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Clinico microbiological profile of endophthalmitis in a tertiary eye care centre of North India

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Abstract
Objective: To assess the prevalence of different types of endophthalmitis and identify the microbial etiology of infectious endophthalmitis.
Methods: A prospective, observational study was carried out in 120 cases of endophthalmitis admitted in RIO, PGIMS Rohtak during the time period of 1/1/2018-1/1/2020. After detailed history and thorough ocular examination, diagnosis of endophthalmitis was made and vitreous sample was taken for direct microscopic examination and culture sensitivity.
Results: Out of 120 patients of endophthalmitis, post-operative endophthalmitis (80%) was most common type followed by post traumatic (17.5%) and endogenous (2.5%) type. Staph epidermidis was found to be the most common etiological agent in post-operative endophthalmitis and post-traumatic endophthalmitis cases while Candida albicans was the most common isolated organism in endogenous endophthalmitis cases.
Conclusion: Staphylococcus epidermidis was the most common isolated organism in post-surgery and post traumatic cases of endophthalmitis, but fungi was the most common etiology in endogenous endophthalmitis cases.

Keywords: Endophthalmitis, ocular trauma, post cataract, vitreous culture

Introduction

Endophthalmitis is a severe vision threatening catastrophic complication of intraocular surgery, microbial keratitis and open-globe injuries which may lead to irreversible loss of vision in the infected eye. Endophthalmitis is an infection of the vitreous and/or aqueous by microbial agents like bacteria or fungi. If intraocular infections is caused by viruses or parasites, it is usually considered as a types of uveitis rather than endophthalmitis [1].

Endophthalmitis can be either exogenous, where microbes on the ocular surface or from an external source are introduced into the eye or endogenous where endophthalmitis is caused by hematogenous spread of pathogens during septicaemia. Majority of endophthalmitis cases are exogenous. Exogenous endophthalmitis is further categorised into post-cataract, post-traumatic, and bleb related depending on the risk factors [2].

Incidence of endophthalmitis and spectrum of causative microbes varies by its category. The rate of endophthalmitis after cataract surgery is found to be approximately 0.1% while the rate after penetrating ocular injuries varies from 1 to 18% [2]. Majority of endophthalmitis cases are found to be post-operative and post-traumatic worldwide, with postoperative endophthalmitis cases constituting 40 to 80% and posttraumatic cases accounting for 2 to 15% of all endophthalmitis cases in different parts of world [2-9]. In 2004, FDA approved use of intravitreal anti-vascular endothelial growth factor (anti-VEGF) drugs to treat neovascular age-related macular degeneration, after that there has been a rapid surge in the use of intravitreal drugs. Some canters has also reported post-intravitreal injection endophthalmitis to be more common than post-operative endophthalmitis [3, 10].

The source of infection in exogenous endophthalmitis can be the ocular surface in postoperative, post-injection, keratitis-related, bleb-related or device-related endophthalmitis cases or it can be the environment in post-traumatic cases. While in endogenous endophthalmitis, source of pathogens is hematogenous seeding secondary to a transient focus or an ongoing infection [6].

Endophthalmitis cases most commonly present with decreased vision associated with ocular

pain, discomfort and a red eye. Constitutional symptoms such as fever are classically absent in exogenous cases but usually present in endogenous endophthalmitis cases [11]. On ocular examination, hypopyon is seen in 80% of post-cataract endophthalmitis cases [12]. Bacterial endophthalmitis has an acute onset with diffuse intraocular inflammation while fungal endophthalmitis typically has a subacute onset with symptoms with typical "clump" formation in aqueous/vitreous [13].

