon	-1.002	-2.219 to 0.216	-0.447	0.093
Lack of fundus view	2.119	0.452 to 3.785	0.977	0.02[a]
Supplementary analysis using one eye from each patient (right eye taken for bilateral cases by convention)				
Constant	1.842	-0.972 to 4.657	-	0.129
Age	-0.046	-0.101 to 0.009	-0.563	0.078
Gender (male)	-0.247	-1.373 to 0.88	-0.122	0.536
Background DM	-0.541	-1.436 to 0.355	-0.275	0.151
Positive blood culture	0.648	-1.414 to 2.71	0.33	0.391
Positive intraocular fluid culture	-0.497	-2.036 to 1.042	-0.231	0.379
Unilateral involvement	0.93	-0.203 to 2.062	0.432	0.08
Time lapsed from ocular symptom to EKE diagnosis	-0.119	-0.299 to 0.061	-0.491	0.126
Presenting VA in logMAR	0.983	0.201 to 1.766	0.763	0.028[a]
Hypopyon	-0.504	-1.919 to 0.911	-0.248	0.339
Lack of fundus view	2.406	0.17 to 4.642	1.224	0.042[a]

CI: Confidence interval; DM: Diabetes mellitus; EKE: Endogenous *Klebisella* endophthalmitis; VA: Visual acuity. [a]*P*<0.05 was taken as significant.

Statistical Analyses and Prognostic Factors Poor prognostic factors of final visual acuity are summarised in Table 3. Multivariate linear regression showed that unilateral involvement (*P*=0.035), poor presenting visual acuity (*P*=0.031) and lack of fundus view (*P*=0.02) were prognostic factors for poor visual outcome when each eye were analysed. Supplementary analysis using one eye model for bilateral cases, where right eye was analysed by convention, showed similar findings for poor presenting visual acuity (*P*=0.028) and lack of fundus view (*P*=0.042). But the effect of unilateral involvement lost statistical significance (*P*=0.08).

Cases Highlights No clear septic source could be identified in 2 cases (Table 1, No.7 and No.13) after extensive investigations. The diagnosis of endogenous *Klebsiella* endophthalmitis in the 2 cases was confirmed by positive culture of intraocular fluid only. *Klebsiella* is a normal flora in the gastrointestinal tract. It was unlikely a coincidence that both cases shared the similarity of having gastrointestinal pathologies (rectal cancer in No.7 and recurrent intestinal obstruction in No.13). In a separate report[13], it was postulated that bacteria gained access into the bloodstream *via* mucosal defect of the tumour in case No.7 (Figure 1). Therefore, it is advisable to offer gastrointestinal workup for cases of endogenous *Klebsiella* endophthalmitis without apparent septic source.

Clinical signs of endophthalmitis include conjunctival injection, hypopyon, vitritis and subretinal abscess. However, 2 cases of the series (Table 1, No. 9 and 10) were documented with no conjunctival injection at initial examinations. Therefore, absence of conjunctival injection does not preclude the possibility of endophthalmitis.

One patient with background acute leukaemia (Table 1, No.14) had neutropenic fever and persistent *Klebsiella* bacteraemia for 6wk before developing endophthalmitis. She was seen by ophthalmologist as an asymptomatic consult 6wk prior to ocular involvement. Initial ocular examination was normal. It was until the development of eye redness when ophthalmologist was consulted once again and endogenous endophthalmitis was diagnosed (Figure 2). Despite blood culture yielded extended spectrum beta-lactamases producing *Klebsiella pneumoniae*, her vision remained relatively good after repeated intravitreal antibiotics injection. This case

