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# Evaluation and Management of Ocular Chemical Injuries with their Visual Outcomes

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**Abstract:** ***Ocular chemical Injury comprises about 8-18% of overall ocular trauma. It is caused by acids and alkalis. Acids cause comparatively lesser severity of burns than alkalis because acids denature the proteins and form a protective layer over the ocular surface. Whereas alkalis penetrate deep and cause severe injury. People of all age group and either gender can be affected, but it is more common in age group of 20-40 years. Ocular chemical injury is the true ocular emergency and requires immediate intervention. It can cause a significant visual impairment in younger economically productive age group. Hence, it is necessary to evaluate the damages caused by it with optimal intervention to restore vision. This study enables the analysis of current management of ocular chemical injury and its effect on the visual outcomes of the patients.***

**Keywords**: ocular, chemical injury, acids, alkalis

## 1.Introduction

Ocular chemical Injury comprises about 8-18% of overall ocular trauma.[1] It is caused by;

1) Acids
2) Alkalis

Acids cause comparatively lesser severity of burns than alkalis because acids denature the proteins and form a protective layer over the ocular surface. Examples are- Sulfuric acid, Acetic Acid, Hydrochloric acid, Sulphurous acid, Hydrofluoric acid. Alkalis penetrate deep and cause severe injury. Hydroxyl (OH) ion causes saponification of the cell membrane constituents which results in cell disruption and cell death and the cation are responsible for the penetration process of respective alkali. Examples- Lime particles, colors used during Indian festivals Ocular chemical injuries produce extensive damage to the ocular surface epithelium, conjunctiva, cornea, and limbal stem cells which results in diminution of vision. Emergency management early and aggressive treatment with close long-term monitoring is the single most important factor in determining the visual outcome.

The severity of chemical injury depends on;

1) Nature of chemical agent
2) Duration of exposure
3) Area of the affected ocular surface

Ocular chemical injuries are classified according to the area of involvement and severity of the ischemia by following classifications.

1) Ropper Hall Classification

**Table 1**

| Grade | Visual Prognosis | Appearance of Cornea | Limbal Ischemia |
|---|---|---|---|
| I | Good | Epithelial Damage | None |
| II | Good | Haze but iris visible | <1/3 |
| II | Guarded | Total epithelial loss with haze that obscures iris details | 1/3 to ½ |
| IV | Poor | Cornea opaque with iris and pupil obscured | >1/2 |

2) Dua Grading

**Table 2**

| Grade | Prognosis | Clock hours of limbal involvement | Conjunctival Involvement | Analogue scale |
|---|---|---|---|---|
| I | Very good | 0 | 0% | 0.0% |
| II | Good | <3/ equal to 3 hours | <30% | 0.1-3%/ 1-29% |
| III | Good to guarded | >3 hours | >30to50% | 3.1-6%/ 30-50% |
| IV | Guarded | >6-9 hours | >50to75% | 6.1-9%/ 51-75% |
| V | Guarded to poor | >9, <12 hours | 75to<100% | 9.1-11.9% / 75.1-99.9% |
| VI | Very poor | 12 hours | 100% | 12%/100% |


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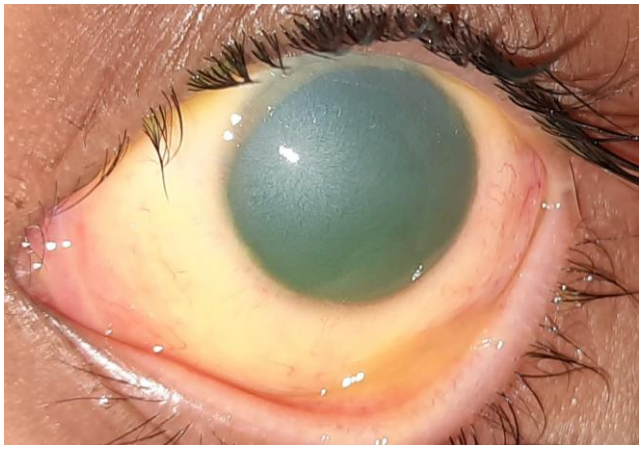

