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Post-Cataract Surgery Fungal Endophthalmitis: 6-Year Experience in Management and Outcomes at a Tertiary Eye Care Center

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Purpose: This study aimed to describe the functional and anatomical outcomes of post-cataract surgery fungal endophthalmitis at King Khaled Eye Specialist Hospital (KKESH).

Patients and Methods: A retrospective analysis of clinical data from a single institution was performed. This study included 29 patients with post-cataract surgery endophthalmitis with suspected or confirmed fungal etiology who presented between January 1, 2017, and December 31, 2022. We evaluated demographics, clinical features, microbiological assessments, and treatment strategies. The effects of various treatments on outcomes were analyzed. The need for additional treatment and functional and anatomical outcomes was also investigated.

Results: The mean time from surgery to the onset of ocular symptoms was 52.1 (SD ± 59.9; range, 3–210) days, and the mean time from surgery to the first visit to KKESH was 81.4 (SD ± 103.5; range, 2–510) days. Low culture positivity was noted in four samples, with two revealing Aspergillus sp. and two revealing Cladosporium sp. Of the 29 patients, 6 underwent pars plana vitrectomy (PPV) and received intravitreal antimicrobial/antibiotic injections. Two of the six patients also underwent simultaneous intraocular lens removal. The average number of additional treatments, regardless of visual acuity, was lower in the PPV group than in the conservative group (0.5 [SD ± 1.1; range, 0–3] and 1.48 [SD ± 1.47; range, 0–6], respectively). In the PPV group, 50% (n=3) of the eyes achieved functional success and 83.3% (n=5) of the eyes achieved anatomical success. In contrast, in the conservative group, 43.5% (n=10) of the eyes achieved functional success and 69.6% (n=16) of the eyes achieved anatomical success.

Conclusion: For post-cataract surgery fungal endophthalmitis, a high index of suspicion and prompt PPV with empirical administration of intravitreal antifungal agents are required to achieve a favorable prognosis.

Keywords: endophthalmitis, fungal, exogenous, pars plana vitrectomy, intraocular lens removal

Introduction

Fungal endophthalmitis is a sight-threatening complication of cataract surgery,[1] with an incidence rate varying between 0.002% and 0.005%.[2] It is usually observed as cluster infections caused by contamination of intraocular irrigation solutions,[3] intraocular lenses (IOLs),[3] viscoelastic material,[1,4] or ventilation system,[3] and hospital construction activity.[3,5] The prognosis of fungal endophthalmitis is generally poor because of its often delayed diagnosis.[1,3] Some investigators have reported factors associated with the prognosis of fungal endophthalmitis, such as corneal involvement and causative fungal organisms.[3,6]

Aggressive treatment may be associated with an improved prognosis.[1] To date, establishing an optimal treatment protocol for improving prognosis has been challenging. This is due to the disease's variable presentation and differences in the virulence of causative fungi.[6] Several modalities have been used to treat this infection, including topical, intravitreal, or systemic administration of antifungal agents and vitrectomy with or without IOL removal.[1,4,6–8]

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Although substantial progress has been made towards understanding the optimal management for post-cataract fungal endophthalmitis, there are still significant knowledge gaps that need to be addressed. Specifically, there is a lack of clarity regarding the comparative effectiveness of early vitrectomy versus conservative management with intravitreal injections, particularly with respect to the functional and anatomical outcomes associated with each approach. Furthermore, while there is some suggestion that IOL removal may be beneficial in fungal cases, there is a lack of robust evidence from large-scale studies to support this approach.[4]

Additionally, the potential influence of specific fungal species on treatment outcomes and the optimal duration of antifungal therapy remains areas of uncertainty. Considering the limited understanding of fungal endophthalmitis and its severe consequences, it is crucial to conduct comprehensive studies that help recognize the variables that impact prognosis and determine the most effective management techniques. This is essential for advancing patient care and visual outcomes in this complex condition.

We performed a retrospective analysis of the clinical outcomes of patients with post cataract-surgery fungal endophthalmitis treated with topical, intravitreal, and systemic antimicrobial drugs with or without pars plana vitrectomy (PPV) and IOL removal. This study aimed to describe the functional and anatomical outcomes of treatment for post-cataract surgery fungal endophthalmitis at King Khaled Eye Specialist Hospital (KKESH).

