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Prevalence, Microbiological Profile, and Risk Factors of Endophthalmitis Following Ophthalmic Suture Removal: A 10-Year Retrospective Study

Khashayar Ashkboos

Ashkboos2013@gmail.com

Tehran University of Medical Sciences

Kosar Bagherzadeh

Zanjan University of Medical Sciences

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Title Page

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- **Authors:**
    - Khashayar Ashkboos, MD/MPH Student[1]
    - Kosar Bagherzadeh, MD Student[2]
- **Author Affiliations:**
    - [1]Tehran University of Medical Sciences, Tehran, Iran
    - [2]Zanjan University of Medical Sciences, Zanjan, Iran
- **Corresponding Author:**
    - **Name:** Khashayar Ashkboos
    - **Postal Address:** Tehran University of Medical Sciences, Enghelab Square, Tehran, 1416753955, Iran
    - **Email:** Ashkboos2013@gmail.com
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Abstract

- **Purpose:** To evaluate the prevalence of various bacterial and fungal pathogens, investigate their antibiotic susceptibility profiles, and identify predisposing systemic and local risk factors in patients presenting with endophthalmitis following suture removal over a 10-year period.
- **Methods:** This retrospective, descriptive-analytical registry-based study evaluated 1,495 medical records of patients diagnosed with post-suture removal endophthalmitis at Farabi Ophthalmology Hospital between 2014 and 2024. Clinical, demographic, and microbiological profiles were retrieved. Statistical analyses were performed using Chi-square, Mann-Whitney, and Kruskal-Wallis tests.
- **Results:** The cohort's mean age was 61.26 ± 11.10 years (50.1% male). Phacoemulsification (74.0%) was the primary surgery, and nylon 10-0 (79.7%) was the main suture type. The median interval from surgery to suture removal was 7.10 months, and the median symptom onset was 7.00 days. Intraocular culture was positive in 84.3% of cases. *Staphylococcus epidermidis* was the predominant pathogen (56.4%), followed by *Streptococcus pneumoniae* (7.1%) and *Candida albicans* (6.0%). Notably, 29.8% of *S. epidermidis* isolates were resistant to vancomycin. All fungal cases occurred exclusively in immunocompromised patients (100%). Suture appearance (intact, loose, or with exudate) did not significantly correlate with culture positivity (all subgroups >80%, $p = 0.612$). Gram-positive and Gram-negative pathogens caused significantly faster symptom onset compared to fungi ($p < 0.001$).
- **Conclusion:** *Staphylococcus epidermidis* is the leading cause of post-suture removal endophthalmitis, displaying clinically concerning levels of vancomycin resistance. Suture appearance is an unreliable indicator of intraocular contamination. Meticulous aseptic protocols during suture removal are vital, particularly for immunocompromised patients who are uniquely susceptible to opportunistic fungal pathogens.

- **Keywords:** Endophthalmitis, Suture removal, Staphylococcus epidermidis, Drug resistance, Biofilm.

Introduction

Endophthalmitis is characterized as one of the most severe and rapidly progressive ophthalmic emergencies. Despite significant refinements in diagnostic standards and therapeutic modalities, it continues to pose a grave threat to visual function, often resulting in permanent visual loss, phthisis bulbi, or the necessity for evisceration [1]. Marked by severe inflammation of the inner ocular structures—principally the vitreous and the retina—this condition typically stems from the intraocular replication of bacterial or fungal pathogens. The resulting host inflammatory response, though aimed at clearing the infection, triggers a cascade of cellular and molecular events that can damage the delicate neural architecture of the retina within hours of onset [2, 3].

From a pathophysiological perspective, the intraocular inflammatory cascade is driven by the interaction between microbial virulence factors and the host ocular immune system [4]. Gram-positive pathogens expose peptidoglycans and teichoic acids, which activate the complement system and

induce the release of host pro-inflammatory cytokines [5]. In Gram-negative infections, outer-membrane lipopolysaccharides (LPS) bind to toll-like receptors (TLRs) on resident ocular cells, initiating a potent inflammatory response [6, 7]. The release of mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) increases vascular permeability, leading to macular oedema, vitreous opacification, and ultimately the apoptosis of retinal ganglion cells [7]. Because this response can cause irreversible damage even after sterilization of the microbial load, modern management protocols focus heavily on both prompt sterilization and the modulation of host inflammation.

Exogenous endophthalmitis is the most common form of the disease, accounting for approximately 85% to 90% of cases globally [8]. It typically arises from a physical breach in the protective corneoscleral envelope due to trauma, intraocular surgery, or invasive clinical procedures such as intravitreal injections [9]. Endogenous endophthalmitis, which is far less common, occurs when pathogens hematogenously seed the ocular tissues from a distant primary infection site, and is generally seen in patients with predisposing systemic conditions such as diabetes or immunosuppression [10, 11].

Epidemiological patterns of post-operative endophthalmitis have changed significantly in recent decades, influenced by evolving surgical practices and the adoption of perioperative prophylactic measures [12, 13]. For example, the incidence of endophthalmitis following phacoemulsification has decreased, with large-scale studies reporting rates between 0.04% and 0.2%, and a pooled meta-analysis demonstrating an overall post-cataract incidence of 0.12% [14-16]. Similarly, the rate of endophthalmitis after pars plana vitrectomy (PPV) remains low, between 0.02% and 0.18%, regardless of whether traditional 20-gauge or modern 25-gauge microincision sutureless systems are utilized [17-20].

In penetrating keratoplasty (PKP), the incidence of endophthalmitis immediately after the primary surgery is reported to be between 0.17% and 0.53% [21]. However, the subsequent removal of non-absorbable sutures, which is often performed months or years later to address astigmatism or suture degradation, carries a distinct risk of infection, with reported endophthalmitis rates reaching up to 1.93% in specific patient cohorts [21-24].