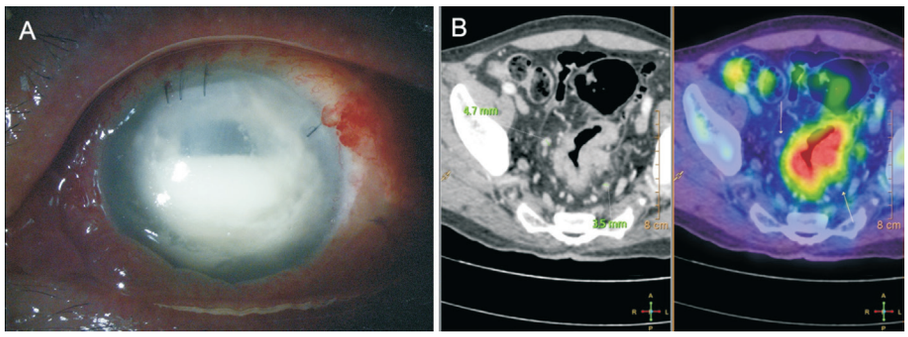

Figure 1 Case of *Klebsiella* endophthalmitis with rectal cancer (Case No.7) A: Slit lamp photo showing rapid development of hypopyon after first pars plana vitrectomy; B: PET-CT revealed hypermetabolic lesion at rectum, compatible with rectal cancer.

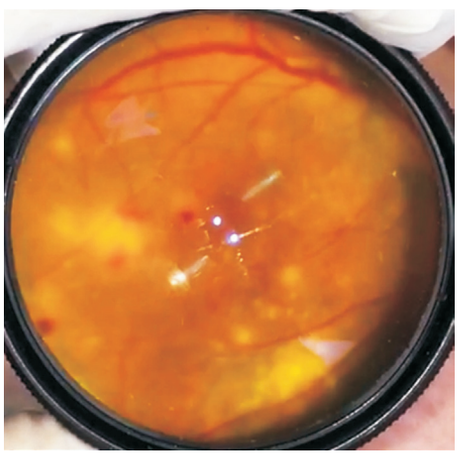

Figure 2 Subretinal abscesses in patient with persistent *Klebisella* bacteraemia documented with smart phone photography in isolation ward.

highlighted the importance of interval re-examination and clinical vigilance towards symptoms of endophthalmitis.

DISCUSSION

General Characteristics of Endogenous Klebsiella Endophthalmitis Despite increased awareness of the condition, visual outcome of endogenous *Klebsiella* endophthalmitis remains poor. This is echoed by the study of another centre in Hong Kong, which reported an even higher evisceration rate of 60%[7].

Emergence of drug-resistant *Klebsiella pneumoniae* had been reported in Asia[14-16]. Of note, the majority of patients in this series (85.7%) were infected with non-resistant strains of *Klebsiella pneumoniae*, suggesting that the standard management of intravitreal ceftazidime remains effective against the cases in this study region.

Klebsiella liver abscess is well recognised as a cause of endogenous endophthalmitis. In contrast to the vast majority of liver abscess (94.7%) in a previous series of endogenous *Klebsiella* endophthalmitis[7], only 64.3% of patients in this series had liver abscess. This should alarm doctors treating patients with *Klebsiella* sepsis that endophthalmitis can still occur without liver abscess. Moreover, ocular symptoms may precede systemic symptoms in some patients (Table 1, No.6). Therefore, systemic sources should be extensively looked for if patient presents with an acute onset of endophthalmitis.

Prognostic Factors Poor presenting visual acuity and lack of fundus view were identified by multivariate linear regression as poor prognostic factors of visual outcome in this study. Despite using individual eye as a unit of measure in regression is a valid analysis[17], caution was exercised to consider unilateral involvement as poor prognostic factor because supplementary analysis using one eye only in bilateral cases failed to identify it as a significant factor. This method of analysis might avoid the potential magnification of effect of shared systemic factors in bilateral cases. Nevertheless, some existing reports did find unilateral involvement a poor prognostic factor[5,8]. The postulation was that bilateral cases tend to present earlier than those with unilateral involvement. However, this study did not find time delay from ocular symptom to endophthalmitis diagnosis a statistically significant factor for poor visual outcome. Lack of fundus view signifies a greater degree of inflammation in the vitreous cavity at the time of diagnosis, which in turn serves as a marker of infection severity. Poor presenting visual acuity had previously been reported as predictors of poor visual outcome[4,8]. Poor presenting visual acuity may be a result of media opacity due to vitritis, which again correlates with the degree of inflammation. At the same time, extensive retinal involvement of the posterior pole of the eye by direct inoculation of *Klebsiella* bacteria through the vascular choroid can cause severe macular dysfunction, leading to a poor presenting visual acuity. Therefore, lack of fundus view and poor presenting visual acuity translate severe degree of infection to poor final visual acuity.