Most common type of endophthalmitis seen worldwide is acute post-cataract endophthalmitis, out of which 30% cases are culture negative. Out of culture-positive cases, 95% of isolates are found to be Gram-positive cocci, out of which coagulase-negative staphylococci is the primary pathogen in 70% of cases. Other pathogens causing acute post-cataract endophthalmitis are Staphylococcus aureus in 10% cases, streptococci in 9%, mixed Gram- positive bacteria in 5%, and Gram-negative bacilli in 6% cases.[14] Chronic post-cataract endophthalmitis is quite rare and most common pathogens are due to fungi or Propionibacterium acnes. If a patient present with persistent endophthalmitis in postoperative period, it should be suspected. If white plaque is present on posterior capsule, it is clue to chronic P. acne endophthalmitis and if there is clumped appearance of intraocular inflammation, it is usually secondary to chronic fungal endophthalmitis [11].

Post-keratoplasty endophthalmitis incidence varies from 0.2% in the acute postoperative period and 0.7% if late presenting cases are also included [15, 16]. Most common cause in post keratoplasty endophthalmitis was Candida in approximately 31% cases. Other pathogens responsible were Pseudomonas, streptococci, staphylococci and mycobacterial species [17].

Incidence of post-injection endophthalmitis is on surge after FDA approval of anti-VEGF injections in 2004. Number of intravitreal injections increased from 83,000 in 2004 to 2.4 million in 2012 as per a study utilizing Medicare database records [18]. Every intravitreal injection carry a 0.05% risk of endophthalmitis, which is quite significant as most patients need multiple intravitreal injections [19].

Incidence of penetrating ocular injuries is around 2 to 3.8/100,000 population in the United States. Risk of post-traumatic endophthalmitis is more in children (5-54%) as compared to adults (0.9 to 18%).[20,21] Risk factors for post-traumatic endophthalmitis are delay in treatment, rural settings of injury, intraocular foreign body, lens capsule disruption and globe rupture. Pathogens causing posttraumatic endophthalmitis are coagulase-negative staphylococci, Bacillus, streptococci, Gram- negative bacilli (Pseudomonas and Klebsiella) and fungi. Bacillus infections are quite fulminant and a ring corneal abscess may be present, while in Clostridium endophthalmitis cases gas bubbles are seen in the anterior chamber with a green-brown colour hypopyon [22].

Bleb-related endophthalmitis has a sudden onset, it occurs months to years following glaucoma surgery in which a "bleb" is created. An infection of bleb or blebitis usually precedes endophthalmitis. It carries a risk of around 1% over 5 years and if blebs are leaking, it increases the risk by 5-fold. Major pathogens responsible for bleb related endophthalmitis are Streptococci, S. aureus, Haemophilus influenzae, and enterococci [23].

Endogenous endophthalmitis can be either bacterial or fungal. Endogenous bacterial endophthalmitis has an acute onset and presents with decreased vision in 90% cases, ocular pain in 50%, hypopyon in 35% cases and vitritis in 33% cases. It is associated with fever in 37% cases [24]. The pathogen is diagnosed by blood or vitreous cultures and common pathogens responsible are S. aureus, streptococci and Gram- negative bacilli such as Escherichia coli and K. pneumoniae. Endogenous fungal endophthalmitis has a silent course and initial presentation is usually chorioretinitis, seen as fluffy white chorioretinal lesions. Common pathogens responsible are Aspergillus, fusarium and Candida [25].

We conducted this prospective, observational study to assess the prevalence of different types of endophthalmitis and identify the microbial etiology of infectious endophthalmitis in a tertiary care centre of North India. As classification of endophthalmitis in different types and identification of common pathogens is essential for its prevention and management.