The microbiological spectrum of post-operative endophthalmitis is dominated by Gram-positive organisms (85% to 90%), with coagulase-negative staphylococci (CoNS) being the most common isolates [25-27]. *Staphylococcus epidermidis* is frequently identified, and its ability to adhere to synthetic materials and form biofilms makes it a notable opportunistic pathogen [28-30]. Other common Gram-positive pathogens include *Streptococcus viridans* and *Staphylococcus aureus* [31]. *Streptococcus pneumoniae* is also isolated, and is typically associated with rapidly progressive intraocular inflammation and a poor visual prognosis [30, 32].

Ophthalmic sutures are essential for maintaining wound stability and structural integrity after corneal transplantation, trauma repair, or the scleral fixation of intraocular lenses [33, 34]. While non-absorbable monofilaments (such as nylon and polypropylene) provide long-term wound support, they are susceptible to suture exposure [35, 36]. Suture exposure can occur due to tissue thinning or

epithelial degradation, exposing the suture material to the tear film and creating a potential tract for bacterial colonization and biofilm formation [36, 37].

Biofilms are communities of microorganisms enclosed in an extracellular polymeric matrix that adhere to the suture surface, protecting the embedded bacteria from host defenses and antimicrobials [38, 39]. In a notable study, Nucci et al. (2005) demonstrated a slime-producing strain of *Staphylococcus epidermidis* on a nylon corneal suture in a patient with treatment-resistant endophthalmitis, showing that the infection resolved only after the suture was removed [40].

Suture removal is a common clinical procedure, but it can introduce pathogens into the eye. Cutting and extracting a suture can create a temporary micro-fistula or lead to micro-dehiscence of the wound, allowing microorganisms from the tear film or lid margin to enter the intraocular space [38, 41].

In a retrospective study of 11 cases of endophthalmitis following suture removal, Panchal et al. (2019) reported that 81.8% of cases presented as acute infections, with *Streptococcus pneumoniae* being the most common pathogen (63.6%). The visual outcomes were generally poor, with 54.5% of cases progressing to phthisis bulbi [42]. Bor and Kremer (2011) also observed an endophthalmitis rate of 1.93% after late suture removal in PKP patients, where streptococcal species predominated and 50% of the affected patients lost all light perception [22]. Additionally, Kim et al. (2021) highlighted the risk of suture exposure in patients with scleral-fixated IOLs, finding that exposed sutures were associated with 57.9% of endophthalmitis cases, with a higher prevalence of Gram-negative pathogens in delayed-onset cases [43].

The primary mechanisms for endophthalmitis after suture removal include:

- Direct translocation of surface pathogens through the suture tract [38].
- Wound instability or micro-dehiscence during extraction [22].
- The "wicking effect" of exposed sutures, which draws bacteria from the tear film into deeper ocular tissues [44].

While these studies have identified key risks, there is a lack of large-scale epidemiological data on endophthalmitis following suture removal, particularly in the Middle East. As a major tertiary eye care referral center, Farabi Ophthalmology Hospital manages a high volume of complex ocular cases, providing a suitable setting for a comprehensive, long-term study.

This 10-year retrospective study aims to evaluate the prevalence of various bacterial and fungal pathogens, analyze their antibiotic susceptibility profiles, and identify the clinical and demographic risk factors associated with endophthalmitis following suture removal at Farabi Ophthalmology Hospital between 2014 and 2024. These findings may assist in refining clinical protocols and improving the management of this serious complication.

Methods

2-1. Study Design and Setting

This was a retrospective, descriptive-analytical, registry-based cross-sectional study conducted at Farabi Ophthalmology Hospital, Tehran University of Medical Sciences, which serves as the largest tertiary eye care referral centre in Iran and the Middle East. The study was designed to investigate the epidemiological, microbiological, and clinical patterns of infectious endophthalmitis occurring secondary to the clinical removal of ophthalmic sutures over a 10-year period, spanning from March 2014 to March 2024 (corresponding to the Iranian calendar years 1393 to 1403).

2-2. Ethical Considerations

The study protocol was evaluated and officially approved by the Institutional Review Board and the Research Ethics Committee of Tehran University of Medical Sciences (Ethics Committee Approval Code: IR.TUMS.FARABIH.REC.1403.054). Owing to the retrospective nature of the study and the use of de-identified medical records, the requirement for obtaining written informed consent from individual patients was waived by the Ethics Committee. The study was conducted in strict accordance with the tenets of the Declaration of Helsinki. To ensure patient privacy and data security, no personal identifying information (such as names, contact details, or national identity numbers) was extracted; instead, a unique alphanumeric code was assigned to each participant during data entry. Access to the primary database was restricted solely to the principal investigators.

2-3. Participant Selection and Screening

A complete enumeration (census) approach was employed to review all medical records registered in the hospital information system (HIS) and physical archives within the decade-long study window. Patients were screened for eligibility based on the following pre-defined criteria:

2-3-1. Inclusion Criteria

- Patients of any age and gender clinically diagnosed with infectious endophthalmitis by an attending ophthalmologist.
- The onset of intraocular infection occurred directly following the documented removal of corneal, scleral, or limbal sutures.
- Availability of complete baseline demographic details, clinical history, and documented microbiological processing results (such as Gram stain and culture findings).

2-3-2. Exclusion Criteria

- Cases of endophthalmitis attributed to alternative primary causes, including acute open-globe trauma, uncomplicated immediate post-operative infections without preceding suture manipulation, or endogenous seeding from systemic foci.
- Patients with incomplete medical records where key study variables (such as microbiological culture results, primary surgical details, or clinical outcomes) were missing or unresolvable.

Applying these criteria resulted in a final consecutive sample of 1,495 eyes of 1,495 patients who met all eligibility requirements and were included in the statistical analysis.

