Original Article

A National Survey of Endophthalmitis Prophylaxis during Cataract Surgery in Pakistan: A 2020 Perspective

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ABSTRACT

Purpose: To assess national endophthalmitis prophylaxis practice patterns during phacoemulsification surgery in Pakistan.

Study Design: Cross sectional survey.

Place and Duration of Study: Eye units registered with the British Pakistani Ophthalmic Society (BPOS) between September and November 2020.

Methods: A survey-based cross sectional study was conducted in Pakistan between September and November 2020. A proforma was designed using a survey client (Survey Monkey) and distributed to the eye units registered with the British Pakistani Ophthalmic Society (BPOS). The survey explored demographic factors, current antibiotic prophylaxis practice during cataract surgery and audit practice in Pakistan.

Results: A total of 339 respondents completed the survey. The survey was representative of ophthalmic surgeons working in the major provinces of Pakistan. A small majority of ophthalmic surgeons provided some form of routine antibiotic prophylaxis (n = 140, 53.8%). Povidone iodine 5% (PVP-I) solution on skin and in the conjunctival sac proved the most popular protocol (n = 163, 66.3%). This was followed by immediate postoperative topical antibiotics (n = 101, 41.1%). Intracameral antibiotic prophylaxis accounted for less than half of current antibiotic practice during cataract surgery in Pakistan (n=99, 40.3%). Most of the respondents did not conduct any audit regarding endophthalmitis (n = 119, 55.6%).

Conclusion: Our survey provides an up-to-date view on the state of antibiotic prophylaxis during cataract surgery in Pakistan and highlights several areas for improvement. This includes policy changes to increase adherence to gold standard antibiotic prophylaxis guidelines, improvement in transparency of surgical outcomes and to audit current postoperative outcomes.

Key Words: Acute postoperative endophthalmitis, Surgical wound infection, Antibiotic, Cataract, Pakistan.

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INTRODUCTION

Endophthalmitis remains one of the most dreaded complications following modern day cataract surgery.¹ Risk factors include surgical factors, such as posterior capsular rupture (PCR), vitreous loss, poor corneal wound integrity, silicon lenses and the type of operative antibiotic prophylaxis, local factors, such as

chronic eyelid disease, and systemic factors, such as older age (above 80) and diabetes.²

A variety of operative protocols have been used in the prevention of postoperative endophthalmitis, including topical/oral antibiotics, use of povidone iodine (PVP-I) solution, subconjunctival injection of antibiotics and antibiotics in irrigating solution.³ In a multicentre, randomised control trial run by the European Society for Cataract and Refractive Surgeons (ESCRS), it was shown that intracameral cefuroxime administered at the time of surgery significantly reduced the risk of developing endophthalmitis following cataract surgery.⁴ This study proved seminal in introducing the concept that intracameral antibiotics may be the new gold standard of antibiotic prophylaxis in cataract surgery. Since then, multiple international centres have adopted the routine use of intracameral injections during cataract surgery and have shown a reduction in the incidence of postoperativeendophthalmitis.^{5,6} A recent Cochrane Review summarises the growing literature that injection with cefuroxime (intracameral antibiotic prophylaxis) lowers the chance of endophthalmitis following surgerv.⁷

Several countries and professional bodies now mandate annual audit of cataract surgery. Such initiatives aid in monitoring practice standards and can ascertain the impact of antibiotic prophylaxis on the annual incidence of postoperative endophthalmitis following cataract surgery as well as provide appropriate guidelines. The Royal College of Ophthalmologists (RCOphth), United Kingdom (UK), deliver an annual national audit that covers endophthalmitis incidence⁸ and the ESCRS have provided recent guidelines on the prevention and treatment of endophthalmitis following cataract surgery.9 However, the practice of antibiotic prophylaxis in many developing countries, such as Pakistan, remains inconsistent and unknown. The collection of robust data allows for the introduction of practice improvement guidelines in developing nations that may have limited resources.