Materials and Methods

Data and Study Design

We retrospectively reviewed 937 electronic charts of patients with post-cataract surgery endophthalmitis with suspected or confirmed fungal etiology who presented to our center and received treatment between January 1, 2017, and December 31, 2022. This study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of KKESH, Riyadh, Saudi Arabia (Institutional Review Board No. RP-22056). Informed consent was not obtained due to its retrospective nature and the lack of identifiable patient data. The data collected included demographics (age, sex, systemic illness, region of referral, history of intraocular surgery or injury, cause of endophthalmitis, prior treatment[s] received), clinical details at presentation (time to development of symptoms, symptoms, laterality, presenting visual acuity [VA], intraocular pressure, and signs), microbiology, treatment (topical, intravitreal, and systemic antimicrobial agents, vitreous surgery, IOL explantation), and outcomes (anatomical and functional).

Patients

A total of 29 consecutive patients with fungal endophthalmitis after cataract surgery were included based on the following inclusion criteria: (1) diagnosis of and treatment for fungal endophthalmitis post-cataract surgery between January 1, 2017, and December 31, 2022; (2) diagnosis of fungal endophthalmitis and a positive culture for fungi; and (3) clinical manifestations corresponding to fungal endophthalmitis (ie prolonged latency period, anterior chamber fibrinous reaction and/or granuloma) despite negative culture results. The exclusion criteria were as follows: (1) cultures positive for bacterial but not fungal endophthalmitis and (2) clinical manifestations not consistent with fungal endophthalmitis.

Treatment Approaches

All patients were referred from secondary care hospitals, and most had undergone vitreous/aqueous tapping and intravitreal injections prior to their arrival at KKESH. The requirement for initial conservative management (ie, observation with topical fortified antibiotics, vitreous tap and intravitreal antibiotic or antimicrobial injection, or anterior chamber washout and intracameral antibiotic injection with IOL explantation) or more aggressive surgical intervention (ie, PPV and intravitreal antibiotic or antimicrobial injection with or without IOL explantation) was determined by the on-call retinal surgeon based on clinical judgment.

Statistical Analyses

Data were analyzed using Microsoft Excel 365 (Microsoft Corporation, Redmond, Washington, USA). Statistical analyses were performed using SPSS version 28 (IBM Inc., Chicago, Illinois, USA). Categorical variables are presented

as frequencies and percentages (no. [%]), whereas continuous variables are presented as means (± standard deviations) and ranges (minimum–maximum). The chi-squared test was used to detect associations, where any output p-value < 0.05 was considered statistically significant.

Results

Demographics and Clinical Presentation

The final analysis included 29 patients. Patient demographics are summarized in Table 1. Most patients (26/29), presented to KKESH between October 2021 and February 2023 and were referred from a specific hospital in Mecca region. All the patients underwent cataract surgery between September 2021 and March 2022. The remaining three patients presented between 2017 and 2020. The mean time from cataract surgery to the onset of ocular symptoms was 52.1 (SD ± 59.9; range, 3–210) days, and the mean time from cataract surgery to the first visit at KKESH was 81.4 (SD ± 103.5; range, 2–510) days. The mean VA at time of referral was 1.8 (SD ± 0.8; range, 0.2–3.0), which was comparable but slightly decreased compared to the mean VA recorded at KKESH, which was 2.0 (SD ± 0.7; range, 0.4–3.0). Before referral to KKESH, most patients received treatment at a secondary care hospital, with vitreous taps and intravitreal antimicrobial injections being the most common forms of treatment. Details of the management prior to referral, along with other pertinent information on presentation, are summarized in Table 2.

Diagnostic Investigations

At the time of presentation, culture samples were aseptically collected for 23 patients, either from a vitreous/aqueous tap or PPV (initial undiluted cutter sample). However, after the initial observation, culture samples were taken from four more patients who required additional treatment in the form of PPV.

Specimens from the patients' eyes were aseptically collected and transported to the laboratory as soon as possible. The microscopic examinations used gram and Giemsa stains to identify the organisms in the samples. The culture media for fungi included blood and Sabouraud dextrose agar. The fungi were cultured at 30°C for at least 4 weeks.