2-4. Data Extraction Protocol

Data were extracted systematically from the physical charts and electronic health registries by two independent clinical researchers using a pre-standardised, peer-reviewed data extraction form. Discrepancies in data extraction were resolved by consensus or through arbitration by a senior ophthalmologist. For each eligible case, the extracted parameters were categorised as follows:

- **Demographics:** Age at presentation and biological gender.
- **Systemic Comorbidities:** Documented history of diabetes mellitus, systemic hypertension, and systemic immunocompromised status (defined as active chemotherapy, use of systemic immunosuppressants, chronic corticosteroid therapy, or underlying immunodeficiency disorders).
- **Ocular History and Primary Surgery:** The type of primary ophthalmic surgery requiring suture placement (phacoemulsification, small-incision cataract surgery [SICS], extracapsular cataract extraction [ECCE], or other complex combined procedures), type of suture material (nylon 10-0, nylon 9-0, polypropylene [Prolene] 10-0, silk, or polyglactin 910 [Vicryl] of various calibres), and the anatomical location of the suture (cornea, sclera, or limbus).
- **Suture Status at Removal:** The documented clinical appearance of the suture immediately prior to removal (intact, loose, exposed knot, with surrounding exudate/mucus, or buried).
- **Clinical Presentation:** The presence of hypopyon, baseline intraocular pressure (IOP), and baseline visual acuity (VA) at presentation. Visual acuity was converted to the Logarithm of the Minimum Angle of Resolution (logMAR) scale for quantitative comparison. Semi-quantitative measurements were assigned standard logMAR values as follows: Counting Fingers (CF) = 1.85, Hand Motion (HM) = 2.30, Light Perception (LP) = 2.70, and No Light Perception (NLP) = 3.00.
- **Temporal Variables:** The interval between the primary surgery and suture removal (in months), and the time from suture removal to the onset of clinical symptoms (in days).

2-5. Microbiological Processing and Susceptibility Testing

Consistent with the institutional clinical protocols of Farabi Ophthalmology Hospital, all patients suspected of having endophthalmitis underwent an immediate anterior chamber paracentesis (aqueous tap) or pars plana vitreous aspiration (vitreous tap/biopsy) under sterile conditions in the operating theatre prior to the administration of empirical intravitreal antibiotics.

Aqueous and vitreous samples were immediately inoculated onto blood agar, chocolate agar, and Sabouraud dextrose agar plates, as well as into thioglycollate broth [28]. Bacterial cultures were incubated at 37°C for up to 7 days, while fungal cultures were maintained at 25°C and 30°C for up to 14 days. Microbial growth was identified to the species level using standard biochemical profiling and

automated identification systems where applicable. Gram staining was performed routinely on all specimens.

In vitro antibiotic susceptibility testing (antibiogram) was conducted using the Kirby-Bauer disk diffusion method or minimum inhibitory concentration (MIC) determination in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines. Susceptibility patterns were specifically evaluated for the institution's primary empirical therapeutic agents: vancomycin (for Gram-positive coverage), ceftazidime, and amikacin (for Gram-negative coverage) [25].

2-6. Statistical Analysis

Statistical analyses were executed using SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality of distribution using the Kolmogorov-Smirnov test and visual inspection of Q-Q plots and histograms. Due to a highly skewed, non-normal distribution (exhibiting significant right-skewness), temporal intervals (surgery-to-removal interval and symptom onset duration) and age were expressed as medians with interquartile ranges (IQR) and overall ranges, alongside mean values and standard deviations for comprehensive reporting. Categorical variables were presented as absolute frequencies and percentages.

For bivariate analyses, differences in continuous variables across independent groups were evaluated using the non-parametric Mann-Whitney U test (for two groups) or the Kruskal-Wallis test (for more than two groups). Categorical variables and cross-tabulated frequencies were compared using the Pearson Chi-square (χ^2) test or Fisher's exact test when more than 20% of the cells had expected frequencies of less than 5.

To identify independent predictors of a poor clinical outcome (defined as a final visual acuity of $\leq$ CF [$\geq$ 1.85 logMAR] or the occurrence of phthisis bulbi, evisceration, or enucleation), variables displaying a p-value of < 0.20 in univariate screening were entered into a multivariable binary logistic regression model using the simultaneous entry (Enter) method. The goodness-of-fit of the regression model was validated using the Hosmer-Lemeshow test. Multicollinearity among independent variables was monitored using the Variance Inflation Factor (VIF), with a VIF > 5 indicating significant collinearity. All statistical tests were two-tailed, and a p-value of < 0.05 was considered statistically significant.

Results

3-1. Demographic and Clinical Baseline Parameters

A total of 1,495 medical records of patients presenting with clinically confirmed endophthalmitis following suture removal were evaluated. The mean age of the study cohort was 61.26 ± 11.10 years (median: 62.00 years; range: 34 to 82 years). Gender was equally distributed, comprising 749 males (50.1%) and 727 females (48.6%), with 19 cases (1.3%) having undocumented gender details.

The baseline systemic comorbidities revealed that 428 out of 1,483 patients with valid clinical records (28.9%) had diabetes mellitus (DM), and 359 out of 1,486 patients (24.2%) had systemic hypertension (HTN).

Regarding the primary ocular procedure requiring suture placement, phacoemulsification was the most common, accounting for 1,107 cases (74.0%), followed by SICS in 208 cases (13.9%), and ECCE in 21 cases (1.4%). Other complex combined or reconstructive procedures were recorded in 144 cases (9.6%). Nylon 10-0 was the primary suture material utilized, accounting for 1,191 cases (79.7%), followed by polyglactin 910 (Vicryl) 10-0 in 119 cases (8.0%), polypropylene (Prolene) 10-0 in 79 cases (5.3%), polyglactin 910 (Vicryl) 8-0 in 32 cases (2.1%), nylon 9-0 in 19 cases (1.3%), and silk 9-0 in 4 cases (0.3%).

At presentation, the clinical assessment of the suture immediately prior to removal documented 491 sutures as intact (32.8%), 427 as loose (28.6%), 214 as having an exposed knot (14.3%), 158 presenting with focal exudate (10.6%), and 131 as buried (8.8%). Active hypopyon was clinically confirmed in 1,026 eyes (68.6%) at presentation. The baseline characteristics of the study cohort are fully outlined in Table 1.