Through a national survey distributed to ophthalmic surgeons operating in Pakistan, our study objectives were to assess national endophthalmitis prophylaxis practice patterns during phacoemulsification surgery in Pakistan. This data will help in finding out adherence of surgeons to national and international clinical standards in clinical practice and identifying strengths and weaknesses in the healthcare system.

METHODS

A cross-sectional survey-based study was conducted by the British Pakistani Ophthalmic Society (BPOS) between the period of 24^{th} September 2020 and 8^{th} November 2020.Study protocol was approved by BPOS before survey distribution to various ophthalmology units across Pakistan via the WhatsApp encrypted messaging platform (WhatsApp Inc, CA, USA). The survey was carried out for service improvement and guidance. Therefore, ethical approval was not required for this study. No personal information was acquired from survey participants and all survey data was handled in a confidential manner.

An 8-item survey was designed following a literature review on international postoperative endophthalmitis audit practice and after expert opinion from members of BPOS. Questions were devised to ascertain demographic details regarding the individual ophthalmology sites performing cataract surgery, the volume of surgery and the details around surgical antibiotic prophylaxis. RZ designed the initial version of the survey and this was subsequently revised through three iterations by BPOS. The survey employed multiple choice questions with either single or multi-select options. An 'other' option was provided where appropriate and respondents were allowed to elaborate on these answers.

Questions 1 to 2 were single – select responses, whilst questions 3 to 8were multi-select responses. 'High-volume' (question 2) was defined as a surgeon who carried out at least 8 cataract operations on a standard morning, afternoon or evening list that lasted between 3 - 4 hours. 'Acute-onset postoperative endophthalmitis' (questions 4 - 5) was defined as iatrogenic infective endophthalmitis that had arisen within 6 weeks following cataract surgery.⁴ The survey was created and disseminated using an online survey client (Survey Monkey, CA, USA).

Data was exported from Survey Monkey as a Microsoft Excel file (Version 16, Microsoft, WA, USA), which was uploaded to Prism (Version 9, Graph Pad, CA, USA) for diagram creation. Data was analysed by two authors (YSB, RZ). Demographic details and survey responses were represented using simple statistics as counts (n) and percentages (%). Multiple responses from the same survey respondent were removed and accounted for by identifying unique internet protocol addresses.

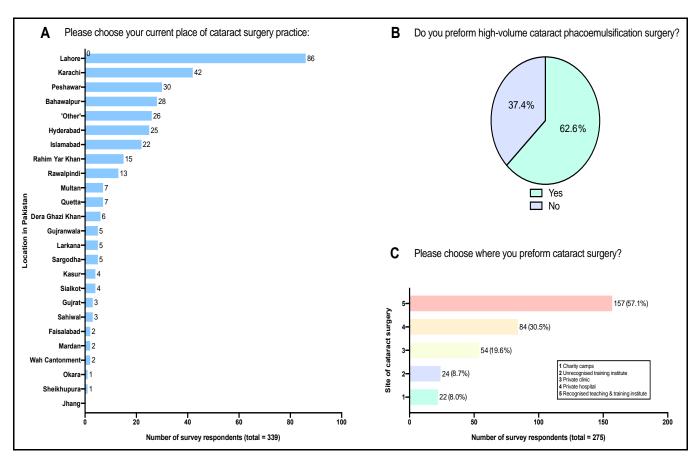
RESULTS

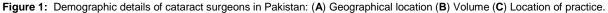
A total of 339responses were received from all four providences of Pakistan and the top 24 most populated cities (Figure 1). Largest responses were from major cities. High volume phacoemulsification was performed by 186 (62.3%) respondents. Majority of the ophthalmic surgeons performed cataract surgery at a recognised teaching, or training institute (n = 157, 57.1%). Other popular sites included private hospital (n = 84, 30.5%), private clinic (n = 54, 19.6%) or unrecognised institute (n = 24, 8.7%). Charity camps were the least popular locations for performing cataract surgery (Figure 1).

