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Research Brief

Ocular surface alterations in critically ill patients: An observational study

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***Background and objectives*:** Critically ill patients in intensive care units (ICUs) are vulnerable to ocular surface disorders due to impaired protective mechanisms, mechanical ventilation, sedation, and adverse environmental conditions. This study aimed to evaluate the prevalence and pattern of ocular surface alterations in ICU patients, identify associated risk factors, and determine microbial profiles in infective kerato-conjunctivitis.

Methods: An observational study was conducted on patients admitted in ICU for more than 72 h. Data on demographics, systemic diagnoses, ocular examinations, including Schirmer's test for severity of dry eye, conjunctival swab cultures, and corneal status were collected and analysed.

Results: Of the 280 patients, with mean ICU stay of 12.6 + 5.1 days, 200 (71.4%) had corneal abnormalities. Keratitis/corneal ulcer was most common (n=88, 31.4%), followed by punctate keratopathy (n=58, 20.7%) and corneal erosion (n=54, 19.3%). Lagophthalmos (n=82, 29.3%) and severe dry eye were significantly associated with corneal pathology (P<0.001). Common pathogens included *Klebsiella sp.* and *Staphylococcus* species. Longer ICU stay and higher severity of illness correlated with increased ocular morbidity. Poor GCS scores, dry eye severity, mechanical ventilation, and conjunctival status were also significant contributors.

***Interpretation and conclusions*:** This study documents the high burden of ocular surface disordersin ICU patients and emphasises the need for routine ocular assessments and structured preventive protocols. Integrating simple eye care measures can mitigate visual complications and enhance overall ICU care quality.

Keywords Dry eye syndrome; ICU; Keratitis; Lagophthalmos; Ocular surface disorders

The ocular surface, comprising the cornea, conjunctiva, tear film, eyelids, and associated glands, is a crucial interface between the eye and the external environment, playing a vital role in the maintenance of visual function and ocular health. A stable tear film is essential for corneal transparency, nutrient delivery and microbial defence; and also contributes to protect the eye from desiccation and mechanical damage.[1] Critically ill patients admitted to the intensive care unit (ICU) are particularly susceptible to ocular surface disorders due to a combination of adverse systemic and environmental factors in ICU. This leads to increased risk of conditions like exposure keratopathy, dry eye syndrome, and infections, which can ultimately impair quality of vision and life, in general, post-recovery.[2] Despite growing recognition of ocular surface disorders in ICU settings, these issues remain under-researched, particularly in developing countries such as India.

The integrity of the ocular surface depends on several protective factors, including complete eyelid closure, a functional Bell's phenomenon (the upward movement of the eye during eyelid closure), a healthy blink reflex, and adequate tear production.[3] In ICU settings, these protective mechanisms are frequently compromised. Many critically ill patients are sedated, mechanically ventilated, or receive neuromuscular blockade, leading to the loss of voluntary eyelid closure and a diminished or absent Bell's phenomenon. This results in lagophthalmos, where the eyelids fail to close completely, leaving the cornea exposed for prolonged

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periods. Additionally, the absence of spontaneous blinking prevents the even-spreading of the tear film, which increases tear evaporation and heightens the risk of ocular desiccation and damage.[4] Systemic conditions such as dehydration, low oxygen levels, and medications like sedatives or muscle relaxants further contribute to reduced tear production, ocular surface drying and epithelial damage.[5,6] Environmental factors, including low humidity and air drafts from ventilators in ICUs, exacerbate drying and damage.[4,7] Research indicates that up to 60% of ICU patients may develop ocular surface disorders, with exposure keratopathy affecting 20–40% of those on ventilators.[8] Broad-spectrum antibiotics used in ICUs may disrupt the ocular surface microbiome, making patients more vulnerable to opportunistic infections.[9] This study intends to assess the prevalence, characteristics, and risk factors of ocular surface changes in ICU patients in a tertiary care center in Northern India.

Methods

This observational study was conducted and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure clear and consistent reporting. The study was performed at the department of Ophthalmology and Intensive Care, Sarojini Naidu Medical College, Agra, India, from April 2023 to November 2024. Ethical approval was obtained from the Institutional Ethics Committee and the informed consent was secured from patients or their legal guardians prior to enrolment. Patient confidentiality was strictly maintained, and clinical interventions were provided for significant ocular findings.