Four samples yielded positive cultures, with two revealing Aspergillus sp. and two revealing Cladosporium sp. (Table 3). Notably, 22 patients underwent a vitreous/aqueous tap with an intravitreal antimicrobial injection before referral, which could account for their low culture positivity (Table 2). Unfortunately, reports from the referring hospitals did not include culture results.

Table 1 Demographics

Variable	Category	No. (%)
Age (years)	Mean (SD)	69.1 (8.7), [49–86}
Gender	Male Female	13 (44.8) 16 (55.2)
Involved eye	Right Eye Left Eye	15 (51.7) 14 (48.3)
Referral region	Mecca Asir AlBaha	26 (89.7) 1 (3.4) 2 (6.9)
Systemic disease	HTN DM Others	22 (95.7) 16 (88.9) 3 (10.3)

Abbreviations: HTN, Systemic Hypertension; DM, Diabetes Mellitus; SD, Standard Deviation.

Table 2 Findings at Initial Presentation

Variable	Category	No. (%)
Time from cataract surgery to symptoms (Days)	Mean (SD)	52.1 (59.9), [3–210]
Visual acuity at the time of referral to KKESH (LogMAR)	Mean (SD)	1.8 (0.8), [0.2–3.0]
Time from exposure to first visit at KKESH (Days)	Mean (SD)	81.4 (103.5), [2–510]
Intravitreal antimicrobial injection before referral	Yes No	22 (75.9) 7 (24.1)
Type of intravitreal antimicrobial before referral	Antibiotics alone Antifungal alone Combination antibiotics and antifungal	7 (24.1) 1 (3.4) 14 (48.3)
Surgery for endophthalmitis before referral	Yes No	1 (3.4) 28 (96.6)
Type of ocular surgery before referral	Anterior chamber washout	1 (3.4)
Initial visual acuity at KKESH (LogMAR)	Mean (SD)	2.0 (0.7), [0.4–3.0]
B-scan findings	Vitreous opacities (total) Details Vitreous opacities (Mild) Vitreous opacities (Moderate) Vitreous opacities (Severe) RC layer thickening Retinal detachment Posterior vitreous detachment	27 (93.1) 11 (40.7) 12 (44.4) 4 (14.8) 1 (3.7) 0 (0.0) 13 (65)

Abbreviations: KKESH, King Khaled Eye Specialist Hospital; SD, Standard Deviation.

Table 3 Treatment Received at KKESH

Variable	Category	No. (%)
Presumed diagnosis at presentation		
	Post Cataract Surgery Endophthalmitis	23 (79.3)
	MK-related Endophthalmitis	4 (13.8)
	Post-operative Inflammation	1 (3.4)
	Retained lens material	1 (3.4)
Initial treatment at KKESH		
	Observation and topical fortified antibiotics	6 (20.7)
	Vitreous tap and intravitreal antibiotic injection	1 (3.4)
	Vitreous tap with intravitreal antibiotic and antifungal injection	15 (51.7)
	Anterior chamber washout and intracameral antibiotics injection with IOL explantation	1 (3.4)
	Pars plana vitrectomy with intravitreal antibiotic and steroid injection	1 (3.4)
	Pars plana vitrectomy and intravitreal antimicrobial injection	5 (17.2)
	PPV and intravitreal microbial injection with IOL explantation	2 (from the 5 mentioned above) (40)

(*Continued*)

Table 3 (Continued).

Variable	Category	No. (%)
Culture results		
Culture sent	Yes	27 (93.1)
	No	2 (6.9)
Positive fungal culture	Yes	4 (13.8)
	No	25 (86.2)
Germ	Aspergillus sp.	2 (6.8)
Identified	Cladosporium sp.	2 (6.8)

Abbreviations: MK:Microbial Keratitis; IOL:Intraocular Lens; PPV: Pars Plana Vitrectomy; KKESH: King Khaled Eye Specialist Hospital.