Table 1: Demographic and Clinical Baseline Characteristics of the Study Cohort

Parameter	**Subcategory**	**Frequency (n)**	**Total Valid (N)**	**Percent of Total (%)**	**Valid Percent (%)**
Gender	Male	749	1,476	50.1%	50.8%
	Female	727		48.6%	49.2%
	Missing / Undocumented	19		1.3%	—
Systemic Hypertension (HTN)	Absent (0)	1,127	1,486	75.4%	75.8%
	Present (1)	359		24.0%	24.2%
	Missing	9		0.6%	—
Diabetes Mellitus (DM)	Absent (0)	1,055	1,483	70.6%	71.1%
	Present (1)	428		28.6%	28.9%
	Missing	12		0.8%	—
Primary Surgery	Phacoemulsification	1,107	1,495	74.0%	74.0%

	SICS	208		13.9%	13.9%
	ECCE	21		1.4%	1.4%
	Other	144		9.6%	9.6%
	Missing / Undocumented	15		1.0%	1.0%
Suture Material	Nylon 10-0	1,191	1,495	79.7%	79.7%
	Vicryl 10-0	119		8.0%	8.0%
	Prolene 10-0	79		5.3%	5.3%
	Vicryl 8-0	32		2.1%	2.1%
	Nylon 9-0	19		1.3%	1.3%
	Silk 9-0	4		0.3%	0.3%
	Missing / Undocumented	51		3.4%	3.4%
Suture Condition at Removal	Intact	491	1,495	32.8%	32.8%
	Loose	427		28.6%	28.6%
	Exposed knot	214		14.3%	14.3%
	With exudate	158		10.6%	10.6%
	Buried	131		8.8%	8.8%
	Missing / Undocumented	74		4.9%	4.9%
Hypopyon	Present	1,026	1,495	68.6%	68.6%
	Absent	414		27.7%	27.7%
	Missing / Undocumented	55		3.7%	3.7%

3-2. Microbiological Profile and Antimicrobial Susceptibility

Intraocular microbiological cultures were positive in 1,260 eyes (84.3%), negative in 220 eyes (14.7%), and missing/unresolved in 15 eyes (1.0%). Gram staining of the specimens demonstrated Gram-positive organisms in 1,026 cases (68.6%), fungal elements in 143 cases (9.6%), and Gram-negative organisms in 79 cases (5.3%). No microscopic growth was identified in 211 cases (14.1%).

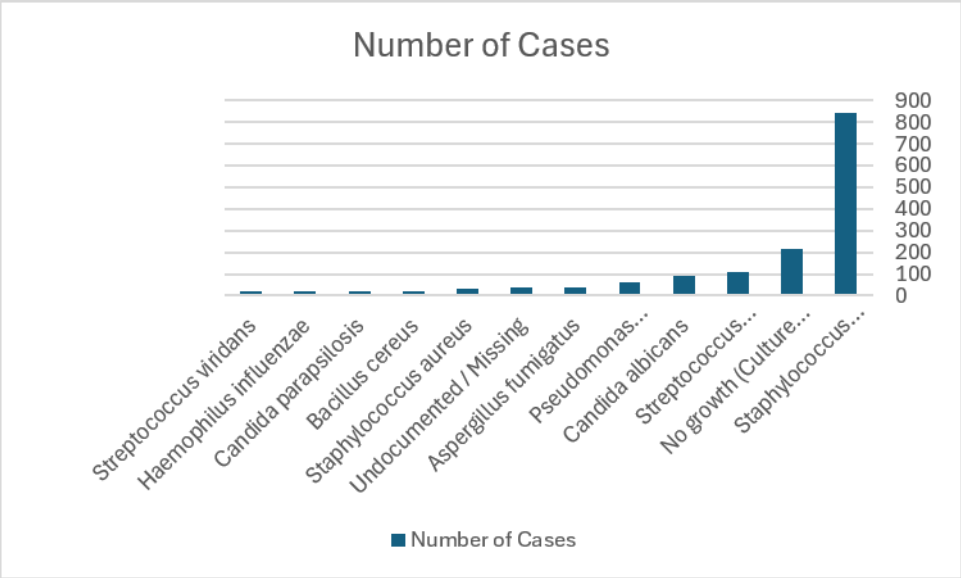


Figure 1: Pathogen Distribution of Post-Suture Removal Endophthalmitis

Among the culture-positive cases, *Staphylococcus epidermidis* was the predominant isolate, recovered from 843 eyes (56.4% of the total cohort; 66.9% of positive cultures). *Streptococcus pneumoniae* was the second most common bacterial isolate, found in 106 eyes (7.1%), followed by the fungal pathogen *Candida albicans* in 89 eyes (6.0%), and *Pseudomonas aeruginosa* in 61 eyes (4.1%). Other isolated species included *Aspergillus fumigatus* (n = 36; 2.4%), *Staphylococcus aureus* (n = 32; 2.1%), *Bacillus cereus* (n = 20; 1.3%), *Candida parapsilosis* (n = 19; 1.3%), *Haemophilus influenzae* (n = 19; 1.3%), and *Streptococcus viridans* (n = 18; 1.2%).

Table 2: Microbiological Culturing Outcomes

Diagnostic Variable	**Subcategory**	**Frequency (n)**	**Total Valid (N)**	**Percent of Total (%)**	**Valid Percent (%)**
Culture Outcome	Positive	1,260	1,495	84.3%	84.3%
	Negative	220		14.7%	14.7%
	Missing / Undocumented	15		1.0%	1.0%
Gram Stain Category	Positive	1,026	1,495	68.6%	68.6%
	Fungal	143		9.6%	9.6%
	Negative	79		5.3%	5.3%
	No growth	211		14.1%	14.1%

	Missing / Undocumented	36		2.4%	2.4%

Table 3: Susceptibility and Resistance Patterns of Key Empirical Antibiotics

Antibiotic Agent	**Sensitive n(%)**	**Resistant n (%)**	**Not Applicable n(%)**	**Not Reported / Missing n (%)**	**Total (N)**	**Valid Tested (n)**	**Adjusted Resistance Rate (%)***
Vancomycin	728 (48.7%)	260 (17.4%)	483 (32.3%)	24 (1.6%)	1,495	988	**26.3%**
Ceftazidime	47 (3.1%)	31 (2.1%)	127 (8.5%)	1,290 (86.3%)**	1,495	78	**39.7%**
Amikacin	57 (3.8%)	25 (1.7%)	126 (8.4%)	1,287 (86.1%)***	1,495	82	**30.5%**

In vitro susceptibility testing (antibiogram) for key therapeutic agents revealed notable resistance patterns. Among the evaluated Gram-positive isolates (n = 988), 728 (73.7%) were sensitive to vancomycin, while 260 (26.3%) exhibited resistance. For Gram-negative isolates, 47 out of 78 tested specimens (60.3%) were sensitive to ceftazidime (39.7% resistant), and 57 out of 82 tested specimens (69.5%) were sensitive to amikacin (30.5% resistant).