Patient recruitment: Eligible participants were patients aged ≥17 yr admitted in ICU for ≥ 72 h. This duration threshold was chosen based on the evidence that ocular surface alterations, such as exposure keratopathy, can manifest within 48–72 h due to sedation, mechanical ventilation and lagophthalmos.[4] Pilot observations in our ICU confirmed early conjunctival congestion and punctate keratopathy within this timeframe, supporting the inclusion of patients with shorter stays to capture early ocular morbidity while accommodating the high patient turnover in our setting. Exclusion criteria included pre-existing ocular conditions, facial trauma, recent ocular surgery, or eyelid abnormalities. Patients were enrolled consecutively *via* purposive sampling, targeting a sample size of 270–300 based on an estimated 20% prevalence of ocular surface alterations (80% power, 5% margin of error).[8,10]

All data were collected by one investigator (VC) on a pre-validated proforma, on the day of enrolment and twice weekly (Monday and Thursday) thereafter until the patient's ICU stay. Available medical records were reviewed for prior ocular history, and family members were consulted when feasible to identify undocumented conditions, especially in comatose and sedated patients.

Data collection: The collected data included demographic details, indication for admission, Glasgow coma scale (GCS) score at admission and ICU severity scores- acute physiology and chronic health evaluation II (APACHE II) and simplified acute physiology score II (SAPS II). Information related to mechanical ventilation, sedation and use of neuromuscular blocking agents, duration of ICU stay (categorised into <10 days and >10 days) and final clinical outcome (discharge/death/referral) was also recorded. Ophthalmic evaluation was conducted using a hand-held slit-lamp (Model PSLAIA-11, Appasamy Associates, Chennai, India) and included: assessment of lagophthalmos (incomplete closure of eyelids) and Bell's phenomenon; conjunctival (congestion, chemosis, discharge) and corneal findings using fluorescein staining under cobalt blue light. Corneal findings were defined as follows: punctate keratopathy (diffuse superficial epithelial staining), corneal erosion (discrete epithelial defects), and keratitis (stromal infiltrates with or without epithelial defects). Schirmer's I test was used to measure tear wetting over 5 min, categorised as normal (>15 mm), moderate (6–14 mm), or severe (<5 mm). Conjunctival or corneal swabs were collected from patients with signs of conjunctivitis or keratitis using sterile cotton swabs. Samples underwent Gram staining, potassium hydroxide (KOH) mount for fungi, and culture on blood agar, MacConkey agar, and Sabouraud's dextrose agar. Microbial isolates were recorded, though antimicrobial susceptibility testing was not conducted due to resource limitations.

Data evaluation: Primary outcomes included the incidence of punctate keratopathy, corneal erosions, keratitis, corneal ulcers, and conjunctivitis. Secondary outcomes assessed correlations between ocular surface alterations and risk factors (*e.g.*, GCS score, ICU stay duration, ventilation, lagophthalmos, Schirmer's test results, ICU severity scores, conjunctival flora). Data were analysed using SPSS version 26. Quantitative variables were reported as mean ± standard deviation,

Table. Baseline characteristics, clinical and ocular profile of ICU patients

Characteristics and profile		ICU patients
Indication for ICU Admission, n (%)	Severe pneumonia	121(43.2)
	Diabetic ketoacidosis	94 (33.6)
	Haemorrhagic stroke	45 (16.1)
	Others	20 (7.1)
Period of stay in ICU	average, days	12.6 ± 5.1
	prolonged stay (>10 days), n (%)	134 (47.9)
GCS score, n (%)	<8 (poor prognosis)	146 (52.1)
	>8 (good prognosis)	134 (47.8)
APACHE II score, n (%)	High risk	109 (38.9)
	Moderate risk	83 (29.6)
	Low risk	55 (19.6)
	Very high risk	33 (11.8)
SAP II Score, n (%)	High risk	142 (50.7)
	Low risk	138 (49.3)
With mechanical ventilation, n (%)		167 (59.6)
Use of neuromuscular blocking agents, n (%)		143 (51.07)
Lagophthalmos, n (%)		82 (29.3)
Conjunctival abnormalities, n (%)	Oedema without congestion	83 (29.6)
	Congestion without discharge	142 (50.7)
	Congestion with discharge (conjunctivitis)	24 (8.6)
Corneal abnormalities, n (%)	Punctate keratopathy	58 (20.7)
	Corneal erosions	54 (19.3)
	Keratitis	88 (31.4)
Schirmer score, n (%)	Very low (Severely deficient tear film)	58 (20.7)
	Moderate (Deficient tear film)	54 (19.3)
Conjunctival Swab, n (%)	Sterile	21 (7.5)
	Bacterial	249 (88.9)
	Fungal	10 (3.6)

