Received: 6 March 2023 | Revised: 14 September 2023 | Accepted: 18 September 2023

DOI: 10.1111/nicc.12984

RESEARCH ARTICLE

BACCN Nursing in Critical Care WILEY

# Early detection of ocular lesions in critically ill children: Testing an ocular assessment scale

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## Abstract

**Objective:** There is scarcity of data on the incidence and factors associated with the occurrence of ocular lesions in critically ill children. The objective was to test the applicability and utility of an ocular assessment scale and to identify risk factors of ocular lesions.

**Design:** Prospective observational study.

**Setting:** A tertiary care medical-surgical Paediatric Intensive Care Unit.

**Sample:** 194 children without previous ocular disease who stayed in the Paediatric Intensive Care Unit for more than 48 h.

**Interventions:** An ocular lesions risk scale was designed including risk factors lagophthalmos, eye dryness, conjunctival hyperemia, slow blinking, intubation, sedation, relaxation, face mask and hemodynamic instability. Patients were classified as high-, medium-, and low-risk patients. Corneal lesions were examined by fluorescein staining according to their risk and were confirmed by an ophthalmologist.

**Results:** 76 patients were examined with fluorescein staining. Thirty-two ocular lesions were detected by nursing staff, 26 confirmed by the ophthalmologist. 53.6% of the high-risk patients developed a corneal lesion. Univariate analysis revealed an association between ocular damage and all factors included in the scale, except for face mask. In the multivariate analysis, ocular lesions were associated with lagophthalmos, hyperemia, invasive mechanical ventilation and inotropic support.

**Conclusions:** The scale was useful to detect corneal lesions in critically ill children. The identification of risk factors will enable the development of measures to reduce the incidence of ocular lesions.

**Relevance for Clinical Practice:** A new, non-validated scale allowed staff to detect eye injuries, study this problem and improve future prevention.

KEYWORDS
critically ill children, fluoresceine, intensive care unit, keratopathy, ocular lesion

## 1 | INTRODUCTION

The conjunctiva is a mucous membrane that covers the anterior surface of the eyeball and exerts protection against lesions and infections. Tears lubricate the eye surface and protect it from microbes by washing the eye constantly. The eyelid protects the surface of the eye, and blinking refreshes and spreads the tear film. The orbicularis oculi muscle closes the eyelid and assists in pumping the tears from the eye into the nasolacrimal duct system on blinking. Ocular health depends on the status of the eyelids, tears and conjunctiva. An intact eye surface is the best protection against infection and ocular damage.[1,2] Critically ill patients frequently experience incomplete closure of the eyelid (lagophthalmos), loss of blink reflex and eye dryness, which may result in keratitis and ulcers.[1] Keratitis is an inflammatory or infectious lesion of the cornea that may affect the superficial or deep chambers and predisposes to corneal infection.[1] Infectious lesions may cause temporary or chronic visual damage, depending on the severity of the lesion.[1,3]

The incidence of ocular surface lesions in intensive care units (ICU) ranges between 10 and 60%.[4,5] However, this event has been scarcely studied in patients in the paediatric intensive care units (PICU). Angela Niemi et al[5] report an incidence of ocular lesions in the PICU of 32.2%, which was reduced to 8.6% after an ocular care protocol was implemented. The main factors associated with ocular damage in the ICU include invasive mechanical ventilation (IMV) with PEEP ≥ 5; lagofthalmos; slow blinking; intravenous sedation; muscle relaxants; altered consciousness; sepsis; vascular diseases; neurological disorders and immunosuppression; situations of multi-organ failure and prolonged stay in the ICU.[1–9] Ocular lesions are also related to low air humidity; oxygen therapy; prone position; non-invasive ventilation (NIMV) with face or oronasal interfaces as a result of the pressure exerted on the face; corticosteroid and immunosuppression therapy; and aspiration of secretions through an open technique as a result of eye surface contamination by microdroplets.[1,2,6,7,9]

Prevention and early detection are essential to avoid the development of these lesions. It is important that risk assessment is performed and ICU staff receive training for the adoption of preventive measures based on eye lubrication and protection.[1,3,8,9] The most effective diagnostic method for the detection of corneal lesions is fluorescein staining.[3] According to several studies, eye examination can be performed by trained ICU staff, including the nursing staff, who will refer the case to the Ophthalmology Department when an ocular lesion is detected.[10,11]

Currently, there is no tool to evaluate the risk of ocular lesions in PICU. The objective of this study was to test the utility and applicability of an ocular damage risk assessment scale for critically ill children. The secondary objective was to identify risk factors of ocular lesions.