Importantly, a focused resistance analysis was conducted for *Staphylococcus epidermidis* (n = 843), the leading pathogen in this cohort. Out of 831 tested *S. epidermidis* isolates, 583 (70.2%) were sensitive to vancomycin, whereas 248 (29.8%) demonstrated in vitro resistance, indicating a significant level of resistance against this first-line empiric therapeutic agent.

3-3. Pathogen Distribution by Primary Surgical Procedure

Bivariate cross-tabulation of the primary surgical procedure against the isolated microbial species demonstrated a highly significant association ($\chi^2 = 182.44$, df = 27, p < 0.001). *Staphylococcus epidermidis* was highly prevalent in eyes that had undergone phacoemulsification (n = 694; 82.3% of *S. epidermidis* cases) and SICS (n = 131; 15.5%).

Significantly, highly virulent and fast-acting pathogens—namely *Bacillus cereus* (n = 20), *Haemophilus influenzae* (n = 19), and *Streptococcus viridans* (n = 18)—were recovered exclusively (100% of cases) from eyes that had primary phacoemulsification cataract surgery. Conversely, *Staphylococcus aureus* showed a distinct distribution, with 18 out of 32 cases (56.3%) isolated from the "other surgical

procedures" subgroup. The detailed distribution of isolated pathogens across different primary surgical categories is summarized in Table 3.

Table 4: Cross-tabulation of Primary Ophthalmic Procedures and Isolated Pathogens

Isolated Pathogen Species	**Phacoemulsification (n)**	**SICS (n)**	**ECCE (n)**	**Other Surgery (n)**	**Undocumented Primary (n)**	**Total Species (n)**
Staphylococcus epidermidis	694	131	10	0	8	**843**
Streptococcus pneumoniae	66	11	1	28	0	**106**
Candida albicans	76	7	1	5	0	**89**
Pseudomonas aeruginosa	53	6	1	0	1	**61**
Aspergillus fumigatus	25	8	1	1	1	**36**
Staphylococcus aureus	9	5	0	18	0	**32**
Bacillus cereus	20	0	0	0	0	**20**
Candida parapsilosis	16	1	0	2	0	**19**
Haemophilus influenzae	19	0	0	0	0	**19**
Streptococcus viridans	18	0	0	0	0	**18**
No growth (sterile)	144	33	5	29	5	**216**
Undocumented Species	24	6	2	4	0	**36**
Total Procedures (n)	**1,107**	**208**	**21**	**144**	**15**	**1,495**

- **Statistical Analysis:** Pearson Chi-Square (χ^2) = **779.969**, Degrees of Freedom (df) = **44**, Asymptotic Significance (2-sided) $p < 0.001$ (Highly Significant).

3-4. Predisposing Systemic Factors and Microbiological Correlations

The relationship between systemic comorbidities and specific microbiological outcomes was analyzed. No significant associations were observed between a history of diabetes mellitus ($p = 0.608$) or systemic hypertension ($p = 0.551$) and the type of isolated pathogen.

However, a highly significant association was identified between the patient's immune status and the isolated microbial species (Fisher's exact test, $p < 0.001$). Fungal pathogens—specifically *Candida albicans* (n = 88; 100%), *Aspergillus fumigatus* (n = 36; 100%), and *Candida parapsilosis* (n = 19; 100%)—were isolated exclusively from patients documented as immunocompromised.

Conversely, immunocompetent patients were primarily affected by bacterial isolates, with 95.3% of *Staphylococcus epidermidis* cases (791 out of 830 valid cases) and 95.0% of *Streptococcus pneumoniae* cases (96 out of 101 valid cases) occurring in patients with normal immune function (Table 4).

Table 5: Patient's Immune Status and Pathogen Crosstabulation

Isolated Pathogen Species	**Immunocompetent (n)**	**Immunocompromised (n)**	**Total Valid Cases (N)**	**Proportion of Fungal Cases in Immunocompromised (%)**
Staphylococcus epidermidis	791	39	830	4.7%
Streptococcus pneumoniae	96	5	101	5.0%
Candida albicans (Fungal)	0	88	88	**100.0%**
Pseudomonas aeruginosa	54	4	58	6.9%
Aspergillus fumigatus (Fungal)	0	36	36	**100.0%**
Staphylococcus aureus	30	1	31	3.2%
Bacillus cereus	20	0	20	0.0%
Candida parapsilosis (Fungal)	0	19	19	**100.0%**
Haemophilus influenzae	15	4	19	21.1%
Streptococcus viridans	15	2	17	11.8%
No growth (sterile)	201	8	209	3.8%
Undocumented / Blank	31	4	35	11.4%

Total (n)	**1,253**	**210**	**1,463**	**14.4%**

- **Statistical Analysis:** Pearson Chi-Square (χ^2) = **952.404**, Degrees of Freedom (df) = **11**, Asymptotic Significance (2-sided) $p < 0.001$(Highly Significant).