**Image 1:** Grade IV Dua's injury with complete corneal edema and 12 clock hours of limbal ischemia

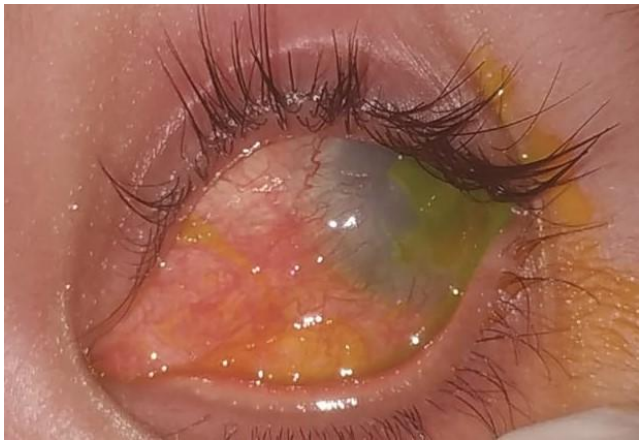

**Image 2:** Long term sequelae-Lower eyelid Symblepharon, conjunctivalisation, vascularization and persistent epithelial defect of cornea in grade VI ocular chemical injury

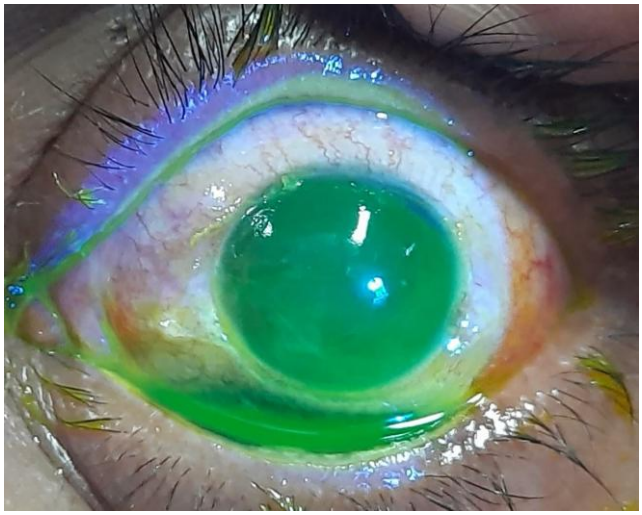

**Image 3:** Grade IV Dua's and Grade III Ropper Hall ocular chemical injury with inferior 4 clock hours of limbal ischemia

## 2.Literature Survey

Ocular surface wound repair mechanisms:

The process of corneal epithelial wound healing is divided into three phases:

1) Cell Migration
2) Cell Proliferation
3) Cell Adhesion

It is a continuous process involving contributions of above all mechanisms depending on the depth and nature of injury.

1. Epithelial cell migration

a) Latent phase-

i. During first 4-6 hours of the injury no significant change in the size of the wound occurs. Size of wound may increase due to sloughing of the necrotic cells at the edge of the wound.
ii. During this phase intracellular synthesis of the structural proteins is increased and polymerization of actin occurs.
iii. Desquamation of the superficial cells and loss of columnar appearance of the basal cells causes progressive thinning at the edge of the wound
iv. Polymorphonuclear neutrophils accumulate in the wound almost after 3 hours. They are principally derived from the tears.
v. Basal and squamous cells show thickening and separation.

b) Linear healing phase-

i. Epithelial cells flatten; move linear till the defect is fully covered.
ii. Actin filaments are involved in the migration of cells. Both basal and suprabasal cells are involved in the migration process.
iii. Migration of the cells occurs in centripetal manner.

c) Epithelial cell proliferation-

i. Following a corneal wound, normal mitotic process in the wounded area is stopped for 1 day accompanied with increased proliferation of the cells in the periphery
ii. Mainly basal cells are involved in the proliferation
iii. Limbal basal epitheliums are a repository for the stem cells.
iv. Stem cells are the progenitor cells that are responsible for tissue regeneration.
v. Stem cell –transiently amplifying cells (TACs)-post mitotic cells (PMCs)-terminally differentiated cells (TDCs)
vi. According to Schirmer et al, corneal basal cells represent TACs, suprabasal cells correspond PMC and TDC.

D) Epithelial cell adhesion-

Soon after the injury fibronectin, laminin, tenascin, fibrin appears on the denuded surface.

Migrating cells develop adhesion plaques with the substrate macromolecules.


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These are cytoskeletal structures that are composed of intracellular stress fibres, plasma membrane and extracellular substances.