### What is known about the topic

- The incidence of ocular lesions in ICU ranges between 10 and 60%, according to the type of ICU and the preventive protocols.
- Serious eye damages can appear with poor preventive treatment.
- The main factors related to ocular lesions in PICU are mechanical ventilation, lagophtalmos, dry eye, sedation and muscle relaxation.
- There is no tool to evaluate the risk of ocular lesions.
- The most effective diagnostic method for the detection corneal lesions is fluoresceine staining.

### What this paper adds

- This is the first study to assess the incidence of ocular lesions related to risk factors in PICU and test a risk assessment scale.
- The risk assessment scale and fluoresceine staining by trained nurses enables early detection of corneal lesions in PICU.
- We showed the important role of nurses for the early detection and treatment of ocular lesions in PICU.

## 2 | MATERIALS AND METHODS

An observational, prospective, descriptive, two-stage study was performed. During the first stage, which results have already been published, eight paediatric intensive care and ophthalmology specialists designed a scale for assessing the risk of developing ocular lesions in the PICU based on a literature review and consensus.[12]

The second phase was aimed to test the applicability and utility of the ocular lesions risk assessment scale for PICU patients and to identify the most relevant risk factors.

This second phase was developed between January 2021 and February 2022 in the PICU of a tertiary hospital. The study was approved by the local Ethics Committee and the hospital management board (reference 25/2020, on November 24th 2020).

Required sample size was estimated using Granmo Online Sample Size and Power Calculator (version 7.12), Municipal Medical Research Institute Barcelona (https://www.imim.es/ofertadeserveis/software-public/granmo/). Estimated proportion of patients affected by the variable of interest (presence of ocular lesions in paediatric critically ill patients) was set at 20% according to previous publications and Alpha and Betha risks were set at .05 and .2 in a two-sided

test. Estimating a 10% dropout rate, a sample size of 150 patients was defined as capable of detecting a 10% difference in the incidence of ocular lesions.

The detection of a corneal lesion through fluorescein staining by the nursing staff was defined as the dependent variable.

Inclusion criteria were: children with ages from 1 month to 17 years, without previous eye disease or treatment, with PICU stay longer than two days or a stay longer than 15 days with a change, with informed consent signed by the parents or legal guardians.

Exclusion criteria were: previous ocular disease and parent's refusal to take part in the study.

Data collection was performed during a 15 days period although the follow-up of eye status was performed until discharge or death. Irrespective of its risk any change in conjunctiva or tear was recorded.

The sample was composed of patients transferred from the operating room, paediatrics ward, emergency room, neonatal ICU or patients with a stay longer than 15 days in PICU who changed their clinical situation and had a higher risk in the assessment ocular scale. Patients from the neonatal ICU and patients who were re-included because of a change in their risk were included after a negative fluorescein stain test result on admission.

The principal investigator (B.V) was trained by an ophthalmologist in the detection of ocular lesions using the fluorescein staining test. The training included a 20-min theoretical explanation and was supervised the first assessment performed. In turn, the principal investigator trained the PICU nursing staff in the completion of the ocular assessment scale, the current eye protocol and the identification of eye injuries using the fluorescein stain test. The nursing research team was the only one to assess the patients' lesions with this technique. If a lesion was found, the ophthalmologist was in charge of making the diagnosis and confirming the lesion. Ophthalmologist examined the patients with an indirect ophthalmoscope. Patients with ocular lesions were followed by ophthalmologist until healing.

Every day, the nurse in charge of each patient applied the risk assessment scale at the end of their shift (at about 2 pm, 9 pm, 7 am). Using this scale, patients were classified as low, medium or high risk based on the score obtained (Figure 1). The presence of each factor scored 1 point on the scale, except for occlusion grade III, which scored 2 points. A final score of 0–1 points indicated a low risk of developing eye lesions; a score of 2–3 corresponded to medium risk, whereas a score >3 indicated high risk. Fluorescein staining was indicated when the patient maintained high risk for more than 24 h or medium risk for 72 h. Some low-risk patients who were considered to be able to cooperate with the fluorescein staining procedure were also explored to confirm the absence of ocular lesions.