Antibiotic prophylaxis against postoperative

endophthalmitis following cataract surgery varied widely amongst survey participants. There were surgeons who provided some form of routine antibiotic prophylaxis against postoperative endophthalmitis as standard operative procedure (140, 53.8%). Whereas others declared no routine antibiotic prophylaxis (107, 41.2%) (Figure 2). PVP – I 5% solution on skin and in the conjunctival sac was the most popular (n = 163, 66.3%). Hundred respondents (43.1%) stated they had an 'other' regimen (off-label antibiotics, such as Moxifloxacin and Vancomycin, n = 51, 51%) for preparing intracameral antibiotics on the day of surgery (Figure 3).

Most survey respondents did not conduct an annual endophthalmitis audit in their respective departments (Figure 4). Majority (n = 47, 41.2%) undertook audit practice for personal development.







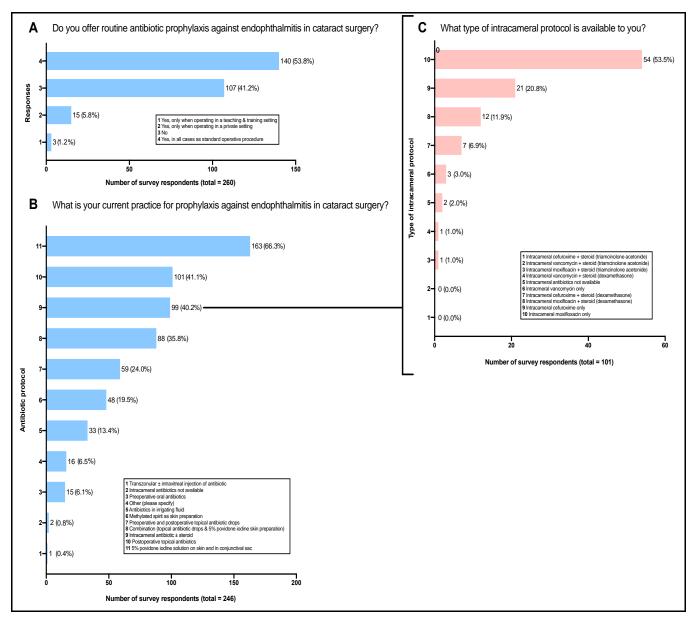


Figure 2: Antibiotic prophylaxis amongst ophthalmic surgeons: (A) Yes / No (B) Type of ABx (C) Type of intracameral ABx.

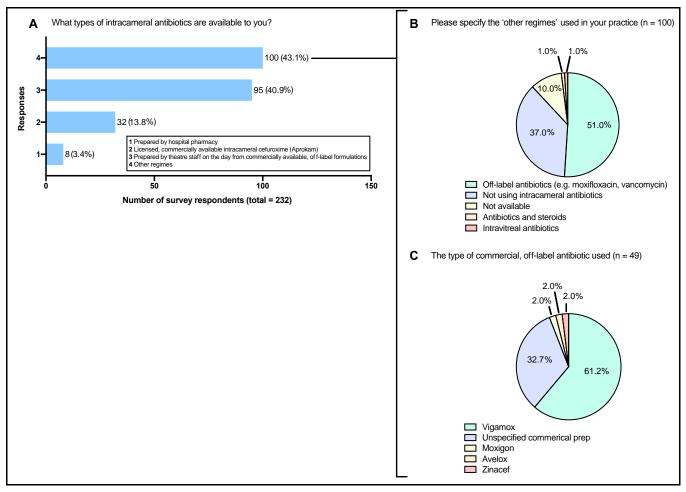


Figure 3: Type of intracameral antibiotics used: (A) Preparation (B) 'Other' regimes (C) Off-label antibiotics.