3-5. Temporal Dynamics of Infection and Suture Parameters

The median time interval from the primary surgical procedure to suture removal was 7.10 months (IQR: 17.10 months; range: 1.00 to 66.00 months). The non-parametric Kruskal-Wallis test showed no significant difference in this surgical-to-removal interval across the different Gram stain classifications (H = 3.12, df = 4, p = 0.538; Mean Ranks: Gram-negative = 654.62, Gram-positive = 728.89, Fungal = 735.59, No growth = 728.80).

The median time from suture removal to the onset of clinical symptoms of endophthalmitis was 7.00 days (IQR: 5.00 days; range: 2.00 to 134.00 days). The Kruskal-Wallis test demonstrated a highly significant difference in the timing of symptom onset across the Gram stain categories (H = 743.15, df = 4, p < 0.001).

Gram-positive (Mean Rank: 555.46, n = 997) and Gram-negative (Mean Rank: 565.66, n = 77) bacterial infections presented significantly faster (hyperacute to acute onset) following suture removal compared to fungal pathogens (Mean Rank: 1190.37, n = 142) and culture-negative cases (Mean Rank: 1301.73, n = 209).

Additionally, Kruskal-Wallis testing indicated a significant difference in patient age across the Gram stain categories (H = 36.38, df = 4, p < 0.001). Patients with Gram-negative infections were significantly older (Mean Rank: 990.37, n = 76) compared to those with Gram-positive (Mean Rank: 722.53), Fungal (Mean Rank: 763.66), or culture-negative (Mean Rank: 663.14) presentations.

Table 6: One-way ANOVA Comparison of Age and Surgery-to-Removal Interval Across Gram-Stain Categories

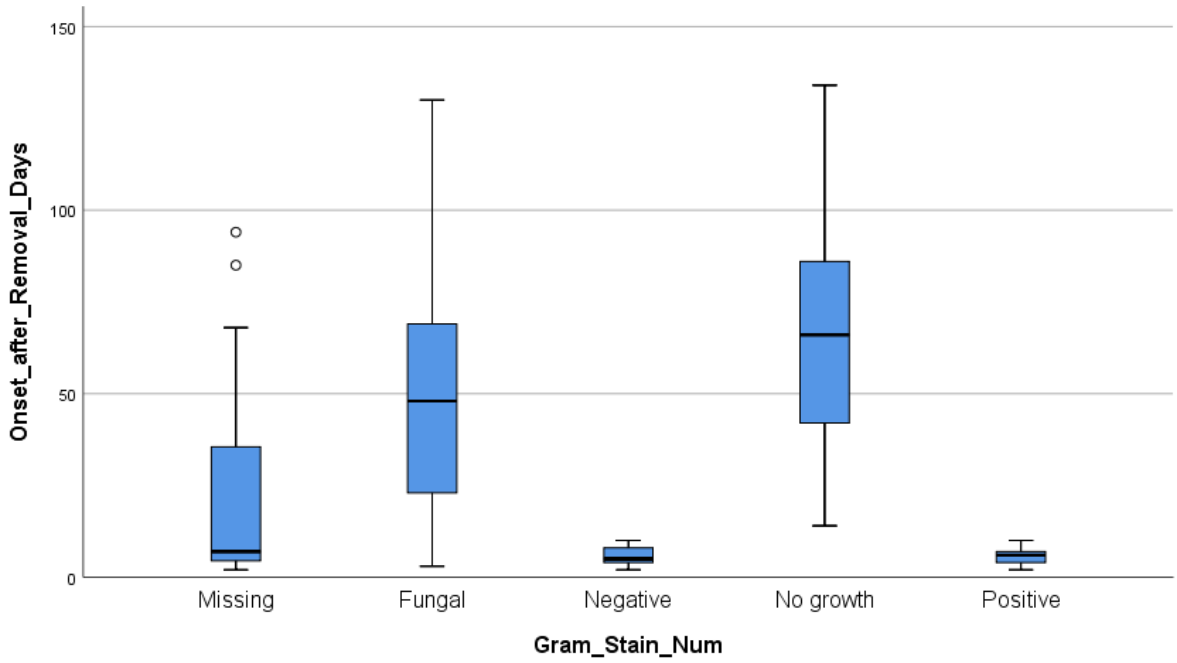
Part A: Descriptive Summary by Group						
Continuous Dependent Variable	**Gram-Stain Category**	N	**Mean**	**Standard Deviation (SD)**	**Standard Error (SE)**	**95% Confidence Interval for Mean**
Age (Years)	Undocumented (Blank)	35	59.60	10.463	1.769	56.01 – 63.19
	Fungal	140	62.07	10.965	0.927	60.24 – 63.90
	Gram-Negative	76	**67.74**	9.549	1.095	65.55 – 69.92
	No growth	207	59.61	11.093	0.771	58.09 – 61.13
	Gram-Positive	1,002	60.98	11.060	0.349	60.29 – 61.67
	Total	**1,460**	**61.21**	**11.079**	**0.290**	**60.64 – 61.78**
Surgery-to-Removal (Months)	Undocumented (Blank)	35	16.55	19.862	3.357	9.73 – 23.37
	Fungal	141	14.33	16.413	1.382	11.60 – 17.07

	Gram-Negative	77	11.59	15.869	1.808	7.99 – 15.19
	No growth	206	13.72	16.431	1.145	11.47 – 15.98
	Gram-Positive	994	13.64	16.050	0.509	12.64 – 14.64
	Total	**1,453**	**13.68**	**16.222**	**0.426**	**12.85 – 14.52**

Part B: ANOVA Summary Table						
Dependent Variable	**Source of Variation**	**Sum of Squares**	**df**	**Mean Square**	F-value	**Significance (p-value)**
Age (Years)	Between Groups	4,015.957	4	1,003.989	**8.345**	<0.001
	Within Groups	175,061.328	1,455	120.317		
	Total	179,077.284	1,459			
Surgery-to-Removal (Mo)	Between Groups	686.251	4	171.563	**0.651**	0.626 (NS)
	Within Groups	381,403.148	1,448	263.400		
	Total	382,089.398	1452			

- *NS: Not Statistically Significant ($p > 0.05$).*

Figure 2: Box Plot of Time to Symptom Onset (Days) Across Gram-Stain Categories



Finally, the clinical appearance of the suture prior to removal (intact, loose, exposed knot, with

exudate, or buried) was evaluated against the culture outcome. Pearson Chi-square analysis showed no significant association between the suture's physical appearance and culture positivity ($\chi^2 = 3.58$, df = 5, p = 0.612). All suture status categories demonstrated high rates of positive intraocular cultures, exceeding 80% across all subgroups: buried (87.0%), intact (85.1%), with exudate (84.8%), loose (83.4%), and exposed knot (80.8%).