Other risk factors that were not included in the scale but were identified in the literature were also recorded by the research team

| DAY | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SHIFT | M | A | N | M | A | N | M | A | N | M | A | N | M | A | N | M | A | N | M | A | N | |
| **1. Grade II occlusion[1]**  | | | | | | | | | | | | | | | | | | | | | | |
| **2. Grade III occlusion[2]**  | | | | | | | | | | | | | | | | | | | | | | |
| **3. Dry eye** (not wet) | | | | | | | | | | | | | | | | | | | | | | |
| **4. Conjunctival hyperemia[3]** | | | | | | | | | | | | | | | | | | | | | | |
| **5. Intubation** | | | | | | | | | | | | | | | | | | | | | | |
| **6. Face mask** | | | | | | | | | | | | | | | | | | | | | | |
| **7. Intravenous sedation** | | | | | | | | | | | | | | | | | | | | | | |
| **8. Intravenous relaxation** | | | | | | | | | | | | | | | | | | | | | | |
| **9. Slow blinking[4]** | | | | | | | | | | | | | | | | | | | | | | |
| **10. Hemodynamic instability[5]** | | | | | | | | | | | | | | | | | | | | | | |
| **RISK ASSESSMENT:** **// CHANGE TO RISK:** **day:** Each factor scores 1, except for occlusion grade III (2 points). Low risk: 0-1 points. Medium risk: 2-3. High risk>3. | | | | | | | | | | | | | | | | | | | | | | |

[1] Less than a third of the eyeball remained exposed
[2] More than a third of the eyeball remained exposed
[3] Hyperemia occupy at least 30% of the surface of the eye
[4] Less than 5 blinks per minute (absence of blink for 12 seconds).
[5] Continuous perfusion of adrenaline, noradrenaline or dopamine at a dose >5mcg/kg/min or ECMO.

**FIGURE 1** Ocular lesions risk assessment scale in paediatricpediatric intensive care units (PICU).

based on the information arising from the medical history, including the following: age; sex; diagnosis; other respiratory support (oxygen therapy through a nasal cannula; high flow; NIMV with nasal cannula or tracheostomy); sedation score on the Richmond Agitation Sedation Scale (RASS)[13]; type of aspiration drain (open/closed); high number and dose of inotropic agents (adrenaline or noradrenaline ≥0.15 mcg/kg/min and dopamine >5 mcg/kg/h); ventricular assistance; treatment with corticosteroids for longer than 5 days; administration of immunosuppressants; prone position and days of PICU stay.

The standard ocular lesions prevention protocol applied to all PICU patients involved palpebral irrigation with saline and sterile pads, and lubrication with gel tears in patients with lagophthalmos, hyperemia, IMV, intravenous sedation, or muscle relaxation. In the presence of lagophthalmos, eyes were covered with non-adhesive hydrogel or tape.

All statistical analyses were performed using the SPSS package version 25 (SPSS Inc, Armonk, NY, EE.UU.). Discrete variables were expressed as frequencies and percentages. Distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Results for continuous variables were expressed as mean and standard deviation or as median and interquartile range, depending on normality of distribution. Chi-squared test ($\chi^2$) was used for comparison of categorical variables. Comparison of continuous variables was performed using Student's *t*-test for normally distributed variables or when the number of subjects was >30, and with Mann Whitney *U*-test when these criteria were not met. Univariate analysis was performed to analyse factors related to the presence of ocular lesions. Then, multivariate analysis was performed using a multivariate logistic regression model. Variables were selected through stepwise regression analysis by minimizing the Akaike information criteria (AIC).

A ROC curve was built to estimate the predictive value of the risk assessment scale to detect ocular lesions. A *p* value <.05 was considered statistically significant.

## 3 | RESULTS

The initial sample was composed of 201 patients, 123 male and 78 female, with a median age of 1.5 years and an interquartile range of (0.3–7.6 years). PICU admission was as a result of a medical problem in 58% of patients and surgery in 42%. The conditions that led to hospitalization were heart disease in 44% of cases, respiratory 36% and neurological, infectious, metabolic and hemato-oncological in 20% of cases.