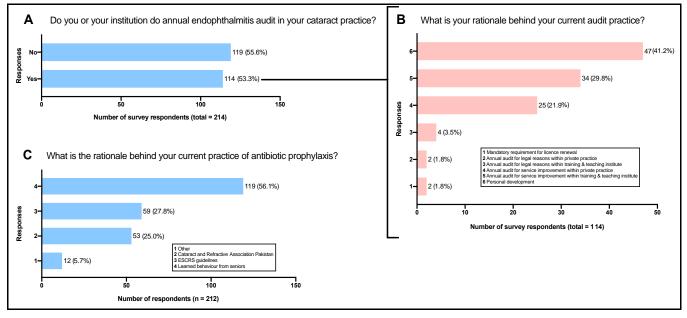


Figure 4: The audit and service improvement practice amongst ophthalmic surgeons: (A) Yes / No (B) Rationale behind audit (C) Rationale behind antibiotic prophylaxis.

DISCUSSION

This survey provides the latest update on cataract surgery practice in Pakistan. Intracameral injection of cefuroxime is the gold standard in cataract surgery for endophthalmitis prevention after several international landmark studies.^{4–6} Our survey demonstrated this was only the third most common (40.2%) endophthalmitis prophylaxis practice in Pakistan, despite evidence showing that the incidence of postoperative endophthalmitis could be reduced to as low as $0.014\%^{10}$ The most common endophthalmitis prophylaxis intervention used in Pakistan was preoperative PVP-I antiseptic solution on the skin and in the conjunctival sac (66.3%). The incidence of endophthalmitis can be reduced up to 4 -fold with PVP – I.¹¹ Novel routes of PVP – I administration are being explored, including intravitreal injection and combining with surgical irrigation fluid.¹²

causative organisms in postoperative The endophthalmitis are Gram-positive bacteria in the overwhelming majority of cases. These are typically coagulase-negative *Staphylococci* (of which Staphylococcus epidermis is the most common) or Staphylococcusaureus.¹³ However, the microbial spectrum of post-cataract endophthalmitis has geographical variation due to antibiotic practice and local antisepsis protocols, with countries such as India and China reporting higher percentages of cultured Gram-negative bacteria and fungal cases.¹⁴

A landmark study in 1995 by the Endophthalmitis Vitrectomy Study (EVS) group¹⁵ set the early standards for the management of postoperative endophthalmitis. The group recommended the omission of systemic antibiotic treatment, due to the potential toxic side effects and low penetrance in the eye. Early pars plana vitrectomy (PPV) was only recommended for individuals presenting after cataract extraction, or lens implantation, with a visual acuity of light perception. Subjects who had a visual acuity of hand motions and above had no advantage with immediate PPV and local antibiotic therapy should remain the mainstay of treatment. Local antibiotics achieve sufficient ocular therapeutic levels to inhibit the growth of many bacteria responsible for endophthalmitis, reducing the risk of systemic toxicity and the need for longer hospital stay.¹⁶

Following the EVS group, the ESCRS study⁴ evaluated the effects of intracameral cefuroxime compared to other antibiotic protocols: no

perioperative antibiotics, topical antibiotics only, combination therapy (topical and intracameral antibiotics) and placebo group. The study concluded that the use of intracameral cefuroxime (injection of 1mg at the end of surgery) reduced the incidence of postoperative endophthalmitis 5-fold, proving superior to other local antibiotic protocols. This evidence of intracameral antibiotics is supported by numerous global studies.⁴⁻⁶ To date, the most commonly used intracameral antibiotics are cefuroxime, moxifloxacin and vancomycin. In Europe, Aprokam® (cefuroxime) has been approved by the European Medicines Agency (EMA) as a commercially available intracameral cefuroxime injection. In US, there is no Food and Drug Administration (FDA) approved intracameral antibiotics, therefore antibiotic solutions need to be constituted prior to injection on the day of surgery. Vancomycin is considered the drug of choice for Gram-positive organisms, including methicillinresistant Staphylococcal species. However, it has no cover for anaerobic or Gram-negative organisms. Moxifloxacin (for example, Vigamox[®], Auromox[®]) is another alternative with a broad spectrum of coverage, including Gram-positive, Gram-negative and Pseudomonas, but may be becoming less effective due to growing resistance.¹⁷

In India, a country that conducts over one million routine cataract operations each year and has close proximity to Pakistan, Moxifloxacin has been a staple brand of locally manufactured intracameral injection since 2013 due to two Indian pharmaceutical companies. After a recent online survey of cataract practice in India, it was established that intracameral Moxifloxacin contributed to 90% of antibiotic prophylaxis.¹⁸ Out of the three commonly used intracameral antibiotics, Cefuroxime had the greatest evidence having been studied in randomised control trials (RCT) and large prospective studies,^{4–6} as well as gained approval by European regulatory bodies.

