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Annals of Ophthalmology and Visual Sciences

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The Ocular Microbiome in Diabetes: A Comprehensive analysis

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Received: Mar 17, 2025

Accepted: Apr 02, 2025

Published Online: Apr 09, 2025

Journal: Annals of Ophthalmology and Visual Sciences

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Abstract

Background: Diabetes may alter conjunctival flora, increasing ocular infection risk.

Aim: To compare conjunctival flora and antibiotic sensitivity in diabetic (with/without retinopathy) and non-diabetic Individuals.

Methods: Samples from 30 type 2 diabetic and 30 non-diabetic patients (≥18 years, no ocular diseases) were cultured on blood and MacConkey agar, with sensitivity tested via Kirby-Bauer method (CLSI 2024). Vision, fundus, and slit-lamp exams were conducted.

Results: Diabetic patients exhibited distinct flora and sensitivity patterns, indicating higher infection susceptibility.

Conclusion: Findings suggest tailored ocular infection management is needed for diabetics.

Keywords: Diabetes mellitus; Conjunctival flora; Antibiotic sensitivity; Diabetic retinopathy; Ocular microbiome; Endophthalmitis; Kirby-bauer method; Type 2 diabetes; Microbial culture; Ocular complications.

Introduction

Diabetes mellitus a chronic disease characterised by abnormal glucose metabolism which results in hyperglycemia. Currently there is increase in cases of diabetes worldwide. Diabetes is associated with many complications such as diabetic foot ulcer, diabetic nephropathy, diabetic neuropathy [1]. Eye complication associated with diabetes includes glaucoma, cataract, and diabetic retinopathy [2].

Conjunctiva is in contact with environment and expose to various microorganisms but healthy conjunctiva has lysozymes, complement, IgA, IgG which removes the organisms [3].

Diabetics are prone to ocular complications due to delayed wound healing of stroma and epithelium, increase in metaplasia and decrease in goblet cells of conjunctiva, alter in immune response of eyes as there is decrease in cellular immunity and cytokine production. Alteration in immune response results in change in microbiome of eyes. This alteration in microbiome increases the chances of endophthalmitis in diabetic patients [4]. Majority of cases of endophthalmitis are due to normal conjuctival flora, including *Coagulase negative staphylococcus spp, Staphylococcus aureus* [5].

Cite this article: Babu B, Riyaz E, Khushboo, Nachiketa, Pundla N, et al. The Ocular Microbiome in Diabetes: A Comprehensive Analysis. Ann Ophthalmol Vis Sci. 2025; 8(1): 1050.

The culture remains gold standard technique for detection microorganism [3]. There are other techniques such as Next generation sequencing [6]. Conjuctival flora of diabetic and non-diabetic individuals varies. Therefore, this study aims to analyze the conjunctival flora and antibiotic sensitivity patterns in diabetic and non-diabetic individuals.

Aim

The study aims to examine the conjunctival flora and antibiotic sensitivity patterns in diabetic patients, with or without diabetic retinopathy, compared to a non-diabetic population.

Material and methods

Study design

Descriptive study.

Place of study

Tertiary healthcare centre in eastern India.

Sample size

This study included a total of 60 participants: 30 patients with type 2 diabetes mellitus and 30 non-diabetic individuals. A detailed history was recorded for all participants, including disease duration for diabetic patients, along with laboratory parameters such as HbA1c, fasting and postprandial blood sugar levels, and Renal Function Tests (RFT). Ocular assessments, including visual acuity using Snellen's chart, a detailed fundus examination using indirect ophthalmoscope and 20D lens, and slit-lamp examination, were performed for all participants.

Inclusion criteria: Patients aged 40 years and older, with or without diabetes mellitus, attending the Ophthalmology Outpatient Department (OPD) were eligible for inclusion.

Exclusion criteria: Pre-existing ocular diseases such as conjunctivitis, blepharitis, nasolacrimal duct obstruction, Contact lens users and on any ocular medications.

Sample collection

Inferior Conjuctival sample collected using sterile swabs after applying local anaesthesia with topical Proparacaine 0.5% w/v. In order to prevent contamination from eyelid margin, eyelashes lower eyelid was pulled down and using sterile cotton swab was swept 5 times over lower conjuctival surface from nasal to temporal side. Sample was sent immediately to microbiology laboratory. Sample was cultured over blood agar and MacConkey agar incubated at 37 degrees Celsius. Plates were examined after 24 hrs and 48 hrs before reporting as culture negative. Any growth obtained were further processed. Organism were identified manually and antibiotic sensitivity were performed manually using the Kirby-Bauer disk diffusion method. For antibiotic sensitivity Clinical Laboratory Standards Institute (CLSI 2024) were followed.

Results

During the study total 120 conjuctival swabs form 60 patients from both the eyes were collected. Age group of diabetic patient ranges from 55-70 years and non-diabetic group 40-70 years. Diabetic patients were further classified based on duration of diabetes as shown in Table 1, based on type of drug taken as shown in Table 2. Gender wise distribution of study population Figure 1.

Table 1: Duration of diabetes.

Duration	Numbers of diabetic population
<5 years	9
5-10 years	5
>10 years	16

Table 2: Treatment taken.