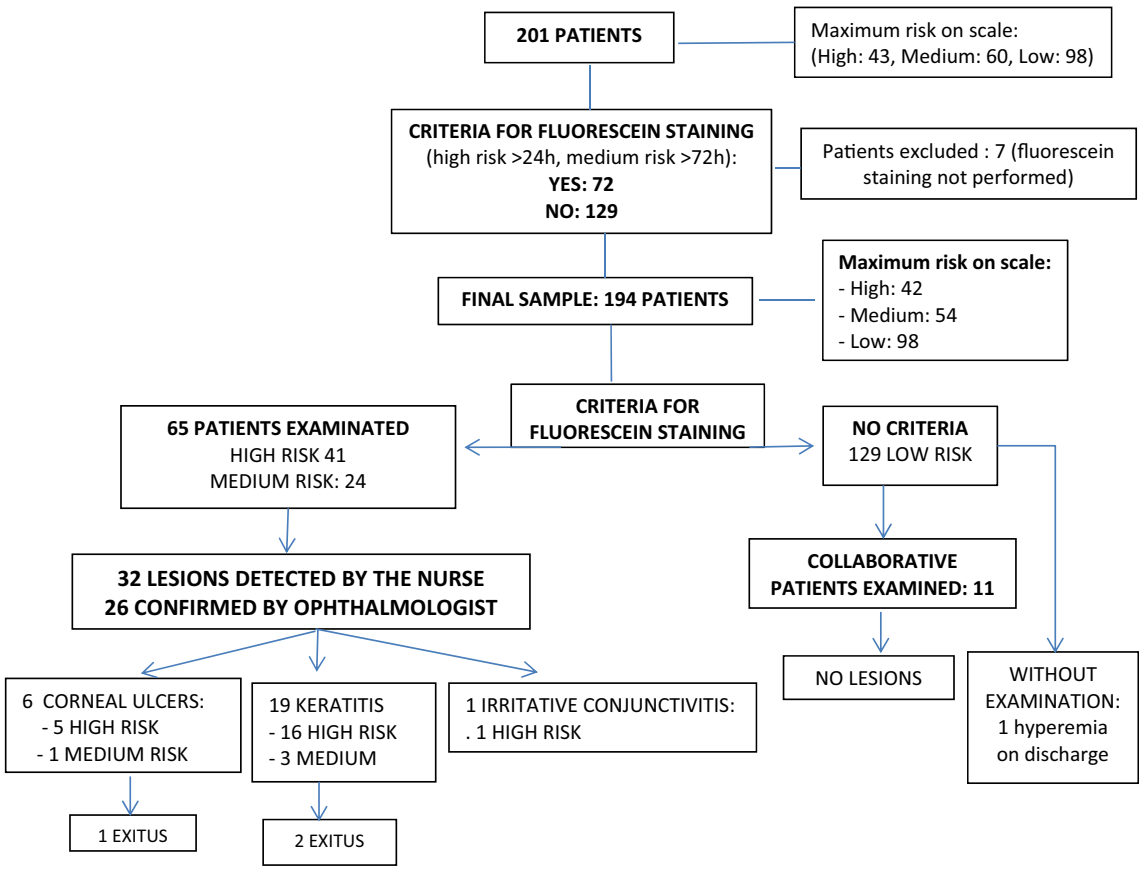


**FIGURE 2** Flowchart of the study.

### 3.1 | Incidence of ocular lesions and evolution

Figure 2 shows the flowchart of the study and the evolution of patients.

Of the 201 patients, in seven cases that were indicated to explore it could not be carried out as a result of organizational problems and work overload, and were excluded from risk factors analysis. So the final sample was 194. A total of 76 patients were evaluated with fluorescein (41 high risk, 24 medium risk and 11 low risk). Eleven low-risk patients who were considered to be able to cooperate with the fluorescein staining procedure were explored and no lesion was observed in these patients. Of the 65 patients with medium or high risk that were explored (41 with a high risk of more than 24 h and 24 with a medium risk of more than 72 h), 32 (49.2%) showed abnormalities after a nurse exploration. In 26 patients (40%) ocular lesions were confirmed by the ophthalmologist (53.6% of the high-risk patients and 12.5% of the medium-risk patients). Ocular lesions appeared at an average of 5.7 days (DS 3.6). There were six cases of corneal ulcer (five patients with high risk and one with medium risk), one irritative conjunctivitis (high risk) and 19 keratitis (three medium risk and 16 high risk).

The nursing staff suspected ocular lesions in 32 patients. Ophthalmologists confirmed the existence of eye lesions in 26 patients (81.2% of lesions detected by the nursing staff ).

Three patients with ocular lesions died (one with an ulcer and two with keratitis). The remainder of patients with an ocular lesion had a good course and all were discharged from the PICU without any ocular lesion or with a good course of the ulcer.

### 3.2 | Risk ocular factors

The frequency of ocular lesion risk factors is shown in Table 1. The factors associated with ocular lesions with statistical significance on univariate analysis are shown in Table 2.

In the patients with lagophtalmos, 72.7% with grade III and 37.2% of patients with grade II developed an ocular lesion. Lagophtalmos (grade II and grade III) was associated with eye dryness ($p < .01$).

Duration of lagophtalmos, dry eye, hyperemia, slow blinking, inotropic support, sedation, maximum and medium risk on the risk assessment scale, and a mean score on the RASS scale were higher in patients with ocular lesions than in patients without them (Online Annex 1). There was no statistically significant relationship between ocular lesions and the duration of IMV.