Vinculin, talin, fibronectin, are the family of very late activating integrins. Their attachments are mediated by intracellular actin in the absence of hemidesmosomes. They act as receptors for fibronectin, laminin and other adhesion molecules. They provide anchorage. Fibrin and fibrinogen stimulate epithelial cells to release tissue plasminogen activator which causes conversion of plasminogen to plasmin which lyses the adhesion of cells to substrates and cause the cells to move forward and form new adhesions. The rapidity of the hemidesmosomal formation depends on the integrity of basement membrane at the time of injury.

Alkali induced defects show delay in marked healing even in the areas of intact basement membrane. It is due to accumulation of keratocytes, cellular debris, polymorphonuclear neutrophils. They prevent the anchoring of basement membrane to their substrates.

Role of limbal stem cells in corneal wound healing:

The concept of involvement of the limbal epithelium in the regeneration and renewal of the corneal epithelium was first proposed by devanger and evansen in 1971 [(2).] Limbal stem cells possess pleuripotent stem cells which are capable of regenerating specific differentiated cells in body. According to the X, Y, Z hypothesis proposed by Thoft and Friend, epithelium is maintained by continuous centripetal movement of the peripheral corneal epithelium. These basal cells lie deep in a thickened epithelial cell layer, tightly attached to the underlying basement membrane. They have a rich blood supply and appear as ridges (Vogt). These are known as limbal palisades of Vogt. are poorly differentiated and maintain their stemness through a combination of inherent cellular characteristics and the presence of favourable microenvironment at limbus. Transient amplifying cells or daughter cells are derived from limbal stem cells, maintain epithelial mass during epithelial turnover and wound healing. Corneal epithelial regeneration occurs regeneration of the corneal epithelium occurs in a centripetal and a circumferential fashion. Conjunctival stem cells are located in the fornices and they migrate in a centripetal fashion for healing of forniceal and bulbar conjunctiva. Limbus is more vascular as compared to the central cornea which is avascular. Vasculature at limbus provide nutrition and increased interaction of blood borne cytokines. [(3)] In cases of complete debridement of corneal epithelium and limbal epithelium, the surrounding conjunctival epithelium can resurface the cornea. This process is called as trans differentiation. Complete transdifferentiating is a rare phenomenon. Experimental studies have shown that it may be due t few retained stem cells. Following severe chemical injuries, resurfacing of the corneal epithelium is associated with the conjunctivalisation, deep stromal vascularisation, persistence of goblet cells within the corneal epithelium and recurrent erosions.

Pathophysiology and clinical course of ocular chemical injury:

The clinical course of ocular chemical injury:

1) Immediate
2) Acute
3) Early reparative (8–20 days)
4) and late reparative phases

1) Immediate phase: It begins from the time a chemical agent comes in contact with the ocular surface[4]. The factors for estimating the extent of ocular chemical injury and prognosis include total area of the corneal epithelial defect, the area of the conjunctival epithelial defect, the amount of clock hours or degrees of limbal involvement, the area and density of corneal opacification, and increased IOP on presentation and lens clarity.

2) Acute phase-

The first seven days after chemical eye injury constitute the acute phase of recovery. During this time, various inflammatory actions begin to take place over the ocular surface. In this stage, usually IOP (intraocular pressure) rises in a bimodal manner.[5]

Early reparative phase-

Early reparative phase starts 8-20 days after the injury. In this phase, the immediate regeneration of ocular surface epithelium and acute inflammatory events occur. Its further proceeds to chronic inflammatory response, stromal repair, and scarring.[6,7] In this stage various digestive enzymes such as collagenase, metalloproteinase, and other proteases are released from the polymorphonuclear leukocytes and the healing epithelium. Due to their action a persistent corneal epithelial defect can get converted to ulcer[8, 9, 10, 11].

Late reparative phase-

This sets in after 3 weeks of initial injury. In this phase completion of healing occurs. Complications if any, also occur in this phase. Breakdown of own ocular tissues leads to the chronic inflammatory reaction. These damaged tissue products act as new antigens. This causes invasion of the leukocytes and macrophages.[12, 13] Rise in IOP occurs which is resistant to the treatment. It may need long term antiglaucoma therapy or surgical therapy. Complication like corneal scarring, dry eye, symblepharon, cicatricial entropion or ectropion may occur subsequently.

## 3.Problem Definition

Ocular chemical injuries produce extensive damage to the ocular surface epithelium, conjunctiva, cornea, and limbal stem cells which results in diminution of vision. Emergency management is the single most important factor in determining the visual outcome. Ocular chemical injury is the true ocular emergency and requires immediate intervention. It can cause a significant visual


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impairment in younger economically productive age group. Hence, it is necessary to evaluate the damages caused by it with optimal intervention to restore vision. This study enables the analysis of current management of ocular chemical injury and its effect on the visual outcomes of the patients.

