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# **BMJ Open** Comparison of the aetiology, microbiological isolates and antibiotic susceptibilities of endophthalmitis between children and adults in southern China: a retrospective, cohort study

Yao Yang 💿 , Jiaqi Lin, Yujie Li, Xiaohu Ding, Manli Liu, Jieting Zeng, Xiaofeng Lin, Fang Duan

### ABSTRACT

**Objectives** To compare aetiology, microbiological isolates and antibiotic susceptibilities of endophthalmitis between children and adults.

Design Retrospective observational study.

**Participants** Patients admitted to Zhongshan Ophthalmic Center between January 2013 and December 2019 with clinically diagnosed endophthalmitis were included. **Outcome measures** The aetiology, microbiological isolates and antibiotic susceptibilities of endophthalmitis were analysed.

Results Of 1803 patients, 430 (23.8%) were aged ≤16 years. In both children and adults, the main aetiology was trauma (85.6% vs 64.7%, p<0.05). Streptococcus species (spp.) (28.8%) were most prevalent in paediatric post-traumatic endophthalmitis; whereas, coagulasenegative staphylococci (36.9%) were dominant in adults In postoperative endophthalmitis, all children had bacterial infections, while fungal infections accounted for 12.5% in adults. In endogenous endophthalmitis caused by fungi, Candida was most prevalent in adults (26.9%); whereas, all causative fungi involved filamentous fungi in children. Isolated bacteria in children presented a higher susceptibility in 7 of 11 antibiotics compared with those in adults. Levofloxacin had the highest susceptibility rate in children (97.9%), and ofloxacin had the highest susceptibility rate in adults (90.6%).

**Conclusion** The main aetiology was trauma, with a higher proportion in children than in adults. The microbial profile of paediatric endophthalmitis was different from those of adults. Susceptibilities of causative bacteria to most antibiotics were higher in children than in adults.

### INTRODUCTION

Endophthalmitis is a rare but devastating condition that results in visual impairment and even blindness. Endophthalmitis usually occurs because of an external source, such as open globe injury, intraocular surgery or infective keratitis, or it emerges from systemic pathogen dissemination. The most common aetiologies for endophthalmitis

### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used the clinical records from a large tertiary ophthalmic centre to derive a cohort to include a large number of patients with endophthalmitis that enhances the robustness of the study.
- ⇒ This study described differences between children and adults with endophthalmitis, which have received less attention before.
- ⇒ This study had a lack of follow-up, because many patients with endophthalmitis referred from all over China, which makes follow-up difficult.

are post-traumatic and postoperative endophthalmitis, and various studies have reported the incidence of endophthalmitis to be between 4% and 30% after open globe injury.<sup>1</sup> Endophthalmitis occurring after cataract surgery is the most common type of postoperative endophthalmitis, with reported incidence rates ranging from 0.03% to 0.2%.<sup>2</sup>

ĝ An analysis of the microbiological spectrum of endophthalmitis is helpful for guiding empirical therapy before causative <u>0</u> isolates are identified. Several studies have reported that coagulase-negative staphylococcus is the most common pathogen associated with both post-traumatic endophthalmitis and postoperative endophthalmitis in all age groups.<sup>3 4</sup> However, fewer studies have included paediatric endophthalmitis **3** patients alongside adults. Al-Rashaed *et al*<sup> $\delta$ </sup> reported Streptococcus species (spp.) as the leading isolate in paediatric patients with post-traumatic endophthalmitis. Similarly, in a previous study, we reported that Streptococcus spp. were the most prevalent isolates in the paediatric population,<sup>6</sup> suggesting a difference in the microorganism spectrum between children and adults. It is known that