GCS, Glasgow Coma Scale; APACHE II, acute physiology and chronic health evaluation II; SAP II, simplified acute physiology II

and categorical variables as frequencies and percentages. Associations between ocular findings and risk factors were assessed using Cochran-Mantel-Haenszel (CMH) tests. Pearson's or Spearman's correlation coefficients evaluated relationships between continuous variables (*e.g.*, ICU stay duration, Schirmer's results). Multivariate logistic regression was performed to identify independent predictors of ocular complications, controlling for confounders such as age, ICU stay duration, and mechanical ventilation. A *P* value <0.05 was considered statistically significant.

Results

A total of 280 patients (119, 42.5 % females), with mean (SD) age of 45.2 (16.8) yr were enrolled in the study. **Table** summarises the baseline characteristics, clinical profile and ocular findings of study patients. Patients with diabetic ketoacidosis (n=94, 33.6%) exhibited the highest prevalence of ocular surface disorders (78.7%, *P*=0.002), followed by pneumonia (45.9% punctate keratopathy, *P*=0.01) and stroke (32.56% erosions, *P*=0.03). About 60% of ocular abnormalities were detected within seven days of ICU admission, emphasising early onset.

Inadequate eye closure or lagophthalmos was observed in about one-thirds of patients while more than two-thirds of the patients (n=200, 71.43%) exhibited keratopathy or corneal involvement. Lagophthalmos was found to be strongly associated with corneal pathology (*P*<0.001, **Fig. 1**); GCS scores <8 had significantly higher (37.67%) keratopathy incidence (*P*=0.003, **Fig. 1**). Longer ICU stays (>10 days) was associated with increased punctate keratopathy (43.3%) and corneal ulcers (22%) compared to shorter stays (*P*<0.001, **Fig. 1**). Higher APACHE II (38.9% high risk) and SAPS II scores were associated with worse corneal outcomes (*P*<0.01). Muscle relaxant use (51.1%) and mechanical ventilation (59.6%) were also found to be significant risk factors for punctate keratopathy (*P*<0.01). Abnormal tear production was also significantly associated with corneal damage (*P*<0.001). Conjunctival swabs identified *Klebsiella* (n=120,42.8%) and *Staphylococcus species* (n=129,46.1%) as predominant pathogens.

The Cramér's V correlation heatmap revealed the strength and direction of associations between categorical variables (**Fig. 2**). Strong positive correlations (Cramér's V ≥ 0.8) were observed between positive conjunctival Swab and mechanical ventilation (0.78). Moderate correlations (0.4 ≤ Cramér's V< 0.8) were noted between several pairs, including lagophthalmos and conjunctival abnormality, and GCS and mechanical Ventilation. Weak correlations (Cramér's V< 0.4) were found in most other variable pairs, such as sex and duration of stay in ICU and APACHE II and GCS score. No cases of permanent