Discussion

4-1. Summary of Primary Findings

This retrospective registry-based study represents, to our knowledge, the largest cohort to date (1,495 cases) evaluating the epidemiological, microbiological, and clinical parameters of endophthalmitis following ophthalmic suture removal. Our investigation yielded several key clinical insights. First, post-suture removal endophthalmitis is primarily an acute clinical event, with symptoms manifesting within a median of 7.00 days following the procedure. Second, *Staphylococcus epidermidis* was identified as the leading causative pathogen, representing 56.4% of all cases and 66.9% of positive cultures. Third, a high level of in vitro resistance (29.8%) to vancomycin was identified among the *S. epidermidis* isolates, which represents a notable challenge to first-line empirical therapeutic protocols. Fourth, the physical or clinical appearance of the suture prior to extraction (buried, intact, loose, or with exudate) did not significantly correlate with culture outcomes, with culture positivity rates exceeding 80% across all subgroups. Finally, patient systemic immune status was strongly associated with specific pathogen categories, as demonstrated by the exclusive (100%) isolation of fungal species from immunocompromised patients, while Gram-negative pathogens were isolated from significantly older patients.

4-2. Comparison of Microbiological Spectrum and Surgical Factors

The microbiological spectrum identified in this large cohort exhibits notable differences when compared to earlier, smaller series in the literature. In the multicentre study by Panchal et al. (2019), *Streptococcus pneumoniae* was identified as the predominant pathogen, accounting for 63.6% of culture-positive cases, with a strong clustering of infections among pediatric patients [42]. Similarly, Bor and Kremer (2011) reported a predominance of streptococcal species (75% of cases) in patients developing endophthalmitis following late suture removal after penetrating keratoplasty (PKP) [22].

While streptococcal species, particularly *S. pneumoniae* (7.1%) and *S. viridans* (1.2%), represented a clinical component of our cohort, the overwhelming dominant pathogen was *Staphylococcus epidermidis* (56.4%). This difference is likely due to the surgical characteristics of our study population. Unlike previous studies that focused primarily on keratoplasty-related suture complications [22, 38], 74.0% of our patients had undergone phacoemulsification as their primary procedure. The high prevalence of phacoemulsification-related suture removals in our center, combined with the standard commensal nature of *S. epidermidis* on the eyelid and conjunctival surface, likely accounts for its dominance in this cohort [28, 45].

Furthermore, we identified a highly significant association between the primary surgical type and the isolated microbial species ($p < 0.001$). Highly virulent and fast-acting organisms, such as *Bacillus*

cereus (n = 20), *Haemophilus influenzae* (n = 19), and *Streptococcus viridans* (n = 18), were isolated exclusively from patients who had previously undergone phacoemulsification cataract surgery. These findings suggest that different surgical settings may establish distinct microenvironments or anatomical vulnerabilities, influencing the colonization patterns of specific pathogens [33].

4-3. Emerging Antibiotic Resistance Patterns

One of the most notable and clinically concerning findings of this study is the high rate of antibiotic resistance among the isolated pathogens. Traditionally, vancomycin has been regarded as the gold standard empirical agent for Gram-positive coverage in suspected endophthalmitis, with resistance rates historically reported as negligible or near zero [26, 28]. However, our in vitro susceptibility analysis revealed that 26.3% of all tested Gram-positive specimens, and specifically 29.8% of *Staphylococcus epidermidis* isolates, exhibited resistance to vancomycin.

This resistance rate is higher than those reported in historical databases and presents a challenge to empirical treatment protocols [25]. The rise in resistance may be driven by the frequent perioperative use of topical antibiotics (such as fluoroquinolones and aminoglycosides) in patients who undergo complex or repeated ocular procedures, which can exert selective pressure on the ocular surface commensal flora [30]. Additionally, we observed a ceftazidime resistance rate of 39.7% among Gram-negative isolates and an amikacin resistance rate of 30.5%.

These findings indicate a decline in the susceptibility of Gram-negative ocular pathogens, consistent with global trends in antimicrobial resistance [33]. Given these patterns, clinicians must remain vigilant, and tertiary eye centers should regularly audit local susceptibility profiles to guide empirical therapy.

4-5. Host Immunological Status and Fungal Pathogenesis

Our analysis identified a strong correlation between the systemic immune status of the patient and the class of the invading pathogen ($p < 0.001$). Crucially, 100% of the fungal endophthalmitis cases—comprising *Candida albicans* (n = 88), *Aspergillus fumigatus* (n = 36), and *Candida parapsilosis* (n = 19)—occurred in patients documented as immunocompromised. This finding is consistent with the pathophysiology of opportunistic fungal infections, which rarely establish intraocular disease in the presence of intact host defenses [27].

In immunocompromised individuals, such as those undergoing active chemotherapy, receiving systemic immunosuppressants, or on chronic topical corticosteroid therapy post-keratoplasty, local ocular defense mechanisms are compromised. This includes a reduction in tear-film immunoglobulins (IgA) and impaired macrophage and polymorphonuclear leukocyte activity at the ocular surface [37, 46].

In this state of impaired immunity, opportunistic fungi colonizing the lid margins or conjunctival sac can infiltrate the suture tract during or after extraction, slowly proliferating within the vitreous or anterior chamber [27].

Conversely, immunocompetent individuals in our study were affected almost exclusively by bacterial pathogens, with 95.3% of *S. epidermidis* and 95.0% of *S. pneumoniae* infections occurring in this group. This suggests that bacterial entry is driven primarily by physical breaches in the ocular envelope rather than systemic immune dysfunction.