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between children and	aduits				
	Paediatric		Adults		Ρ
	n	%	n	%	
Post-traumatic	368	85.6	889	64.7	< 0.05
Without IOFB	321	74.7	484	35.3	
With IOFB	47	10.9	405	29.5	
Postoperative	17	4	205	14.9	< 0.05
Cataract surgery	5	1.2	130	9.5	
Secondary IOL implantation	4	0.9	8	0.6	
Glaucoma surgery	5	1.2	34	2.5	
Vitrectomy	0	0	19	1.4	
Intraocular injection	1	0.2	4	0.3	
Keratoplasty	2	0.5	6	0.4	
Scleral buckling	0	0	2	0.1	
Others	0	0	2	0.1	
Endogenous	35	8.1	163	11.9	0.031
Keratitis-associated	10	2.3	116	8.4	< 0.05
Total	430		1373		

IOFB, intraocular foreign body; IOL, intraocular lens.

children are not equivalent to adults. To date, few studies have compared the endophthalmitis characteristics of paediatric and adult patients in the same area and over the same timeframe.

In this study, we reviewed data concerning 1803 consecutive inpatients who had been clinically diagnosed with endophthalmitis. We aimed to (i) describe the aetiology of endophthalmitis in both children and adults, (ii) compare the causative isolates of different types of endophthalmitis between children and adults, and (iii) analyse antibiotic susceptibility between children and adults. Our findings present valuable information in terms of empirical therapy for this disease.

### **MATERIAL AND METHODS**

This study was performed in compliance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University (2019KYPJ050). The requirement for written informed patient consent was waived given the retrospective nature of the study.

### **Study population**

Data concerning 1803 consecutive inpatients who had been clinically diagnosed with endophthalmitis were retrospectively collected at Zhongshan Ophthalmic Center, southern China, from January 2013 to December 2019.

### **Procedures**

We collected demographic data such as patient age and sex. Patients were diagnosed with endophthalmitis by a senior ophthalmologist based on their medical history and clinical manifestations, including the presence of corneal oedema, hypopyon, anterior chamber cells and inflammation in the vitreous. All patients were administered topical antibiotics after clinical diagnosis. The choice of antibiotics initially depends on the ophthalmologist's empirical judgement of the infection and **u** subsequently be adjusted according to smear or culture results. Surgical treatments, including intravitreal injection of antibiotics, pars plana vitrectomy and enucleation, were performed based on the assessment of the ophthalmologist. All patients with endophthalmitis were then 8 divided into four groups according to aetiology, namely, post-traumatic, postoperative, endogenous and keratitisassociated endophthalmitis. Patients were also divided according to age into paediatric (0-16 years) and adult  $(\geq 17 \text{ years})$  groups.<sup>7</sup>

Pathogen culture was undertaken using patients' aqueous humour or vitreous humour or eye contents (intraocular fluid cultures). Aqueous/vitreous taps for use culture were performed during surgery. Aqueous humour from the anterior chamber was aspirated through the corneal limbus with a needle (0. 45 mm\*16 mm RWLB) on a 1-mL syringe. Vitreous specimens were collected through the pars plana prior to antibiotic injection or 5 vitrectomy via a needle or vitrector (suction 0-500 mm te Hg). Eye contents removed during enucleation were collected. The samples were inoculated in culture bottles, BACT/ALERT SA and BACT/ALERT SN, (BioMerieux, Inc., Marcy-l'Étoile, France) for the growth of bacterial cultures and potato glucose agar for the growth of  $\blacksquare$ fungal cultures, respectively.<sup>8-10</sup> Anaerobic bacteria were cultured in an anaerobic environment consisting of an anaerobic gas-producing bag, an oxygen indicator and an anaerobic culture bag. The samples were placed in a culture instrument until they were reported positive. The contents of positive bacterial culture bottle were transferred to Columbia blood agar medium and cultured for 24-48 hours to obtain pure colony. All bacterial isolates were subjected to species identification on an automated microbiological system Vitek 2 Compact (BioMérieux, Inc., Marcy-l'Étoile, France); all fungi isolates were identified by experienced technicians according to fungal morphology. Antibiotic susceptibility testing of the isolated bacteria was performed using both the Kirby–Bauer disc diffusion method and the broth dilution method according to the performance standards for antimicrobial susceptibility testing described by the Clinical and Laboratory Standards Institute guideline. (1) Kirby–Bauer disc diffusion method, the standardised bacterial fluid was inoculated to the MH agar plate. Antimicrobial-impregnated disks which contain antibiotics with different concentration gradients were placed on the surface of the agar. The plates were incubated at 35°C for 16-18 hours. And then, the diameter of the