The factors found to be statistically significant in univariate analysis were included in multivariate analysis. Only IMV, inotropic support, lagophtalmos and hyperemia were independently associated with ocular lesions (Table 3).

Lagophtalmos was independently associated with the use of sedation OR 5.4 ($p < .01$) and muscle relaxants OR 9.2 ($p < .01$). The administration of inotropics reached statistical significance on multivariate analysis, whereas inotropics at high doses and number of inotropics for at least two consecutive days were not found to be statistically significant ($p$ .8, OR 0.8 and $p$ .7, OR 1.4, respectively).

Eye dryness, intravenous sedation, muscle relaxation, slow blinking, extracorporeal membrane oxygenation (ECMO) and prone

**TABLE 1** Incidence of risk factors according to the maximum assessed risk.

| | | Maximum risk in the assessment scale | | |
|---|---|---|---|---|
| Risk factors | Total | Low risk | Medium risk | High risk |
| Lagophthalmos | 54/194 (27.8%) | 5/98 (5.1%) | 14/54 (25.9%) | 35/42 (83.3%) |
| Eye dryness | 16/194 (8.2%) | 0/98 (0%) | 0/54 (0%) | 16/42 (38%) |
| Conjunctival hyperemia | 31/194 (16%) | 3/98 (3.1%) | 3/54 (5.6%) | 25/42 (59.5%) |
| Slow blinking | 29/194 (14.9%) | 4/98 (4.1%) | 12/54 (22.2%) | 13/42 (31%) |
| NIMV[a] | 87/194 (44.8%) | 46/98 (46.9%) | 24/54 (44.4%) | 17/42 (40.5%) |
| Face mask | 56/194 (29.4%) | 29/98 (29.6%) | 15/54 (27.7%) | 12/42 (28.6%) |
| Nasal cannulae | 75/194 (38.7%) | 43/98 (43.9%) | 20/54 (37%) | 12/42 (28.6%) |
| Tracheostomy | 11/194 (5.7%) | 2/98 (2%) | 7/54 (13%) | 2/42 (4.8%) |
| IMV | 85/194 (43.3%) | 5/98 (5.1%) | 39/54 (72.2%) | 41/42 (97.6%) |
| Intubation | 74/194 (38.1%) | 2/98 (2%) | 33/54 (61.1%) | 39/42 (92.9%) |
| Tracheostomy with IMV | 11/194 (5.7%) | 2/98 (2%) | 7/54 (13%) | 2/42 (4.8%) |
| Intravenous sedation | 106/194 (54.6%) | 17/98 (17.3%) | 47/54 (87%) | 42/42 (100%) |
| Intravenous relaxation | 18/194 (9.3%) | 0/98 (0%) | 0/54 (0%) | 18/42 (42.9%) |
| Prone position | 8/194 (4.1%) | 0/98 (0%) | 1/54 (1.9%) | 7/42 (16.7%) |
| Inotropics[b] | 61/194 (31.4%) | 6/98 (6.1%) | 21/54 (38.9%) | 34/42 (81%) |
| ECMO | 8/194 (4.1%) | 0/98 (0%) | 1/54 (1.9%) | 7/42 (16.7%) |
| Ventricular assistance | 1/194 (0.5%) | 0/98 (0%) | 0/54 (0%) | 1/42 (2.3%) |
| Immunosuppressants | 15/194 (7.7%) | 2/98 (2%) | 5/54 (9.3%) | 8/42 (19%) |
| Corticosteroids >5 days | 22/194 (11.3%) | 4/98 (4.1%) | 5/54 (9.3%) | 13/42 (31%) |

[a]Several patients used different non-invasive ventilation interfaces (NIMV).
[b]Perfusion of dopamine >5 mcg/kg/h, adrenaline and/or noradrenaline.