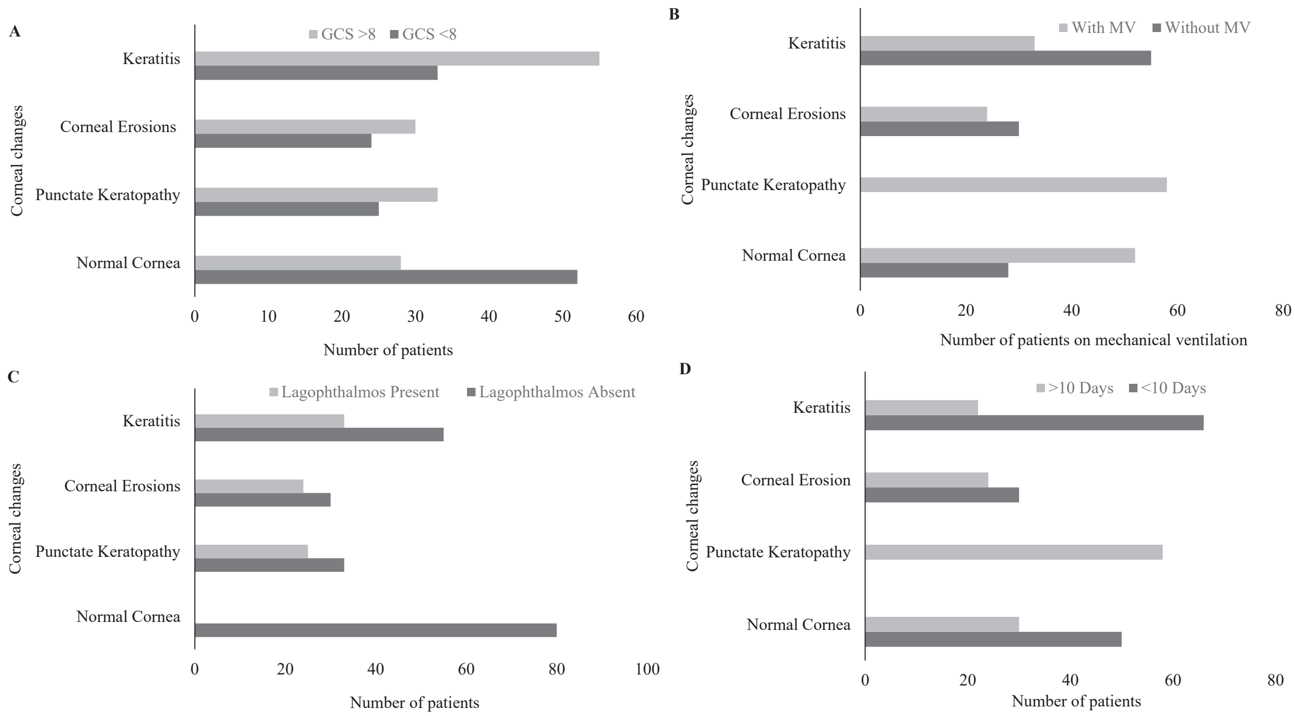

Fig. 1. Graphical representation of corneal changes with respect to various risk factors- GCS Score, mechanical ventilation, lagophthalmos and duration of ICU stay.

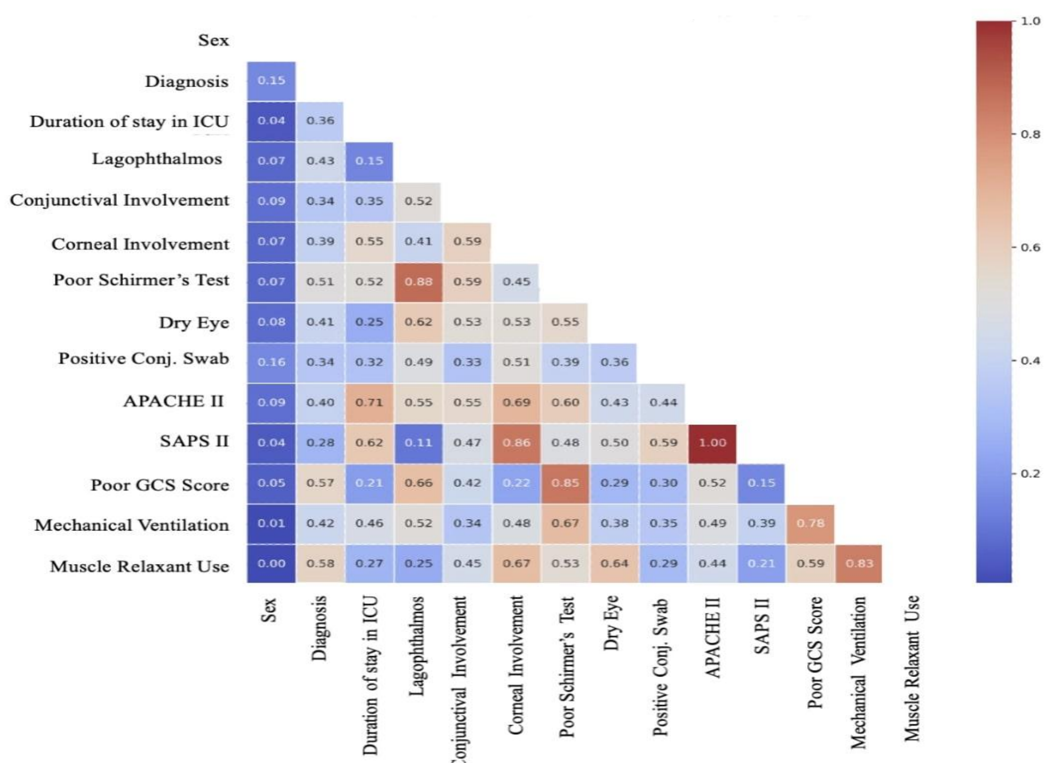

Fig. 2. Cramér's V correlation heatmap depicting strength and direction of associations between categorical variables. Stronger associations are indicated by warmer colours. (*Source*: Generated using R software, version 4.3.1; *https://www.r-project.org/*).

visual loss or corneal perforation were observed during the study period. Temporary tarsorrhaphy was performed in 5 patients (1.79%) with severe exposure keratopathy to prevent further corneal damage, all of whom showed improvement in corneal findings by the end of their ICU stay.