Ophthalmological Screening Recommendations Controversies exist in asymptomatic ophthalmological screening for patients with *Klebsiella* sepsis. Some suggested universal ophthalmological screening for all cases of *Klebsiella* sepsis and supported the argument with a lower evisceration rate after implementation of a regional universal screening program after the year 2000[5]. However, there was no difference in final visual acuity in their study. The lower

evisceration rate could have been the result of increased clinical awareness, improved systemic infection control and better instrumentation in pars plana vitrectomy. Others recommended screening only for cases of *Klebsiella* liver abscess[18]. On the other hand, a substantial proportion of cases would be missed as hepatobiliary system infection only accounted for 64.3% in our series.

In general, the occurrence of endophthalmitis in *Klebsiella* sepsis is rare. Our study identified only 18 eyes in 14 patients within a period of 12 years in a major regional tertiary centre which serves a population of over 1 million. The reported endophthalmitis rate of *Klebsiella* liver abscess in Asia ranges from 3% to 7%[4,19-20]. Only 3.8% of patients with *Klebsiella* bacteraemia was found with endophthalmitis[21]. As shown in our study where majority of eyes were symptomatic (88.9%), the cost-effectiveness of asymptomatic screening is questionable, especially in a region with tight resources. The universal poor visual outcome reported across studies[4-8] and the lack of standardised treatment beyond initial intravitreal antibiotics injection, have further weakened the argument for asymptomatic ophthalmological screening. By far, no study has successfully shown a delay in recognition of *Klebsiella* endophthalmitis has a significant effect on visual outcome. Our study also fails to show *via* multivariate linear regression the significant effect on final visual acuity by a delay from ocular symptom onset to endophthalmitis diagnosis.

Considering the heterogeneous nature of primary infection sites, it is difficult to provide a recommendation on targets for asymptomatic screening. Exemplified by 2 of the cases in this study (Table 1, No.9 and 14), patients can develop endogenous endophthalmitis even after normal initial ophthalmological examinations. Therefore, a normal examination during asymptomatic screening might create a false sense of security to the clinicians managing the *Klebsiella* sepsis. Moreover, asymptomatic screening might not be feasible in some units, where inpatient ophthalmological service is not available.

Nevertheless, screening should be considered in patients who cannot express their ocular symptoms, for example cases in intensive care unit or with cognitive impairment, as recommended by some authorities[6]. As shown in this series, lack of conjunctival injection does not preclude the possibility of endophthalmitis. It might be difficult to spot early signs of endophthalmitis in non-communicable patients. Excluding the exceptional case of persistent *Klebsiella* bacteraemia due to acute leukaemia (Table 1, No.14), where a long-time lapse of 42d from systemic symptom onset to ocular symptom had occurred, mean time from systemic symptom onset to ocular symptom in our study was 3.38±3.01d. Therefore, an ophthalmic examination performed within 1wk of systemic infection symptom onset, as recommended in a study[21], will theoretically identify most of the cases of endogenous *Klebsiella* endophthalmitis.

Strengths and Limitations This is a study in an endemic region with a long study period of 12y. The study was conducted in a major tertiary hospital in the region where on-site ophthalmological consultation and assessment was readily available. Statistical analysis was performed using a multivariate model, which took the effect of multiple factors and variables into consideration. By performing linear regression with final visual acuity as the dependent variable, this study avoided arbitrarily dividing the continuous nature of visual outcome into dichotomous nature of good or poor visual acuity as previous reports did.

Limitations of our study include the retrospective nature and the relatively small number of cases. Missing data was inevitable due to the retrospective nature. Lack of standardised treatment algorithm complicated meaningful analysis of the effect of ocular treatment on visual outcome.

In conclusion, visual outcome of endogenous *Klebsiella* endophthalmitis remains poor. Poor presenting visual acuity and lack of fundus view predict poor final visual acuity. High index of suspicion for endophthalmitis is important in *Klebsiella* sepsis patients complaining of ocular symptoms. Ophthalmological screening is recommended in non-communicable patients with *Klebsiella* sepsis, and the suggested time frame would be within one week of systemic infection symptom onset. Interval re-examination should also be considered in cases where systemic infection is not yet controlled.

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