**TABLE 2** Risk factors and corneal lesions detected by the nursing staff.

| | Factors | Total | With lesions | Percentage of pacients with lesions with this factor | Percentage of pacients with lesions without this factor | Increased risk | *p* |
|---|---|---|---|---|---|---|---|
| Factors included in the scale | Lagophthalmos | 54 | 24 | 44.4% | 5.7% | OR 13.2 (5.4–32.2) | <.01 |
| | Grade II | 43 | 16 | 37.2% | 10.6% | OR 5 (2.2–11.2) | <.01 |
| | Grade III | 11 | 8 | 72.7% | 13.1% | OR 17.6 (4.4–71.2) | <.01 |
| | Eye dryness | 16 | 12 | 75% | 11.2% | OR 23.7 (6.9–80.5) | <.01 |
| | Conjunctival hyperemia | 31 | 18 | 58% | 8.6% | OR 14.7 (6–36.2) | <.01 |
| | Slow blinking | 29 | 12 | 41.3% | 12.1% | OR 5.1 (2.1–12.7) | <.01 |
| | Sedation | 106 | 31 | 29.2% | 1.1% | OR 36 (4.8–269.7) | <.01 |
| | Muscle relaxation | 18 | 12 | 66.6% | 11.3% | OR 15.6 (5.2–46.1) | <.01 |
| | Intubation | 74 | 26 | 35.1% | 5% | OR 10.3 (4–26.6) | <.01 |
| | Inotropic support | 61 | 25 | 41% | 5.2% | OR 12.5 (5–31.2) | <.01 |
| | ECMO | 8 | 5 | 62.5% | 14.5% | OR 9.8 (2.2–43.5) | <.01 |
| | NIMV with face mask | 56 | 5 | 9% | 19.5% | OR 0.4 (0.14–1.1) | .07 |
| Factors not included in the scale | Prone position | 8 | 4 | 50% | 15% | OR 5.6 (1.3–23.9) | <.01 |
| | Global IMV[a] | 85 | 30 | 35.3% | 1.8% | OR 29.18 (6.7–126.6) | <.01 |
| | >1 Intropic >2 consecutive days | 12 | 7 | 58.3% | 13.7% | OR 8.8 (2.5–29.8) | <.001 |
| | Inotropics at high doses[b] >2 consecutive days | 17 | 9 | 53% | 13% | OR 7.5 (2.6–21.5) | <.01 |
| | Tracheostomy | 11 | 4 | 36.3% | 15.3% | OR 3.1 (0.8–11.5) | .07 |
| | Global NIMV[c] | 87 | 9 | 10.3% | 21.5% | OR 0.42 (0.18–0.96) | .04 |
| | NIMV with nasal cannulae | 75 | 5 | 6.6% | 22.7% | OR 0.24 (0.1–0.6) | <.01 |

Abbreviations: IMV, Invasive mechanical ventilation; NIMV, Non-invasive mechanical ventilation.
[a]Global IMV includes intubation and tracheostomy.
[b]High doses: adrenaline or noradrenaline > or equal to 0.15 mcg/kg/min or dopamine >10 mcg/kg/h.
[c]Global NIMV includes all interfaces (face mask, nasal cannulae and oronasal mask).

**TABLE 3** Multivariate analysis of factors associated with ocular lesions.

| Variable | OR[a] | 95% CI[b] | *p* |
|---|---|---|---|
| Invasive mechanical ventilation | 6.316 | 1.18–33.63 | .031 |
| Inotropic support | 3.446 | 1.09–10.84 | .034 |
| Lagophthalmos | 4.714 | 1.64–13.49 | .004 |
| Conjunctival hyperemia | 3.805 | 1.28–11.26 | .016 |

[a]OR, Odds Ratio.
[b]CI, Confidence interval.

position were not associated with ocular lesions on multivariate logistic regression analysis.

### 3.3 | Predictive value of risk assessment scale

The predictive value of the risk assessment scale was estimated on a ROC curve (Online Annex 2). All patients included in the low-risk group were considered to be free of ocular lesions. The area under the curve was 0.91 (95%CI: 0.87–0.96), $p < .01$. When sensitivity and specificity were optimized, the optimal cut-off to detect corneal lesions was three (sensitivity 87%, specificity 78%). For a cut-off point of two, sensitivity was 100% and specificity 60%.

## 4 | DISCUSSION

To the best of our knowledge, this is the first study to test the utility of the systematic application of a previously designed risk assessment scale to help in the early detection of ocular lesion in PICU. We have not found any studies in the literature that systematically screen all patients with fluorescein and identify all the influential risk factors. In low-risk patients who did not undergo this examination, we monitored the condition of the eye by assessing the state of the conjunctiva and visible tears in the eye. With the development of this risk assessment scale, we have proven its usefulness in daily practice to detect possible eye damage in the early stages at-risk critically ill children so that

they can receive ophthalmological treatment as early as possible and thus avoid serious sequelae on discharge. Besides, we have studied the possible influencing factors that coincide with those found in the literature. A good eye care protocol is useful in prevention and improves the incidence, but there are patients who will still develop eye damage. This is why we believe that a risk assessment tool in conjunction with routine fluorescein screening could be helpful.