Table 2         Comparison of the call	ausative isola	tes of endopl	nthalmitis be	etween chi	dren and ad	dults		
	Post-traumatic Postopera		tive Endogenous			Keratitis-associated		
	Children	Adults	Children	Adults	Children	Adults	Children	Adults
Causative isolates	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gram-positive cocci	54 (51.9)	148 (49.2)	3 (60.0)	28 (70.0)	3 (37.5)	12 (23.1)	2 (100.0)	2 (12.5)
Coagulase-negative staphylococci	14 (13.5)	111 (36.9)	1 (20.0)	18 (45.0)	-	5 (9.6)	1 (50.0)	1 (6.3)
Streptococcus spp.	30 (28.8)	9 (3.0)	2 (40.0)	1 (2.5)	1 (12.5)	3 (5.8)	1 (50.0)	1 (6.3)
Enterococcus spp.	2 (1.9)	11 (3.7)	-	9 (22.5)	-	3 (5.8)	-	-
Kocuria spp.	3 (2.9)	6 (2.0)	-	-	-	1 (1.9)	-	-
Granulicatella spp.	-	4 (1.3)	-	-	1 (12.5)	-	-	-
Leuconostoc spp.	1 (1.0)	3 (1.0)	-	-	-	-	-	-
Others	4 (3.8)	4 (1.3)	-	-	1 (12.5)	-	-	-
Gram-positive bacilli	19 (18.3)	35 (11.6)	-	1 (2.5)	-	5 (9.6)	-	-
Bacillus cereus	8 (7.7)	19 (6.3)	_	-	_	1 (1.9)	_	_
Bacillus subtilis	3 (2.9)	3 (1.0)	-	_	_	_	-	_
Propionibacterium acnes	2 (1.9)	2 (0.7)	_	1 (2.5)	_	1 (1.9)	_	_
Others	6 (5.8)	11 (3.7)	-	_	-	3 (5.8)	-	_
Gram-negative cocci	1 (1.0)	3 (1.0)	-	-	-	1 (1.9)	-	-
Neisseria spp.	1 (1.0)	3 (1.0)	-	-	-	1 (1.9)	-	-
Gram-negative bacilli	18 (17.3)	75 (24.9)	2 (40.0)	6 (15.0)	2 (25.0)	14 (26.9)	-	7 (43.8)
Pseudomonas aeruginosa	1 (1.0)	11 (3.7)	1 (20.0)	2 (5.0)	2 (25.0)	1 (1.9)	-	6 (37.5)
Enteric bacilli	3 (2.9)	12 (4)	-	-	-	-	-	-
Aeromonas spp.	2 (1.9)	6 (2.0)	-	-	-	-	-	1 (6.3)
Acinetobacter spp.	1 (1.0)	5 (1.7)	-	1 (2.5)	-	1 (1.9)	-	-
Xanthomonas spp.	1 (1.0)	5 (1.7)	-	-	-	2 (3.8)	-	-
Serratia spp.	2 (1.9)	3 (1.0)	-	2 (5.0)	-	-	-	-
Escherichia coli	2 (1.9)	2 (0.7)	-	1 (2.5)	-	1 (1.9)	-	-
Pantoea spp.	3 (2.9)	-	-	-	-	-	-	-
Klebsiella spp.	-	2 (0.7)	-	-	-	6 (11.5)	-	-
Haemophilus influenzae	-	-	1 (20.0)	-	-	1 (1.9)	-	-
Others	3 (2.9)	29 (9.6)	-	-	-	2 (3.8)	-	-
Fungus	12 (11.5)	40 (13.3)	-	5 (12.5)	3 (37.5)	20 (38.5)	_	7 (43.8)
Aspergillus spp.	6 (5.8)	12 (4.0)	-	3 (7.5)	-	-	-	2 (12.5)
Candida spp.	1 (1.0)	4 (1.3)	-	1 (2.5)	-	15 (28.8)	-	-
Fusarium spp.	2 (1.9)	9 (3.0)	-	1 (2.5)	1 (12.5)	2 (3.8)	-	3 (18.8)
Mucor	-	4 (1.3)	-	-	1 (12.5)	-	-	-
Penicillium	-	1 (0.3)	-	-	1 (12.5)	_	-	-
Blastomyces dermatitidis	-	1 (0.3)	-	-	-	-	-	-
Other filamentous fungi	1 (1.0)	6 (2.0)	-	-	-	3 (5.8)	-	2 (12.5)
Uncertain	2 (1.9)	3 (1.0)	-	-	-	-	-	-
Total	104 (100)	301 (100)	5 (100)	40 (100)	8 (100)	52 (100)	2 (100)	16 (100)