Discussion

This study highlights the significant burden of ocular surface disorders among ICU patients in a tertiary care setting in Northern India. Key risk factors include lagophthalmos, prolonged ICU stays, mechanical ventilator, severity of illness, and abnormal tear production. The predominance of pathogens like *Klebsiella* and *Staphylococcus* species underscores the need for vigilant infection control measures.

This study, conducted in a high-volume ICU, found a 71.4% keratopathy prevalence—exceeding the 5.9-60% range from prior studies—and a 78.7% rate in DKA patients, underscoring systemic illness impacts on tear film deficits.[11,12] Lagophthalmos occurred in 29.3% of patients, aligning with Jammal *et al*[8] observation of lagophthalmos in 31% cases, heightening the risk of exposure keratopathy. If neglected, keratopathy may advance to widespread epithelial erosion, chronic epithelial defects, stromal degradation, vascularisation, squamous metaplasia, and secondary infections, potentially resulting in substantial vision loss.[12] *Klebsiella* dominated isolates, matching Mela's findings, with respiratory secretions during suctioning as a primary infection source.[13] Respiratory secretions are considered the primary source of ocular surface infections, with aerosols generated during tracheal suctioning and direct contact from suction catheters playing significant roles. Suctioning from the trunk side and eye covering may reduce ocular surface infections.[14]

High APACHE II and SAPS II scores indicated illness severity, concurrent with Saritas *et al*.[2] Further, impaired neurological function, as indicated by GCS score of <8 in 52.1% patients was observed to be a strong risk factor for lagophthalmos and tear film instability. Mechanical ventilation and muscle relaxant use were found to be other risk factors along with conjunctival congestion and conjunctivitis as frequently encountered indicators of ocular surface disorder, similar to observations in previous researches.[8,15,16] Our findings on corneal abnormalities align with Chang and Adepoju, who linked corneal ulcers to diabetes, a prevalent comorbidity in our cohort.[17] Age-related tear instability and comorbidities likely explain older patients' vulnerability, while younger patients' resilience to ocular surface disorders. Clinically, these age-related differences suggest that middle-aged and older ICU patients require more intensive ocular monitoring and preventive interventions to mitigate corneal pathology. Younger patients, while less affected, still warrant routine assessments to prevent complications. The color-coded Cramér's V heatmap showed a strong ventilation- positive conjunctival swab link, supporting the need for infection control measures.

This study has several limitations. Single-center design may limit the external validity of the findings. Patient demographics, ICU protocols, and resource availability may differ across other settings, potentially affecting the generalisability of the observed prevalence of ocular surface disorders. Second, the absence of post-discharge follow up restricts our understanding of long-term ocular outcomes. Antibiotic resistance profiles for bacterial isolates were not assessed, being beyond the scope of the study, potentially affecting the generalisability of infection management recommendations.

The study emphasises the critical importance of routine ocular assessments and the implementation of standardised eye care protocols in ICU to enhance patient outcomes and reduce the risk of long-term ocular morbidity. Future research should incorporate multicentre designs, longitudinal follow up post-discharge, multiple investigators to minimise bias, and control groups to better isolate ICU-related risk factors for ocular surface disorders.

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शोध-संदेश

आईसीयू में भर्ती गंभीर रूप से बीमार मरीजों में नेत्र संबंधी विकारों का खतरा अधिक होता है, जिसका मुख्य कारण लैगोफ्थाल्मोस (आंखों का सिकुड़ना), गंभीर शुष्क नेत्र, मैकेनिकल वेंटिलेशन और बीमारी की गंभीरता है। कॉर्नियल जटिलताओं को कम करने और आईसीयू देखभाल की समग्र गुणवत्ता में सुधार के लिए नियमित नेत्र परीक्षण और सरल निवारक नेत्र देखभाल प्रोटोकॉल आवश्यक हैं।

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