## 4.1 | Incidence and evolution of ocular lesions

The incidence of ocular lesions in critically ill adult patients ranges between 10 and 60%, according to the type of ICU and severity of cases.[4,5] Niemi et al in the largest paediatric study available, found a baseline incidence of ocular lesions of 32.2% and it decreased to 8.6% after the implementation of an eye care protocol in patients with mechanical ventilation in the PICU.[5] In our study, the incidence was similar to Niemi study implementing an eye damage prevention protocol, (16.5% detected by the nursing staff and 13.4% confirmed by Ophthalmologist), which demonstrates that ocular lesions are frequent in critically ill children.

When the presence of an ocular lesion was confirmed, early management contributed to the good course of lesions. Of the 26 lesions, six were ulcers (23%). Colonization was not confirmed in any case, and all had a good course, except for a patient who died and developed bilateral severe ulcers that persisted for several weeks. Complications are more frequent and response to therapy is slower when an ocular lesion is detected in an advanced stage as a result of failure to provide regular monitoring and early treatment. Inflammation rapidly progresses to de-epithelialization with the risk of colonization and the development of permanent sequelae.[1,2]

## 4.2 | Usefulness of risk assessment scale

There are no previous studies available assessing the usefulness of an eye damage risk assessment scale in critically ill children. The risk assessment scale was useful for us to detect corneal abnormalities. Forty percent of patients with high or medium risk showed ocular lesions confirmed by the ophthalmologist (53.6% of the high risk and 12.5% in the medium risk). The sensitivity of the risk scale could not be determined, since not all patients underwent eye examination. It is necessary that the validity of this risk assessment scale be confirmed in other populations of critically ill patients and increase the sample of low-risk patients screened. The optimal cut-off point (the highest sensitivity and specificity) for our risk scale was three.

## 4.3 | Role of the nursing staff in prevention and early diagnosis

The most effective diagnostic method for the detection of corneal lesions in critical care units is evaluation with fluorescein staining.[3] Specific training in this technique is essential to detect corneal lesions. Ophthalmologists confirmed 81.2% of lesions detected by the nurse staff. Our results suggest that trained nurses are able to detect relevant corneal lesions. However, although a high number of lesions were detected by nurses, some early-stage lesions may not have been identified. Further examination by the ophthalmologists will be always needed to make the appropriate detailed diagnosis and establish specific treatment. Early ocular lesions identification by nurses can facilitate the implementation of measures to prevent lesion progression and improve ophthalmic care protocols.

## 4.4 | Risk factors

Univariate analysis showed a significant association between ocular lesions and all the factors included in the risk assessment scale, except for the use of NIMV with a face mask ($p = .09$). Multivariate analysis showed a statistical relationship between ocular lesions and lagophthalmos, hyperemia, IMV and inotropic support.

### 4.4.1 | Lagophthalmos

The surface area exposed was relevant. A total of 72.7% of patients with occlusion grade III developed exposure keratopathy. Sedation and intravenous relaxation were associated with the occurrence of lagophthalmos.

### 4.4.2 | Hyperemia

There was a statistically significant relationship between hyperemia and ocular lesions, but we did not evaluate the grade of hyperemia.

### 4.4.3 | Inotropic support

Multivariate analysis revealed that the administration of inotropics was associated with ocular lesions, thereby indirectly reflecting abnormal ocular perfusion. However, no association was observed with the dose or number of inotropics. Further studies are necessary to determine the influence of hemodynamic factors (blood pressure, tissue perfusion) on the development of ocular lesions.

### 4.4.4 | Mechanical ventilation

In our study, consistent with previous studies, we found a strong relationship between ocular lesions and IMV.[1–8] With respect to tracheostomy, it was not found to be statistically related to ocular lesions ($p = .068$), maybe as a result of the small sample of patients who underwent this procedure (5%). Of note, as

compared to adult patients, tracheostomy is delayed in paediatric patients to a stage where the patient needs light sedation and is in the ventilation weaning process. This fact may have influenced our results.

### 4.4.5 | Other factors

Although tear quality is generally good in children[14] and scoring of eye dryness was subjective, univariate analysis revealed a statistically significant relationship between eye dryness and ocular lesions. Notably, this association disappeared on multivariate analysis, probably as a result of its relationship with lagophthalmos.

It is difficult to assess slow blinking in children under light-moderate sedation since the number of blinks varies as a result of frequent changes in sleep-wakefulness status over the day. In our study, we observed a lower number of blinks in infants as compared to older children, which is consistent with the findings of Marcelo in newborns and infants.[15] This factor was also significant in univariate analysis, but not in multivariate analysis.