Material and Methods

A prospective, observational study was carried out on 120 cases of endophthalmitis admitted in RIO, PGIMS Rohtak during the time period of 1/1/2018-1/1/2020 after taking their informed consent. A detailed history was elicited in every patient regarding their demographic details, clinical presentation and interval between surgery/trauma and onset of symptoms. A detailed ocular examination was done in every patient including presenting visual acuity and thorough slit lamp examination for corneal edema, anterior chamber exudates and vitreous exudates. USG B scan was done for posterior segment evaluation in eyes with hazy media which was obscuring the details of fundus. A clinical diagnosis of endophthalmitis was made based on clinical findings and vitreous sample was taken for direct microscopic examination and culture sensitivity. Vitreous aspiration was done at the pars plana 3mm away from the limbus with a sterile tuberculin syringe and a 26-gauge needle. Undiluted vitreous sample of about 0.2 ml was collected and sample sent immediately to laboratory for microbiological analysis. After collection of vitreous specimen, patient was given intravitreal ceftazidime 2.25 mg/ml and vancomycin 1mg/ml as per treatment guideline for endophthalmitis. Patients with suspected fungal infection were also administered intravitreal amphotericin B (5 microgram/0.5 ml). All patients were treated with systemic and topical antibiotics as per protocol. Patients with visual acuity less than 1/60 were planned for emergency pars plana vitrectomy and in such patients vitreous biopsy was collected from the mid vitreous cavity by applying aspiration with a 2 cc disposable syringe plugged into the suction tubing of the vitreous cutter. For getting a better recovery of microorganism in vitreous tap, an undiluted sample should be taken before starting the infusion fluid.

For identification of causative organism, direct microscopic examination was done after staining with Gram, Giemsa and Calcofluor staining. For culture, six culture Medias were used i.e 5% sheep blood agar, 5% sheep blood chocolate agar, brain heart infusion (BHI) broth, thioglycolate broth, Robertson's cooked meat broth and Sabouraud dextrose agar (SDA). All culture Medias were kept for two weeks in case of no growth or before declaring the sample as sterile. Only unequivocal or significant culture results were considered. A culture was considered significant only when there was a confluent growth in any solid media; and/or

growth in more than one medium; and/or growth in one medium with presence of organism in direct microscopy.
Data was collected and analysed using Microsoft Excel spread sheet. Then statistical analysis of data was done with SPSS (Statistical Package for Social Sciences) ver. 21.0.

Results

A total of 120 patients with clinical presentation of endophthalmitis presenting to RIO, PGIMS Rohtak during time period of 1/1/2018-1/1/2020 were enrolled in the study after taking a detailed informed consent. The mean age of patients in our study was found to be 54.6±18 years. The most common subtype of endophthalmitis was post-operative endophthalmitis in 96 patients (80%) followed by post-traumatic in 21 patient (17.5%) and endogenous in 3 cases (2.5%) {Figure 1}.

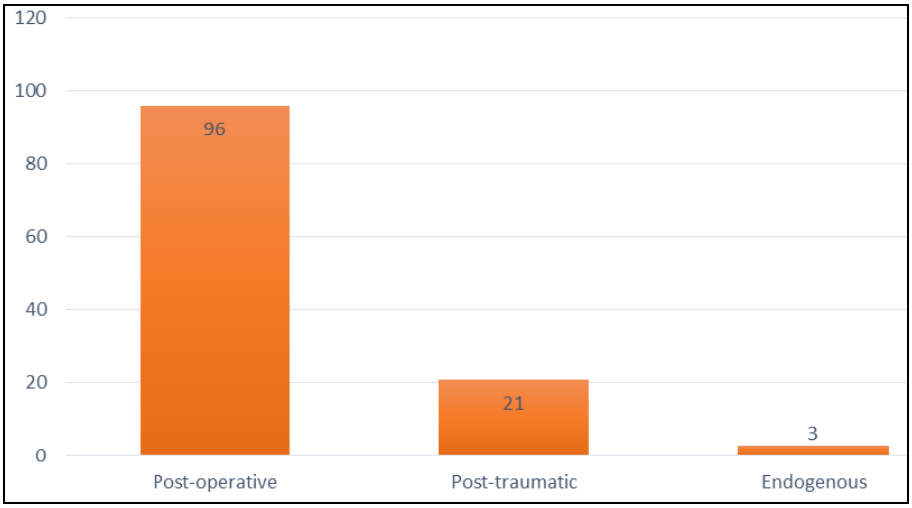

Fig 1: Prevalence of different types of Endophthalmitis

Out of 120 patients, only 90 patients (75%) had positive culture report of vitreous specimen while rest 25% showed no microorganism in culture report and were reported as sterile after 2 weeks.