area without obvious bacterial growth was measured to determine the sensitivity of bacteria to antibiotics. (2) In broth dilution method, the standardised bacterial fluid and the drug-sensitive test culture medium were mixed completely in the ratio of 1:100. Equivalent bacterial fluid mixture (100  $\mu$ L) was added to the plates with

wells containing antibiotics with different concentration gradients and antimicrobial susceptibility reagents. The plates were incubated overnight. The lowest antibiotic concentration which successfully inhibits the growth of bacteria (no bacterial growth) is minimum inhibitory concentration. Bacterial susceptibilities were recorded as 'sensitive', 'intermediate' or 'resistant'. For our study purposes, 'sensitive' and 'intermediate' susceptibilities were both considered 'sensitive'. The following antibiotics were used for susceptibility tests: fluoroquinolones (moxifloxacin, levofloxacin and ofloxacin), cephalosporins (ceftazidime, cefazolin and cefuroxime), aminoglycosides (tobramycin, amikacin), penicillin, meropenem, linezolid, vancomycin and neomycin. The susceptibility of vancomycin and moxifloxacin have routinely been tested from 2017. However, we only began routine penicillin susceptibility testing in 2016.

### **Patient and public involvement statement** None.

### **Statistical analysis**

All analyses were performed using SPSS V.16.0 (SPSS Inc., Chicago, IL, USA). Characteristics of the study population, the aetiology of endophthalmitis, the culture results and the susceptibility data are summarised using means and SD for continuous variables and percentages for categorical variables. Differences in categorical variables were assessed using an  $x^2$  test, and p<0.05 was considered significant.

### RESULTS

During the study period, we collected data concerning 1803 patients diagnosed with endophthalmitis. There were 430 (23.8%) patients aged  $\leq 16$  years (average age, 6.19±3.43 years; range, 2 months to 16 years; males, 71.2%). Among the 1355 patients aged  $\geq 17$  years, the average age was 46.72±15.12 years and the proportion of males was 76.1%, which was significantly greater than that of the paediatric group (p=0.006).

The aetiologies of endophthalmitis are listed in table 1. In the paediatric group, 85.6% of the patients developed endophthalmitis after eye trauma and 12.8% (47/368) presented with a retained intraocular foreign body (IOFB). Among the remaining patients, 4% were diagnosed with endophthalmitis after intraocular surgery, most commonly after cataract and glaucoma surgery (29.4%, 5/17 patients), followed by endogenous endophthalmitis (8.1%) and keratitis-associated endophthalmitis (2.3%). In the adult group, post-traumatic endophthalmitis was identified in 64.7% of patients, among whom, the proportion of those with IOFB-related endophthalmitis was 45.6% (405/889), which was considerably greater than that of the paediatric group (45.6% vs 12.8%), p<0.05). Postoperative endophthalmitis was observed in 14.9% of patients, with cataract surgery (63.4%, 130/205)being the leading cause. A total of 11.9% of patients had endogenous endophthalmitis, and 8.4% of patients had keratitis-associated endophthalmitis.