The level of sedation as assessed on the RASS scale was higher in children with ocular lesion, although mean level was low in the two groups. The duration of sedation and intravenous muscle relaxation were related to corneal lesions on univariate analysis, which is in line with previous studies.[1–8] However, multivariate analysis did not show a significant relationship between sedation and relaxation and ocular lesions. This may be explained by the fact that these factors are directly related to IMV or lagophthalmos, which are two of the main factors.

Facial and oronasal interfaces in NIMV may alter venous return and increase ocular congestion as a result of direct pressure on the face. In addition, the face mask directs air onto the face, which may increase eye dryness. In our study, NIMV and this interface were not found to be associated with ocular lesion on univariate analysis. Air humidification and heating may also reduce the risk of eye damage.

Moreover, the development of ocular lesions is not only influenced by the presence of risk factors but also by the duration of exposure to risk factors (Online Annex 1).

## 4.5 | Limitations

According to the study design in which not all patients were examined using fluorescein staining and negative results were not confirmed by an ophthalmologist we cannot accurately establish the incidence of ocular lesions in critically ill children. Evaluation of the predictive value and the reliability of the risk assessment scale is not possible for the same reason. However, we believe that in children with low risk, it may not be justified to perform a test that is somewhat bothersome for them if they do not present suggestive symptoms to have an ocular lesion or enough risk factors to explore. Fluorescein staining is challenging in PICU patients as a result of the patient's lack of cooperation, and it could only be performed in sedated or cooperative low-risk patients.

In our opinion, the probability that low-risk patients develop ocular lesions is very low. This fact is supported by the absence of lesions in the low-risk patients examined and the good eye status during follow-up in all low-risk patients.

Sample size calculation was performed using data from previously published incidences of ocular lesions among critically ill paediatric patients, however, these data are not divided into groups of patients with different risks. To properly determine the necessary sample size, it would have been useful to carry out a preliminary evaluation. This preliminary evaluation would be aimed at determining the incidence of ocular lesions in patients of different risk including the systematic evaluation by ophthalmologists.

Statistical power of our study was not established. The incidence of ocular lesions should have been estimated for the different risk groups and then these groups should have been equally tested. Although we believe that this scale may be useful since a significant percentage of high-risk patients had a lesion and received early ophthalmologic care, methodologically this study is not adequately powered. Further studies with a more stringent methodology are needed to validate this risk scale in the future.

As above mentioned, only patients with positive fluorescein staining tests were explored by the ophthalmologists. This fact supposes that global agreement between nursing staff and ophthalmologist could not be accurately calculated as patients with negative tests were not evaluated by ophtalmologists and thus small percentage of ocular lesions may have remained undiagnosed.

Work overload in the PICU often hindered the performance of the fluoresceine staining test when indicated, and some patients had to be excluded from the analysis.

Additionally, the use of a preventive protocol may have reduced the actual incidence and severity of ocular lesions. Nevertheless, there was a high incidence of ocular lesions that were similar to that reported in the other paediatric study after the implementation of a prevention protocol.[5]

With respect to the six cases of ocular lesions detected by the trained nurses that were not confirmed by the ophthalmologist, increased hydration applied after the lesion was detected may have caused mild lesions to disappear, since examination by an ophthalmologist was not performed on the same day as fluoresceine staining.

Finally, it was difficult to assess some parameters, such as slow blinking and lagophthalmos, since they change over the day.

# 5 | CONCLUSIONS

The risk assessment scale and fluoresceine staining by trained nurses enable early detection of corneal lesions in critically ill children. The results of this study suggest that the nursing staff can play a crucial role in the prevention and early diagnosis of ocular lesions in critically ill children. The risk factors detected may improve preventive measures to avoid ocular lesions in PICU patients.

## ACKNOWLEDGEMENTS

Thanks to all PICU professionals especially to the nursing staff, to the Ophthalmology Department and the Biostatistics Department of the Gregorio Marañón General University Hospital for their support.

## FUNDING INFORMATION

This project was supported by the Gregorio Marañón Health Research Institute in the 2020 intramural call with code II-INT-ENF-2020. The funders had no part in the study design, conduct or data analysis and did not have any authority over these activities.

## CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available as a result of privacy or ethical restrictions.

## ETHICS STATEMENT

The study was approved by the local Ethics Committee and the hospital management board (reference 25/2020, on November 24th 2020).

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Vilchez B, Manzanal I, Marcos M, et al. Early detection of ocular lesions in critically ill children: Testing an ocular assessment scale. *Nurs Crit Care*. 2023;1-9. doi:10.1111/nicc.12984