Postoperative Endophthalmitis

The mean age of patient in this group of endophthalmitis was 60.4±12 years and M: F ratio was 3:2. All patients were having unilateral endophthalmitis and other eye was unaffected. Right eye was involved in 40% cases and left in 60% cases.

Table 1: Demographic details of study objects

	Post-operative Endophthalmitis, n=96	Post-traumatic Endophthalmitis, n=21	Endogenous Endophthalmitis, n=3
M:F Ratio	3:2	6:1	1:2
Incidence (%)	80	17.5	2.5
Mean age ±SD	60.4±12	32.4±15	66.2±11

Out of 96 cases of post-operative endophthalmitis, 90 patients had an acute presentation and only 6 patients had chronic presentations. Mean time of presentation between surgery and presentation to the tertiary referral centre was 10±2 days in acute cases. The most frequent surgery responsible for postoperative endophthalmitis was cataract surgery in 90 patients, par plana vitrectomy in 2 patients, bleb-associated in 1, intravitreal Ozurdex injection in 1 patient, silicone oil removal in 1 patient and post-keratoplasty in 1 patient. {Figure 2}

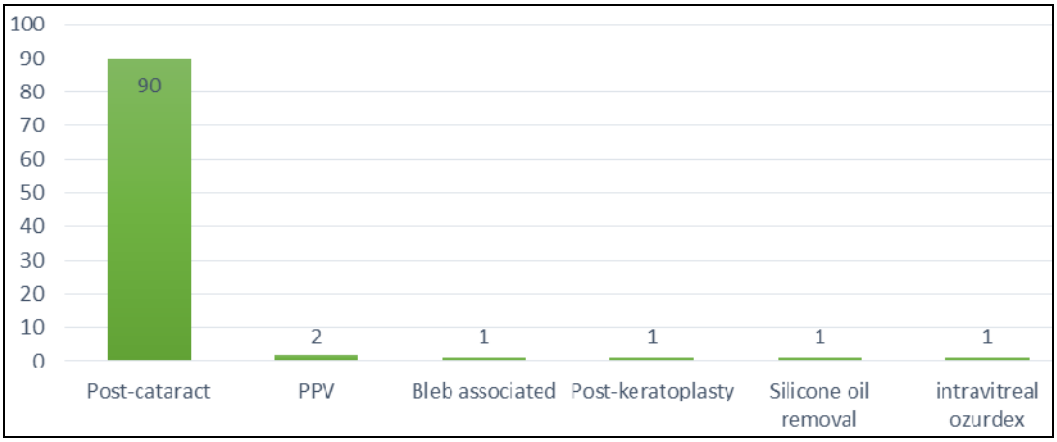

Fig 2: Risk factor for post-operative Endophthalmitis

In 70 patients, culture reports were positive while 26 patients were found to be culture negative even after 2 weeks. The most common isolated pathogen was Staphylococcus epidermidis (48.5%) followed by Streptococcus viridans (34.2%). {Table 2}

Table 2: Microbiological Spectrum of Post-operative Endophthalmitis pathogens

Organism	Number	Percentage
Staphylococcus epidermidis	34	48.5%
Streptococcus viridians	24	34.2%
Staphylococcus aureus	2	2.85%
Streptococcus pneumoniae	1	1.42%
Enterococcus	1	1.42%
Pseudomonas aeruginosa	4	5.7%
E. coli	1	1.42%
Enterobacteriaceae	1	1.42%
Fusarium	2	2.85%

Post-Traumatic Endophthalmitis

The mean age of 21 patients with post traumatic endophthalmitis was 32.4±15 years, which was much younger age group than post-operative endophthalmitis cases. Out of 21 patients, 18 (85.7%) were men and 3 (14.3%) were females with a M: F ratio of 6:1 which was significantly higher than postoperative endophthalmitis cases. Culture report were positive in 16 samples and Staphylococcus epidermidis was most common isolated pathogen followed by Pseudomonas aeruginosa.