Pathogen cultures were performed for 1394 (77.3%) of the 1803 patients, of which 1253 (69.5%) were

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cultured from intraocular samples. In 16 patients, both the vitreous humour and aqueous humour were sent for culture; 40.9% (614/1039) of the cultures were positive for vitreous humour, 36.7% (126/199) of cultures were positive for aqueous humour and 45.2% (17/31) of the culture were positive for eye contents. In total, 502 (36.0%, 502/1394) patients had positive cultures, 20 had double infections and 3 patients had triple infections (total number of isolates, n=528). Among these, 59.1% were gram-positive bacteria, 24.4% were gram-negative bacteria and 16.5% were fungal isolates.

endophthalmitis, with Streptococcus spp. (28.8%) being the most prevalent organism in the paediatric group, followed by coagulase-negative staphylococci (13.5%), Bacillus cereus (7.7%) and Aspergillus spp. (5.8%). In patients aged ≥17 years, coagulase-negative staphylococci were most prevalent (36.9%), followed by *B. cereus* (6.3%)and Aspergillus spp. (4.0%). All isolates in the paediatric group with postoperative endophthalmitis were bacterial; whereas, fungal isolates were identified in 12.5% of 5 patients aged  $\geq 17$  years. In terms of endogenous cases, Pseudomonas aeruginosa (25%) was the most common isolate in the paediatric group; whereas, Candida spp. (28.8%) were dominant in the adult group. Both isolates ated involved in keratitis-related endophthalmitis in the paedi-G atric group were gram-positive bacteria; whereas, 43.8% of the isolates in patients aged  $\geq 17$  years with keratitisrelated endophthalmitis were fungi.

The total susceptibility rates of the isolated bacteria are shown in table 3. In general, isolated bacteria were highly sensitive to levofloxacin and ofloxacin in both the paediatric and adult groups (97.9% vs 94.8% and 89.3% vs 90.6%, respectively). The sensitivity rates to ceftazidime were 69.2% and 76% in paediatric and adult groups,  $\blacktriangleright$ respectively. In addition to levofloxacin and ofloxacin, gram-positive bacteria isolates from the paediatric group were highly susceptible to linezolid (100%), vancomycin **Z** (88.9%) and moxifloxacin (80.0%); whereas, gramnegative bacteria were highly sensitive to meropenem (100%) and neomycin (91.7%). In the adult group, gram-positive bacteria were highly sensitive to linezolid (99.1%) and vancomycin (97.5%); whereas, gramnegative bacteria presented the highest susceptibility to meropenem (93.2%).

Coagulase-negative staphylococci and *Streptococcus* gp. exhibited high sensitivity to vancomycin (98.7%, 100%) and cefuroxime (100%, 95%). *Enterococcus* spp. exhibited a notable susceptibility to linezolid (100%) yet displayed a lower sensitivity rate to vancomycin (50%). *B. cereus* showed high sensitivity to levofloxacin (100%), tobramycin (100%) and amikacin (88.9%). The predominant gram-negative isolate, *P. aeruginosa*, showed high susceptibility to levofloxacin (100%), meropenem (100%), amikacin (100%) and tobramycin (95.8%).