Treatment Strategies and Outcomes

The on-call retinal surgeon at KKESH administered the initial treatment based on the clinical findings and personal judgment (Table 3). Of the 29 patients, 6 underwent Pars plana vitrectomy with Alcon Constellation® system, and intravitreal antimicrobial/antibiotic injections (1 patient received an antibiotic injection alone, whereas 5 patients received a combination of antibiotics and antifungal injections). Two of the six patients who underwent an initial vitrectomy also underwent IOL removal. The remaining patients received conservative management—six received topical fortified antibiotics; one underwent a vitreous tap with intravitreal antibiotic and steroid injection; one underwent anterior chamber washout, intracameral antibiotic injection, and IOL removal; and the remaining fifteen patients underwent a vitreous tap with intravitreal antibiotic and antifungal injections.

After initial management, 18 patients required additional treatment, 17 of whom were from the non-PPV group and only 1 in the PPV group; however, this difference was not statistically significant (p = 0.265) (Table 4 and Table S1).

We examined the average number of additional treatments based on VA (Table 5). In the PPV group, those with HM or better VA required an average of 0.75 (SD ± 1.3; range, 0–3) additional treatments, whereas those with light perception (LP) or worse VA required no additional treatment. However, in the conservative group, those with HM or better VA required an average of 1.47 (SD ± 1.5; range, 0–6) additional treatments, and those with LP or worse VA required 1.50 (SD ± 1.1; range, 0–3) additional treatments.

In addition, we explored functional and anatomical outcomes to determine treatment success (Table 4). A successful functional outcome was defined as having an attached retina and a best-corrected VA (BCVA) of ≥ 1.30 (20/400). However, a successful anatomical outcome was defined as having an attached retina with a BCVA of ≥ 2.4 (LP). In the PPV group, 50% (n = 3) of the eyes achieved functional success, and 83.3% (n = 5) achieved anatomical success. In contrast, in the conservative group, 43.5% (n = 10) of the eyes achieved functional success and 69.6% (n = 16) of the eyes achieved anatomical success. The mean BCVA at the last follow-up was 1.7 (SD ± 0.9), and the average duration of follow-up was 15.8 (SD ± 20.4; range, 2–86) months (Table 6).

Table 4 Comparison of Outcomes Between Initial Vitrectomy vs Non-Vitrectomy Eyes

Outcome	Pars Plana Vitrectomy Eyes (n = 6)	Non-pars Plana Vitrectomy Eyes (n = 23)	*p*-value
Required Additional Treatments	1 (16.7)	17 (73.9)	0.265
Functional* Success	3 (50)	10 (43.5)	
Anatomical• Success	5 (83.3)	16 (69.6)	

Notes: *Attached retina and BCVA ≥ 20/400: 13 (44.8). • Attached and BCVA ≥ LP: 21 (72.4).
Abbreviations: BCVA, Best Corrected Visual Acuity; LP, Light Perception.

Table 5 Treatment and Outcomes Based on Presenting Visual Acuity

Variables	Pars Plana Vitrectomy Eyes (n = 6)		Non-pars Plana Vitrectomy Eyes (n = 23)	
Visual acuity	HM or better (n = 4)	LP or worse (n = 2)	HM or better (n = 19)	LP or worse (n = 4)
Average number of additional treatments	0.75 (range: 0–3)	0 (0.0)	1.47 (range: 0–6)	1.50 (range: 0–3)
Functional success	3 (75)	0 (0.0)	10 (52.6)	0 (0.0)
Anatomical success	3 (75)	2 (100)	13 (68.4)	3 (75)

Abbreviations: HM, Hand Motion; LP, Light Perception.

Table 6 Findings at Last Follow-Up

Variable	Category	No. (%)
Final visual acuity		
At discharge (LogMAR)	Mean (SD)	1.8 (0.7)
At the last follow-up (LogMAR)	Mean (SD)	1.7 (0.9)
Final anatomical outcome		
	Attached retina	21 (77.8)
	Corneal opacity	5 (17.2)
	Detached retina	4 (14.8)
	Evisceration	3 (10.3)
	Phthisis bulbi	1 (3.4)
	Hypotony	1 (3.4)
	Optic nerve pallor	1 (3.4)
	Sterile anterior segment inflammation	1 (3.4)
	Retro-corneal membrane	1 (3.4)
Total months of follow-up	Mean (SD)	15.8 (20.4), [2–86]

Abbreviation: SD, Standard Deviation.