## 4.Methodology

Aims and Objectives:

1. Identification of the causes and risk factors which have effect on final visual outcome.
2. Grading of the injury according to the presentation.
3. To determine the final visual outcome.

**Study design: Longitudinal study**

Materials and Methods:

The study was conducted in compliance with the institutional ethical committee and study protocol. The study was in compliance with the ICMR guidelines for biomedical research in human subjects, 2017.

Subjects were recruited from, Outpatient, Inpatient Department of Ophthalmology Department, casualty of tertiary institute from June 2018 to January 2021.

After the subjects have met the inclusion/exclusion criteria, and are willing to sign the informed consent document, they were enrolled in study.

Inclusion Criteria:

1) Ocular chemical injury with both acids and alkalis.
2) All ocular chemical injuries including grade I to IV of Ropper hall classification and grade I to VI of Dua's classification of ocular chemical injuries.
3) Subjects up to 60 years of age.
4) Subjects of either gender.
5) Subjects without having previously existing ocular surface disorders.

Exclusion Criteria:

1) Subjects with previously existing ocular surface disorders.
2) Subjects more than 60 years of age.

**Study Method**

At first visit thorough history of the patients including name, age, sex, address, contact information, chief complaints, history of presenting illness, past, personal and family history was taken. Thorough ocular examination of the patient and grading of the injury was done. In ocular examination, visual acuity, examination of eyelids, cornea, conjunctiva, anterior chamber, Iris, pupil, lens and fundus examination. After immediate management is done, and patients were met with inclusion and exclusion criteria, an informed consent in the language which patient understands, was taken. Patients were followed up. There were 9 follow up visits. These included visits on day1, day3, day 5 day 7, day 14, day 21, day28, day 56 and day 74 of initial chemical injury. On every follow up visit, visual acuity, examination of eyelids, cornea, conjunctiva, anterior chamber, iris, pupil lens and fundus examination were done and any improvement or worsening was monitored.

## 5.Results and Discussion

Ocular chemical injuries produce extensive damage to the ocular surface including conjunctival, corneal epithelium and limbus. It ranges from minor injuries to extensive injuries. Ocular chemical injuries cause delayed epithelialization of ocular surface, persistent inflammation, and progressive tissue melting. In long term complications, it may result in healing with vascularization, scarring and keratinization, symblepharon formation. Thus, in acute stage, most important aspect of management is to reduce inflammation and promote epithelialization.

Incidence in our study:

In the present study, majority of the population affected was younger age group. Maximum patients were in age group from 20 to 40 years (64 patients) 3 cases were less than 10 years of age and 11 cases above 40 years of age.54 males and 34 females were affected as given in table 3 and 4.

**Table 3:** Distribution of the study subjects based on the age group

| Age group | Frequency | Percentage |
|---|---|---|
| **<10** | 3 | 3.41 |
| **11 to 20** | 23 | 26.14 |
| **21 to 30** | 37 | 42.05 |
| **31 to 40** | 14 | 15.91 |
| **41 to 50** | 7 | 7.95 |
| **51 to 60** | 3 | 3.41 |
| **>60** | 1 | 1.14 |
| **Total** | 88 | 100.00 |
| **Mean** | 26.64 | |
| **SD** | 11.02 | |
| **Range** | 9 to 83 | |

**Table 4:** Distribution of the study subjects based on the gender

| Gender | Frequency | Percentage |
|---|---|---|
| **Female** | 34 | 38.64 |
| **Male** | 54 | 61.36 |
| **Total** | 88 | 100.00 |

Form of injury in all cases was accidental. Alkali injuries were common (73.86%). Overall lime was the most common agent causing injury (44.38%). Gulal was the next common chemical agent. All the injuries caused by gulal were from a common gathering in Indian festivals like Ganesh Visarjan, Holi.