	Children			Adults		
	Gram-positive	Gram-negative	Total	Gram-positive	Gram-negative	Total
Ofloxacin	63/66	10/11	73/77	83/93	36/42	119/135
	95.5%	90.9%	94.8%	89.2%	85.7%	90.6%
Levofloxacin	69/71	23/23	92/94	136/165	80/86	216/251
	97.2%	100.0%	97.9%	82.4%	93.0%	89.3%
Moxifloxacin	4/5	1/1	5/6	63/77	9/11	72/88
	80.0%	100.0%	83.3%	81.8%	81.8%	81.9%
Vancomycin	8/9	-	-	77/79	_	-
	88.9%			97.5%		
Linezolid	9/9	-	_	114/115	_	_
	100.0%			99.1%		
Meropenem	1/2	11/11	12/13	29/36	41/44	70/80
	50.0%	100.0%	92.3%	80.6%	93.2%	88.2%
Penicillin	22/43	2/4	24/47	24/113	10/29	34/142
	51.2%	50.0%	51.1%	21.2%	34.5%	30.7%
Cefazolin	23/29	7/20	30/49	40/48	15/70	55/118
	79.3%	35.0%	61.2%	83.3%	21.4%	50.9%
Cefuroxime	51/66	10/24	61/90	60/87	36/91	96/178
	77.3%	41.7%	67.8%	69.0%	39.6%	58.6%
Ceftazidime	22/32	14/20	36/52	71/88	51/68	122/156
	68.8%	70.0%	69.2%	80.7%	75.0%	76.0%
Tobramycin	41/75	21/25	62/100	116/185	83/103	199/288
	54.7%	84.0%	62.0%	62.7%	80.6%	67.3%
Amikacin	12/41	13/16	25/57	30/51	62/84	92/135
	29.3%	81.3%	43.9%	58.8%	73.8%	60.9%
Neomycin	31/40	11/12	42/52	54/66	35/40	89/106
	77 50/	91 7%	80.8%	81.8%	87.5%	82.9%

### DISCUSSION

In this study, we compared the aetiology, microbiological isolates and antibiotic susceptibilities of endophthalmitis between children and adults in the same area and over the same timeframe. Data concerning 1803 patients with clinically diagnosed endophthalmitis were analysed, of whom 23.8% were patients aged  $\leq 16$  years. Traumatic endophthalmitis was the most common aetiology, and the most common isolates differed between the groups. Streptococcus spp. were the most common isolates in the paediatric group; whereas, coagulase-negative staphylococci were predominant in the adult group. Endogenous endophthalmitis had similar rates of fungal infections in the two groups, but filamentous fungal infections were prevalent in children while Candida was predominant in adults. The causative bacteria in children were most susceptible to levofloxacin in children, while the causative bacteria in adults were most sensitive to ofloxacin. Gram-positive bacteria were highly susceptible to vancomycin and linezolid; whereas, gram-negative bacteria

, and Trauma was the most prevalent aetiology in both groups in our study, although the proportion of post-traumatic endophthalmitis in children was significantly greater than that in adults (85.6% vs 64.7%, p<0.05). Previous studies have shown that the main aetiology of endophthalmitis has varied across different areas and countries in adultdominated populations. For example, data from the USA indicated that the main aetiology of endophthalmitis was postoperative infection; whereas, in China, the main aetiology has been reported to be post-traumatic infection.<sup>38</sup> However, two other studies from the USA reported that trauma was the main aetiology of paediatric endophthalmitis,<sup>1112</sup> which was consistent with our findings; however, the proportion of patients with traumatic endophthalmitis was lower in those studies than in our study. Rishi *et al*<sup>13</sup> reported that IOFB-related endophthalmitis accounted for 4% of paediatric post-traumatic endophthalmitis cases; whereas, the proportion of IOFB-related

endophthalmitis cases across all age groups reported in other studies ranged from 24% to 53%.<sup>14–16</sup> Our findings indicated a similar trend; that is, the proportion of IOFB-related endophthalmitis in the paediatric group was considerably lower than that in the adult group (12.8% vs 45.6%, p<0.05).