4-5. Temporal and Age Dynamics

The temporal characteristics of symptom onset varied significantly across Gram-stain categories ($p < 0.001$). Gram-positive and Gram-negative bacterial infections presented with a rapid, acute onset (median of 7 days), whereas fungal cases presented with a delayed onset.

This clinical timing aligns with the known growth kinetics and virulence mechanisms of these pathogens. Highly virulent bacteria, such as *S. pneumoniae* and *P. aeruginosa*, replicate rapidly and release destructive extracellular enzymes (such as pneumolysin and elastase) that trigger an immediate host inflammatory response [3, 5]. In contrast, fungal pathogens multiply slowly and elicit a low-grade, granulomatous inflammatory response, leading to a delayed clinical presentation that can sometimes be mistaken for sterile post-operative inflammation or graft rejection [27].

We also observed that patients presenting with Gram-negative infections were significantly older (Mean Rank: 990.37; $p < 0.001$) than those with Gram-positive or fungal infections. This age-related susceptibility may be linked to senile changes in the ocular surface microenvironment, such as chronic tear film instability, decreased tear lysozyme levels, and microvascular insufficiency at the limbus or sclera, which can facilitate colonization by Gram-negative bacilli (such as *Pseudomonas*) in elderly individuals [15].

4-6. Suture Status and the Biofilm/Wicking Mechanism

A key finding of this study was that the clinical appearance of the suture prior to removal (intact, loose, exposed, with exudate, or buried) did not correlate with culture outcomes ($p = 0.61$). All categories showed high rates of positive intraocular cultures, exceeding 80% across all subgroups, including sutures documented as intact (85.1%) and buried (87.0%). This is a clinically important finding, as it indicates that a suture's benign physical appearance does not rule out microbial colonization.

This phenomenon is explained by the ability of bacterial pathogens, particularly *Staphylococcus epidermidis*, to form biofilms on synthetic materials [39]. Even on an intact or partially buried nylon suture, colonizing bacteria can produce a protective extracellular polymeric substance (EPS) matrix, embedding themselves on the suture surface [40, 47].

During suture extraction, the physical movement of the suture through the corneal or scleral tissue can shear this biofilm, inoculating viable bacteria directly into the suture tract [38]. Additionally, through the "wicking effect," the micro-fistula left behind immediately after suture removal can draw tear film fluids containing these mobilized bacteria into the anterior chamber before the tract can close naturally [36, 44].

4-7. Clinical Implications and Recommendations

Given that over 80% of suture removals in patients who developed endophthalmitis were associated with positive cultures regardless of suture appearance, several preventative measures should be considered:

- **Pre-Procedural Antisepsis:** The application of 5% povidone-iodine (betadine) to the conjunctival sac and lid margin is essential prior to any suture manipulation. It is highly effective in reducing the ocular surface bacterial load and is not subject to antimicrobial resistance [48].
- **Technical Precision:** Suture cutting should be performed as close to the tissue entrance as possible, ensuring that the exposed, potentially contaminated portion of the thread is not pulled through the stromal suture tract [38].
- **Post-Procedural Prophylaxis:** A short course of broad-spectrum topical antibiotics (e.g., a fourth-generation fluoroquinolone) should be prescribed for 5 to 7 days following suture removal to protect the micro-tract during epithelial closure.
- **Surgical Suture Removal in High-Risk Cases:** In uncooperative pediatric patients, suture removal should be performed under general anesthesia or deep sedation to prevent micro-dehiscence or tissue laceration due to sudden movement [42].

4-8. Study Strengths and Limitations

The primary strength of this study is its large sample size (1,495 cases) collected over a 10-year period from a single tertiary referral center, providing robust statistical power. Additionally, the study offers a comprehensive evaluation of both clinical and microbiological parameters in this specific patient population.

Howbeit, several limitations must be acknowledged:

- **Retrospective Design:** The study relied on historical medical records, leading to missing data in some parameters, such as missing baseline age in 7.4% of cases.
- **Single-Center Study:** Although Farabi Hospital is the national referral center and represents a diverse patient pool, the findings may not fully reflect the microbiological profiles of other regional centers.
- **Lack of a Control Group:** The study did not include an uninfected control group (patients who underwent suture removal without developing endophthalmitis), which limited our ability to calculate relative risk or odds ratios for specific risk factors.
- **Absence of Long-Term Visual Acuity Outcomes:** Due to the referral nature of our institution, many patients returned to their local ophthalmologists after acute management, preventing the systematic collection of long-term visual outcomes for the entire cohort.

5. Conclusion

In conclusion, endophthalmitis following suture removal is a serious complication that presents as an acute infection, with *Staphylococcus epidermidis* serving as the primary causative pathogen. Crucially, the clinical appearance of the suture prior to removal is an unreliable predictor of microbial contamination, as high culture-positivity rates were observed across all suture states. The high rate of vancomycin resistance (29.8%) among *S. epidermidis* isolates is a notable finding that highlights the need for ongoing surveillance of local resistance patterns. Additionally, systemic immune status was strongly associated with pathogen type, with fungal infections occurring exclusively in immunocompromised patients. Meticulous aseptic techniques, the routine use of pre-procedural povidone-iodine 5%, and careful post-procedural monitoring are essential to minimize the risk and impact of this complication.

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Khashayar Ashkboos and Kosar Bagherzadeh. The first draft of the manuscript was written by Khashayar Ashkboos, and both authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Approval

This retrospective chart review study involving human participants was conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval was granted by the Ethics Committee of Tehran University of Medical Sciences, Farabi Eye Hospital (Approval Code: IR.TUMS.FARABIH.REC.1403.054).

Consent to Participate

Informed consent was officially waived by the Ethics Committee of Tehran University of Medical Sciences in view of the retrospective nature of the study, and because all procedures performed were part of routine clinical care.

Consent to Publish

Not applicable. This retrospective study did not include any individual participant's identifying details, clinical photographs, or sensitive personal data.