Duration	Numbers of diabetic population
Oral hypoglycaemic drug	24
Insulin	4
Combination	2

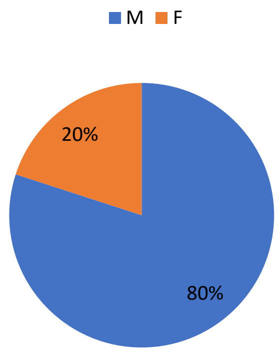

Figure 1: Gender wise distribution of study population.

Gender wise distribution in diabetic and non-diabetic study population as shown in Table 3.

Table 3: Gender wise distribution.

	Male	Female
Diabetic	22	8
Non-Diabetic	26	4

Most common organism isolated was *Coagulase negative staphylococcus* (CONS) in 03 diabetic patients and 01 in non-diabetic population.

Table 4: Organism isolated from study population.

Growth obtained	Non diabetic	Diabetic
Coagulase negative staphylococcus (CONS)	1	3
Staphylococcus aureus (MRSA)		1
Staphylococcus aureus (MSSA)		1
Klebsiella spp		1
>10 years	>10 years	16

Table 5: Association of treatment and organism isolated in diabetic patient.

Organism isolated	Oral hypoglycaemic	Insulin	combination
Coagulase negative staphylococcus (CONS)	2	1	
Staphylococcus aureus (MRSA)		1	
Staphylococcus aureus (MSSA)	1		
Klebsiella spp		1	

Organisms were tested for antimicrobial sensitivity testing. *Coagulase negative staphylococcus* isolated from non-diabetic group was found 100% sensitive to Oxacillin, Erythromycin, Clindamycin, Ampicillin, Ciprofloxacin, Gentamycin, Linezolid, Clarithromycin and Vancomycin.

Coagulase negative staphylococcus isolated from diabetic group 33% was found resistant to Oxacillin, Clindamycin, Erythromycin, ampicillin, clarithromycin.

Staphylococcus aureus isolated from diabetic group was 100% resistant to oxacillin, ampicillin, and clarithromycin.

Klebsiella spp isolated from diabetic group was resistant to Ciprofloxacin, ampisulbactm and sensitive to Piptaz, amikacin, imipenem, gentamycin, amoxicillin-clavulanate, cefexime.

Discussion

This study compared conjunctival flora in diabetic (55-70 years) and non-diabetic (40-70 years) individuals, consistent with Adam et al.'s ranges (38-70 for diabetics, 30-70 for non-diabetics) [5]. Among diabetics, 80% used oral hypoglycemics, 14% insulin, and 6% combination therapy. CoNS was the most common isolate, aligning with Ashtamkar S. et al. and Venkataraman M. et al. [3,7], though Akash Shrivastava et al. found *S. aureus* predominant [8], and Rajeshkannan et al. noted gram-negative organisms [9]. Microbial growth was higher in diabetics (86%) than non-diabetics (14%), supported by Rajeshkannan et al. (68%) [9], Murlidhar CA et al. (62%) [10], and Akash Shrivastava et al. [8]. *Klebsiella spp* in diabetics, also reported by Akash Shrivastava et al. [8], heightens risks of ocular infections like endophthalmitis [11].

Endophthalmitis, a severe intraocular infection, is a significant concern in diabetics due to altered microbiomes and frequent interventions (e.g., intravitreal injections), as noted by Fileta et al. [4]. Diabetic patients are at higher risk post-surgery or injection, with pathogens like CoNS and *S. aureus*—common in our study—implicated in 70-80% of cases [5]. A 2023 study by Chen et al. found diabetic patients had a 2.5-fold higher incidence of postoperative endophthalmitis, linked to hyperglycemia-induced immune dysregulation and resistant flora [17]. Prevention involves strict aseptic techniques, preoperative conjunctival swabs to guide prophylaxis, and glycemic control, though compliance is challenging in diabetics [18]. Management is complicated by poor drug penetration into the avascular vitreous, delayed healing, and multidrug resistance, as seen in our resistant isolates [4,19]. Complications include retinal detachment, phthisis bulbi, and vision loss, with a 2024 study by Sharma et al. reporting worse outcomes in diabetics due to chronic inflammation and biofilm formation by resistant organisms [20].

Surgical complications in diabetic eyes, such as during cataract surgery, are exacerbated by microbiome shifts and poor healing, per Zhang et al. (2023) [12]. Hospital-Acquired Infections (HAIs) are also more common, with Gupta et al. (2024) noting resistant MRSA in diabetic conjunctival flora post-hospitalization [14]. Wound healing is impaired by oxidative stress and inflammation, increasing infection persistence and scarring [15].

Perioperative antibiotic prophylaxis is critical in diabetics. Patel et al. (2024) recommend topical fluoroquinolones (e.g., moxifloxacin) pre- and post-surgery to reduce endophthalmitis risk, though resistance as in our *S. aureus* isolates may necessitate alternatives like vancomycin [16]. A 2023 study by Kim et al. advocates intracameral cefuroxime or moxifloxacin in diabetics, reducing infection rates by 60%, though resistant gram-negative organisms like our *Klebsiella spp* require tailored regimens [21]. Frequent monitoring and culture-guided therapy are essential given resistance trends [19].

Conclusion

Diabetic patients showed higher conjunctival microbial growth and resistance, increasing risks of endophthalmitis, surgical complications, HAIs, and poor healing. Enhanced prevention, including perioperative prophylaxis, and aggressive management are vital to mitigate these threats.

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