Table 3: Microbiological Spectrum of Post-traumatic Endophthalmitis pathogens

Organism	Number	Percentage
Staph epidermidis	12	75%
Bacillus cereus	1	6.25%
Pseudomonas aeruginosa	2	12.5%
Enterobacteriaceae	1	6.25%

Endogenous Endophthalmitis

Out of 3 patients of endogenous endophthalmitis cases, culture report was positive in 2 patients. 2 patients were female and 1 was male with a M: F ratio of 1:2. All affected patients were on corticosteroids for some undetermined collagen vascular disease. In 2 culture positive patients, Candida albicans was the only isolated pathogen.

Discussion

The most common subtype of endophthalmitis in our study was post-operative endophthalmitis in 80% cases followed by post-traumatic in 17.5% and endogenous being the least common in 2.5% cases only. Most common factor attributing for endophthalmitis was found to be cataract surgery in 75% cases. Similar results were produced by Pei-Chang *et al* [26] and Somani *et al* [27] in their studies in Taiwan and Canada respectively. As cataract surgery is the most common intraocular surgery performed all over the world, therefore most of the endophthalmitis cases occur post cataract surgery.

In our study, mean age in postoperative, post-traumatic and endogenous endophthalmitis was 60.4±12 years, 32.4±15 years and 66.2±11 years respectively. Males were affected more commonly than females in post-operative and post-traumatic endophthalmitis cases with M: F ratio of 3:2 and 6:1 respectively. In post-traumatic endophthalmitis cases, younger age group was involved with a very significant male predominance due to greater chances of exposure of males to trauma due to outdoor activities. Similar results were shown in a study conducted in Odisha, India by Sharma S *et al* [28].

In our study, the culture positivity rate in postoperative endophthalmitis was 72.9% and most common isolated pathogen was Staphylococcus epidermidis (48.5%) followed by Streptococcus viridians (34.2%). These results were similar to Endophthalmitis Vitrectomy Study which reported 94% Gram- positive cocci and 6% Gram-negative bacilli in post-operative endophthalmitis.[14] However, the published Indian literature from various regions had shown Gram-positive cocci in 10-54% cases, Gram-negative in 26-42% and fungal infection in 16-22% cases of post-operative endophthalmitis.[29-31] This discrepancy can be attributed to method of sample collection, inappropriate sample collection and inappropriate handling.

In post-traumatic endophthalmitis cases, vitreous culture report was positive in 76% cases and most common isolated pathogen was Staphylococcus epidermidis in 75% cases followed by Pseudomonas aeruginosa in 12.5% cases. These results are compatible with studies conducted by Abdulrahman *et al* [32] and Abu el-Asrar *et al* [33].

In our study, culture positivity rate was 66% in endogenous endophthalmitis cases with M: F ratio of 1:2. All affected patients were on corticosteroids for some undetermined collagen vascular disease and Candida albicans was isolated pathogen in two culture positive patients. These results are compatible with a study conducted in India by Maitray A *et al* [34].

Conclusion

In conclusion, this study conducted in North India demonstrates that the most common subtype of endophthalmitis is post-operative and cataract surgery accounts for 80% of total endophthalmitis cases. Numerous studies have concluded Staphylococcus epidermidis to be the most common etiological agent of endophthalmitis, the current study had also shown Staphylococcus epidermidis to be the most common isolated organism in post-surgery and post traumatic cases of endophthalmitis, but fungi was the most common etiology in endogenous endophthalmitis cases.. As post-traumatic endophthalmitis cases affects young productive population of India which can lead to irreversible loss of vision, therefore use of protective eye wear should be emphasised to prevent ocular trauma at workplace. Hence, we strongly recommend vitreous biopsy to be done for culture and sensitivity in every endophthalmitis case. However, based on microbiological spectrum results of our study, empirical use of standard intravitreal therapy (vancomycin and ceftazidime in bacterial endophthalmitis; amphotericin B in fungal endophthalmitis) still holds a place in a developing country like India.

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