Concerning post-traumatic endophthalmitis in our study, gram-positive bacteria were the predominantly detected organisms in both age groups. Recent studies from southern China, northern China, and France reported that Streptococcus spp. were the leading cause of paediatric endophthalmitis.<sup>6 17 18</sup> Sen et al retrospectively enrolled 30 paediatric patients with post-traumatic endophthalmitis in India and reported Streptococci (79%, 16/19) and Pseudomonas (16%, 3/19) were common organisms.<sup>19</sup> In this study, *Streptococcus* spp. were the most prevalent organism (28.8%, 30/104) involved in post-traumatic endophthalmitis in children, but the prevalence was not as high as that reported by Sen et al. Coagulase-negative staphylococci was the second most common organism involved in post-traumatic endophthalmitis in children within our study (13.5%, 14/104). The different sample sizes may have contributed to differences in the proportions of the most common pathogens. In contrast, coagulase-negative staphylococci were the most common causative organisms in adults. Aspergillus spp. were the most prevalent causative fungi and the proportion was similar in both groups (5.8% vs 4.0%). Additionally, B. cereus was prevalent in both children and adults, and P. aeruginosa and Enterococcus spp. were common isolates in adults. Streptococcus spp., Aspergillus spp., B. cereus, P. aeruginosa and Enterococcus spp. have been reported as highly virulent causative organisms of endophthalmitis.<sup>20-24</sup> Although there was some difference in the prevalence of pathogens associated with post-traumatic endophthalmitis between the two groups, most of the pathogens were highly virulent, particularly in children.

Our study revealed that the prevalent aetiology of postoperative endophthalmitis differed somewhat between the two groups: cataract and glaucoma surgeries were the most common aetiology in children; whereas, most infections occurred after cataract surgery in the adult group, which is consistent with previous studies from Germany and the UK.<sup>25 26</sup> Baig *et al*<sup>27</sup> reported that gramnegative bacteria accounted for 51.8% of the cultured isolates of postoperative endophthalmitis in a study conducted in Pakistan. In contrast, gram-positive bacteria were reported as the most prevalent isolates in studies from Norway and Australia.<sup>2 28</sup> Similarly, gram-positive bacteria were the predominant pathogens associated with postoperative endophthalmitis in both groups in our study. Causative pathogens can differ according to the region and environment, which may contribute to the discrepancies reported in these studies. In the paediatric group, five strains were identified, all of which were bacteria. Streptococcus spp. were the most prevalent pathogen (2/5), possibly because culture-confirmed

postoperative endophthalmitis in these children mainly occurred after glaucoma surgery (3/5), and *Streptococcus* spp. have been found to be the predominant pathogens of endophthalmitis after glaucoma surgery.<sup>29</sup> In the adult group, Coagulase-negative staphylococcus was the most common isolate of postoperative endophthalmitis, which is consistent with the findings of previous studies focused primarily on adults.<sup>2 30</sup> In addition, 12.5% of the adults had fungal infections.

Our study showed that the major causative organisms of endogenous endophthalmitis were bacteria in both children and adults, similar to the findings of previous studies from India and Korea.<sup>31 32</sup> Gounder *et al*<sup>33</sup> found that fungal endogenous endophthalmitis affected a younger population than bacterial endogenous endophthalmitis did in a study predominantly comprising adults; however, in our study, the proportion of fungal isolates was similar between children and adults (37.5% vs 38.5%). Studies from Asia, Australia and the USA reported that *Candida* spp. were the most common fungal isolates of endogenous endophthalmitis in studies predominantly involving adults.<sup>33 34</sup> Similarly, *Candida* spp. were the most prevalent isolates in adults in our study. In contrast, all the causative fungi were filamentous fungi in our paediatric group.

The rate of susceptibility of causative bacteria to antibiotics in patients with endophthalmitis has been of concern. Among the 11 antibiotics tested in our study, bacteria in the paediatric group presented greater susceptibility to seven antibiotics than did those in the adult group. The same trend was also identified in Green *et*  $als^7$  study on keratitis, in which cultured organisms of paediatric keratitis showed significantly increased rates of antibiotic susceptibility compared with those in adults. Ofloxacin and levofloxacin had the highest susceptibility rates in the two groups, with levofloxacin reaching 97.9% in children. Among the commonly used cephalosporins apart from ceftazidime, the sensitivity rates of cefazolin and cefuroxime in both groups were less than 70%.