Discussion

This study demonstrated that early pars plana vitrectomy (PPV) with empirical intravitreal antifungal therapy resulted in higher rates of functional and anatomical success compared to conservative management in patients with post-cataract fungal endophthalmitis.

Fungal endophthalmitis is a diagnostic challenge because of its rarity. Previous studies on exogenous fungal endophthalmitis often report infiltrates confined to the anterior chamber, pupillary region, and/or anterior vitreous.[3] Most of our patients had diffuse intraocular inflammation, although corneal edema and anterior chamber fibrin were common findings. For a conclusive diagnosis, it is crucial to send specimens for both bacterial and fungal cultures, because the classic symptoms of fungal endophthalmitis may not always be evident.[3]

Various fungal species of Aspergillus, Fusarium, and Candida can cause post-cataract surgery fungal endophthalmitis,[3,9,10] with Aspergillus sp. being most commonly isolated fungi.[3,6,7] In this study, 50% (n = 2) of the eye specimens yielded positive cultures for Aspergillus sp. Cladosporium sp. was the other isolated fungi. The literature has only reported a few cases of Cladosporium-related endophthalmitis.[11–13]

The visual prognosis of patients with fungal endophthalmitis is generally poor, with the final VA declining to 20/200 or worse, regardless of the causative organism.[1,3,9,10,14] In our study, the VA improved only slightly, and 20.7% (n = 6) of the eyes achieved BCVA of ≥ 20/200; 6.9% (n = 2) achieved BCVA of ≥ 20/40; and 13.8% (n = 4) had no LP (NLP). This was consistent with the findings of Das et al[7] In their study, after treatment, 30.1% of eyes gained a VA of ≥ 20/400; in 7.3% of eyes, VA was ≥ 20/40; and NLP was observed in 13.7% of eyes.[7] However, in a more recent study by Kim et al, who presented an outbreak of fungal endophthalmitis following cataract surgery, the visual outcome was more favorable with a mean BCVA of 20/45, and only 8.8% had VA < 20/200.[1] They hypothesized that the reasons were good initial VA, early detection, early aggressive intervention, and continuous long-term antifungal treatments.[1]

The prolonged latency period of weeks to months for exogenous fungal endophthalmitis can also contribute to the delay in diagnosis.[3] Sen et al reported a mean latency period of 69 (range, 12–180) days in their case series of fungal endophthalmitis after cataract surgery.[6] In the present study, we observed a latency period varying from 3 days to 180 days. Most cases of cluster fungal endophthalmitis occur within 4 weeks.[3] The early presentation suggests the introduction of a large amount of inoculum during surgery.[3] We noted that the majority of cases originated from one region (Mecca) and displayed characteristics typical of fungal endophthalmitis clusters. Given that these patients were referred from a hospital undergoing renovation, we speculated that airborne spores from the construction site may have served as a possible source of the inoculum. However, we did not conduct microbiological studies on the construction site.

Hospitals worldwide are aging, and many may be contaminated by fungal spores.[5] Thus, during hospital construction, it is necessary to perform an aerobiological evaluation for fungal spores.[5] Installing high-efficiency particulate airflow filter air cleaners, using copper-8-quinolinolate-formulated paint, and switching from perforated ceiling tiles to non-perforated ones are some recommended control measures to lower the risk of hospital-associated aspergillosis.[5,15] Other measures include sealing windows, replacing horizontal dust-accumulating blinds with vinyl roller shades, and regularly and systematically cleaning surfaces.[5,15] Additionally, the air conditioning systems should be checked frequently for spores.[5,15]