Our survey of endophthalmitis prophylaxis in cataract surgery demonstrated that intracameral Moxifloxacin was the most popular choice (53.5%) of commercially repurposed and off-label intracameral antibiotic used in Pakistan. This was followed by the gold standard – intracameral cefuroxime (20.8%) – and then combination therapy (Moxifloxacin plus Steroid, 11.9%).

When questioned on the type of preparation of intracameral Moxifloxacin, 61.2% of survey respondents selected Vigamox®, which remains the popular choice amongst ophthalmic surgeons in Pakistan. However, there are several disadvantages regarding Moxifloxacin. Due to a dose-dependent response, an initial high dose maybe required to antibiotic prophylaxis against provide adequate bacterial species: Staphylococcus specific and Pseudomonas.¹³ From anecdotal evidence, it is often routine for ophthalmic surgeons in Pakistan to use one bottle of commercially available antibiotic throughout the day, raising the question of antibiotic lifespan and efficacy as sequential doses are used in multiple theatre cases. Finally, there is a rise of antibiotic resistance to Moxifloxacin due to exposure to bacterial colonies present in the ocular and nasopharyngeal flora.¹⁴ Other intracameral antibiotics that were routinely used by survey respondents included Cefuroxime (20.8%) and Vancomycin (3.0%), which also provide adequate cover for certain bacterial species. However, resistance may also be developing to these traditional intracameral antibiotics.⁴ This raises concerns for developing nations, such as Pakistan, who do not routinely conduct audits in cataract surgery and may not spot trends in growing antimicrobial resistance.

The optimum distribution of surgical care in middle to low-income countries is debated amongst national policy makers and governments. There is lack of infrastructure in delivery of safe surgical care, maldistribution of a surgical workforce and reduced healthcare funding in low - income countries. Our survey shows there is a wide distribution of cataract practice in Pakistan, ranging from the private to charitable sector, which can lead to an unequal distribution of postoperative endophthalmitis cases. Independent and private practices are more likely to have state-of-the-art technology, sterile equipment, cleaner airflow systems and personal protective equipment that contribute to reduced complications following cataract surgery. Recognised training institutes are more likely to have recognised training programmes, centralised cataract services for a particular region and optimised theatre protocols. In comparison, charity camps may operate in less sterile environments, use only basic antiseptic protocols and re-use surgical instruments amongst cases. Despite these factors, the outcomes between larger, recognised cataract units and cataract camps are not dissimilar with respect to visual acuity and complication rates.¹⁹ This might be explained by the fact that the same local ophthalmic professionals that operate in larger units,

or privately, may undertake charitable work in cataract camps. There is also an increasing influx of foreign ophthalmologists that are running charitable organisations and outreach programmes to contribute to the improvement of reversable causes of blindness.

Finally, there is new evidence exploring the outcomes of manual small - incision cataract surgery (MSICS), which tends to be more commonly performed in low-resource and charitable settings due to the superior cost-benefit analysis to traditional phacoemulsification. Studies have shown postoperative endophthalmitis rates with MSICS are high-income comparable to countries using phacoemulsification.²⁰

The technical skills of an ophthalmic surgeon is another important factor in considering postoperative cataract surgery outcomes. A large cohort study observed that newly-qualified surgeons undertaking independent practice were 9 times more likely to have high complication rates (greater than 2%), including endophthalmitis, when compared to surgeons in their tenth year of practice.²¹