and cefuroxime in both groups were less than 70%. Vancomycin is a sensitive antibiotic for gram-positive bacterium-induced endophthalmitis, with a sensitivity  $f_{100}$ rate of 97.7%–100% reported in previous studies.<sup>435</sup> Similarly, both groups in our study showed high susceptibility of gram-positive bacteria to vancomycin (adult group, 97.5%; paediatric group, 88.9%). Linezolid has been reported as a synthetic antibiotic for treating infections caused by multiresistant bacteria such as Streptococcus, methicillin-resistant Staphylococcus aureus and vancomycinresistant enterococci.<sup>36</sup> Das et al reported that the sensitivity of gram-positive cocci to linezolid was 93.3% after **8** cataract surgery for endophthalmitis in India.<sup>37</sup> In our study, gram-positive bacteria also showed an ideal sensitivity rate of more than 99% to linezolid in both groups, with Enterococcus spp. displaying a remarkable susceptibility of 100% to this antibiotic. In addition to quinolones, gram-negative bacteria were highly sensitive to meropenem in both groups (adult group, 93.2%; paediatric group, 100%). The susceptibility rates to ceftazidime, which is commonly used, were 69.2% in the adult

group and 76.0% in the paediatric group. Therefore, quinolone antibiotics, such as levofloxacin and ofloxacin, are ideal treatment choice for infectious endophthalmitis; however, only topical use is recommended for children. As gram-positive bacteria were highly sensitive to vancomycin and gram-negative bacilli were relatively sensitive to ceftazidime in both groups, the combined use of vancomycin and ceftazidime for intravitreal and intravenous injections is still recommended in empirical therapy for clinically diagnosed endophthalmitis.

In our study, the positive culture rate of different intraocular specimens cultured via traditional methods ranged from 36.7%-45.2%. Previous studies reported negative culture rates of up to 60% from aqueous tap biopsies and up to 55% from vitreous tap biopsies.<sup>38</sup> Since culturenegative endophthalmitis is common, new microbiological diagnostic methods offer alternative diagnostic tools for endophthalmitis. Kosacki et al reported that in the event of negative culture results, 16S rRNA PCR may allow for positive pathogen identification.<sup>39</sup> Chen et al reported that, compared with traditional culture, metagenomic next-generation sequencing had a greater positive rate for identifying pathogens in endophthalmitis patients (88.89% vs 27.78%).<sup>40</sup> Low *et al* demonstrated the utility of nanopore sequencing in identifying potential pathogens and its bacterial load in endophthalmitis, suggesting further optimisation of a portable, real-time technology for pathogen detection of endophthalmitis.<sup>41</sup> A variety of more precise and accurate microbial detection technologies will help improve the diagnosis and treatment of endophthalmitis and improve patient prognosis.

This study had limitations in terms of its retrospective nature and lack of follow-up. Our study was performed at a large tertiary ophthalmic centre in China, with many patients with endophthalmitis referred from all over China, making follow-up difficult. Furthermore, data concerning most of the initial aetiologies of endogenous endophthalmitis were not available in the medical records. However, we were able to obtain validated data from a relatively large sample size to describe differences between children and adults with endophthalmitis in terms of aetiology, microbiological isolates and antibiotic sensitivities.

In conclusion, we analysed the clinical data of 1803 patients with clinically diagnosed endophthalmitis. Trauma was the main aetiology identified in both children and adults, but it was considerably greater in children than in adults. The microbial profile of paediatric patients with endophthalmitis was different from those of adults. The susceptibility rates of causative bacteria to most antibiotics in children were higher than those in adults. This information may help guide the clinical management of endophthalmitis in both children and adults.

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 $\rm XL$  drafted the final manuscript. FD approved the vision to be submitted. FD is the guarantor.

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Patient consent for publication Not applicable.

Ethics approval This study was performed in compliance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University (2019KYPJ050). The requirement for written informed patient consent was waived given the retrospective nature of the study.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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