A universal standard treatment protocol for fungal endophthalmitis is yet to be established. Nevertheless, multiple investigators have advocated prompt vitrectomy with or without IOL removal.[1,4,14,16] Kim et al demonstrated that immediate vitrectomy with IOL removal results in a lower overall number of additional intravitreal antifungal injections and a higher degree of visual improvement.[1] In a follow-up report, further analysis revealed that IOL removal along with early vitrectomy reduces the incidence of vision-threatening outcomes and treatment burden.[4] The role of vitrectomy lies in its ability to reduce organism burden.[17,18] However, its role should not be limited, as previously suggested by the Endophthalmitis Vitrectomy Study.[19,20] Especially with the advancement of technology, small gauge vitrectomy is associated with increased safety.[4,20,21] Dib et al recommended complete early vitrectomy as the primary treatment for all fundus obscuring acute post-cataract endophthalmitis in LP/HM eyes and some eyes with counting finger (CF) or better VA.[21] They believe that this will rapidly restore and maintain a sterile, nontoxic intraocular environment preventing "endophthalmitis maculopathy".[21] They reported a more favorable final VA, with 79% of the eyes having a VA of ≥ 20/40, 11% having a VA between 20/50 and 5/200, and 10% having a VA of < 5/200.(21) In our study, the PPV group required on average less additional treatments per patient than the conservative group did (0.5 [SD ± 1.1; range, 0–3] and 1.48 [SD ± 1.47; range, 0–6], respectively). The PPV group also achieved higher rates of functional and anatomical success compared to the conservative group (50% and 83.35% and 43.5% and 69.6%, respectively). Our results showed slightly higher percentages than those reported by Narang et al, who demonstrated similarly better functional outcomes in eyes undergoing PPV than in those not undergoing PPV (44.44% and 22.22%, respectively).[3]

Additionally, infectious organisms attach to the surface or haptic of IOL, and the capsule may serve as a scaffold for attachment.[4,22] Removal of IOL, although not routinely performed for bacterial endophthalmitis, is associated with a lower rate of persistent inflammation or recurrence compared to vitrectomy alone.[22–24] Conversely, IOL and capsule removal are more commonly adapted strategies for treating fungal endophthalmitis.[1,3,4,14] This is especially true given the documented resistance of fungi to antifungal treatment, as well as the higher probability of recurrence.[4,10] In this study, two patients who underwent initial vitrectomy also underwent IOL explantation simultaneously. One patient achieved functional and anatomical success, whereas the other achieved anatomical success. None of the patients required any additional treatment.

Furthermore, the optimal timing of adjuvant intravitreal antifungal injections remains controversial. Some may delay their use until microbiological evidence has been confirmed. Sen et al concluded that the early addition of intravitreal antifungal injections can prevent further decline in vision.[6] In our study, 20 eyes received intravitreal antifungal injections at presentation. The role of steroids in the treatment of fungal endophthalmitis has been controversial.[3,6] Some studies have shown promising outcomes with their use.[3,25] None of our patients received intravitreal steroids at presentation, except for one. One patient was initially treated with PPV with intravitreal antibiotics and steroid injections. To control infection, the patient required three additional treatments and underwent evisceration. The type of organism and its virulence may have played a role in the outcome; the culture was positive for Aspergillus sp.

This study has some limitations. First, this was a retrospective study; therefore, no common protocol was followed for the diagnosis and management of fungal endophthalmitis. Second, this study included both culture-positive and possible fungal endophthalmitis cases. Third, prior treatment before referral to our center resulted in a low culture positivity rate and a failure to identify the causative organism. Finally, owing to the small number of patients in each group, we were unable to discern any differences in the clinical outcomes of voriconazole and amphotericin B. Further follow-up studies are required to investigate different variables (ie, age, presence of systemic or ocular disease, type of cataract surgery, media clarity, hypopyon) and their association with treatment outcomes. Despite these limitations the main takeaway from this study is the potential benefit of early aggressive surgical intervention in managing post-cataract fungal endophthalmitis.

Conclusion

We reported a cluster of cases of post-cataract surgery fungal endophthalmitis. A high index of suspicion and prompt PPV with empirical administration of intravitreal antifungal agents are required for a favorable prognosis. The earlier and more diffuse inflammation observed in this study indicates that a significantly high load of fungal inoculum is introduced into the eye intraoperatively. This necessitates more stringent control measures for hospitals undergoing construction. Further studies with more uniform and stricter treatment protocols than those of this study are required to obtain conclusive evidence for the ideal management of post-cataract surgery fungal endophthalmitis.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors have no proprietary, commercial, or non- commercial interest in any materials mentioned in this article.

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