In addition, studies have shown that increasing surgical volume has correlation with better visual acuity outcomes and less complications following cataract surgery.²² An estimate of 350 cataract cases per year, or greater than 2 years of independent surgical practice, have been suggested as requirements to maintain high-volume and low – complication status amongst ophthalmic surgeons. Diminishing returns and statistically insignificant differences are seen beyond these arbitrary values otherwise.²⁰

Clinical audits are a method of ensuring that healthcare is provided in line with set standards. It allows care providers, as well as patients, know if a service is performing well, or if improvements can be made. Just over half of survey respondents did not conduct an annual endophthalmitis audit in their respective departments (n = 119, 55.6%). These figures do not provide confidence in creating standardised and safe cataract surgery practice for Pakistan, especially when audit data remains in the hands of individual surgeons, and latest guidelines from leading professional societies, such as ESCRS, remain ignored.⁴

There is a push for increasing contribution and transparency for national audits of postoperative cataract complications. Examples include the British Ophthalmology Surveillance Unit (BUSO), which runs the National Ophthalmology Database (NOD)⁸;a that specifically measures database outcomes following cataract surgery, including postoperative infections. Unfortunately there are a lack of national registries or audits with respect to postoperative cataract complications in South Asia. Malaysia has been exempla in setting up a national cataract registry Database²³) Eve and inviting (National all ophthalmologists operating within Government and University-funded hospitals participate in this registry, which also explores the incidence of postoperative endophthalmitis and delivers on regular annual reports. Other countries, such as India, are trialling the early stages of a registry and agree that auditing is required to implement uniform national policy and protocol for cataract surgery.²⁴

Reporting standards and registries allow for increased transparency of practice amongst ophthalmologists, set targets for the reduction of postoperative complications, improvement in practice guidelines and associated cost savings.²⁵

To ensure the highest quality of audit and national data registry, BPOS has commissioned and made available a free, state-of-the-art, web-based electronic patient care summary record for all Pakistani ophthalmologists. The electronic record is designed to promote data collection and is capable of generating robust audits of postoperative complications, visual and refractive outcomes following cataract surgery.

Strength of this study is that it looks at the latest update of cataract surgery practice in Pakistan, focusing primarily on postoperative endophthalmitis prophylaxis. It is a heterogenous survey that covers all four provinces of Pakistan and all types of cataract centres, from recognised teaching units to charity eye camps. In addition, the survey questions were internally validated with senior members of BPOS who were highly aware of the type of practice that may be occurring in Pakistan. Through a collaborative effort between BPOS and the Ophthalmological Society of Pakistan, the major hope is this study aids in defining national standards of cataract practice in Pakistan.

Limitations associated with this study include firstly the sample size, which may just contribute to only a snapshot of ophthalmic practice in Pakistan, and not necessarily reflective of the wider ophthalmic community. Secondly, there is a volunteer bias with respect to survey responses, especially if this survey response were disseminated via a professional society with a limited contact list. Thirdly, this study is not generalisable to other developing nations, which will have factors such as local antibiotic practices and environmental factors impacting the postoperative endophthalmitis rates. Finally, certain questions were identified retrospectively to be poorly worded to deliver on an intended outcome (for example, please specify the 'other regimens' used in your practice) and may have been treated as a repeat question. However, discussion points drawn from these biased questions were limited.

CONCLUSION

The burden of postoperative cataract complications, especially infection, is felt largely in developing nations. Our survey provides an up-to-date view on the state of antibiotic prophylaxis following cataract surgery in Pakistan and highlights several areas for improvement. This includes policy changes to increase adherence to gold standard antibiotic prophylaxis guidelines, improvement in transparency of surgical outcomes and to audit current postoperative outcomes.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board.

Conflict of Interest

Authors declared no conflict of interest.

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Authors' Designation and Contribution

Yarrow Scantling-Birch; Foundation year 2 Doctor: Literature Search, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.

Hassan Naveed; Registrar: Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.

Hira Khan; Clinical Year 3 Student: Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review. Ijaz Sheikh; Consultant Ophthalmologist: Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review. Rashid Zia; Lead Ophthalmologist: Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.

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