Evaluation of risk factors in our study:

1) Need of early presentation-


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Majority of cases reported within 6 hours of the injury to the hospital (77.27%). About 12.5% reported between 6 to 24 hours and 2 cases each between 1 day to 1 week, 3 cases between 1 week to 1 month and 5 cases more than 1 month in the present study. In present study, out of 112 eyes presenting within 24 hours of injury, more than 70% patients had good visual outcome (≥6/12). Amongst patients presenting between 24hours to 1 week, 50% (1) patients had good and poor (≤6/60 to LP) visual outcome each. Both the eyes presenting between 1 week to 1 month of initial chemical injury poor final visual outcome. Finally, out of 7 eyes presenting after 1 month of initial chemical injury (2) had fair (≤ 6/12 to <6/60) and 5 patients had poor final visual outcome. (Tables 5 and 6).

Thus, the results of our study were comparable to study conducted by kelin and lobes.

2) Early Intervention-

Early intervention in cases showed good visual outcome.

3) Grade of Injury-

Patients presenting with lower grades of injury had good visual outcomes. Injuries with lower grades and presenting earlier will heal without permanent damage within few days. In our study it was found that all 13 (100%) eyes presenting with Dua's classification Grade I injury had good visual outcomes, while 97.77 % patients of Grade II injury according to Dua's classification had good visual outcome (vision equal to or better than 6/12).22 (53.66%) out of 41 eyes with Grade III injury had good visual outcome, 18 (43.91%) had fair and 1 had poor visual outcome (final vision ≤6/60). There were 18 eyes who presented with Grade IV injury.4 of them had final BCVA between 6/12 and 6/60 and 6 patients had final vision ≤ 6/60.4 patients presented with grade V injury, out of which 3 had poor final visual outcome. Out of 10 eyes presented with Grade VI injury, only one patient had final visual acuity of 6/24. Remaining 10 (90%) eyes had BCVA (Best Corrected Visual Acuity) less than or equal to 6/60. The results were consistent with the previous studies (72), (36).

Similar results were observed using Ropper Hall classification.100 %eyes of Grade1 injury had final BCVA (Best Corrected Visual Acuity) better than or equal to 6/12.97.77% eyes with Grade II injury had, BCVA (Best Corrected Visual Acuity) of better than or equal to 6/12 at final follow up visit. Amongst patients with Grade III injury 75% had BCVA (Best Corrected Visual Acuity) between 6/12 to 6/60 remaining about 25% patients had poor visual outcome with BCVA (Best Corrected Visual Acuity) less than or equal to 6/60. While out of 24 patients presented with Grade IV injury, 6 had fair BCVA (Best Corrected Visual Acuity) (less than or equal to 6/12 more than 6/60) and remaining 18 (75%) eyes had poor final visual outcome. They had BCVA (Best Corrected Visual Acuity) less than 6/60 at final follow up visit.

**Table 5:** Distribution of the study subjects based on Duas grading

| Duas grading | Frequency | Percentage |
|---|---|---|
| **Grade I** | 13 | 10.56 |
| **Grade II** | 45 | 36.58 |
| **Grade III** | 41 | 33.33 |
| **Grade IV** | 10 | 8.13 |
| **Garde V** | 4 | 3.25 |
| **Grade VI** | 10 | 8.13 |
| **Total** | 123 | 100.00 |

4) Surgical management-

Thus, according to Dua's grading, out of 13 eyes presented with grade I injury none required surgical management.3 (6.67%) eyes with Grade II injury, required AMT.26 (63.33%) eyes out of 41 eyes presenting with Grade III Injury required Amniotic Membrane Transplantation (AMT). Out of 10 eyes presenting with Grade IV injury, 8 required AMT, 1 required AMT with symblepharon release surgery. Out of 4 eyes presenting with Grade V injury, 3 required AMT, 1 required AMT with symblepharon release. Out of 10 eyes presenting with Grade VI injuries, 5 required Amniotic Membrane Transplantation, 2 required AMT with symblepharon release, 2 required penetrating keratoplasty and Simple limbal epithelial transplantation. Thus 100% eyes above grade IV injury required some surgical management.

Similar results were observed according to Ropper Hall classification. Surgical management was not required for Grade I injuries.93.33% patients with Grade II injuries did not require any surgical management. Out of 41 eyes presenting with Grade III injuries 26 (6.41%) required AMT. There were 24 patients presenting with Grade IV injuries.100 % eyes required some surgical management.16 eyes required AMT, 2 eyes required penetrating keratoplasty and 2 required SLET.

Final visual outcome-

Final visual outcome depended on Grade of injury. It was observed that according to Dua's grading, 100%eyes of Grade I injury had final visual outcome better than or equal to 6/12.

97.77% eyes with Grade II injuries had final visual outcome better than or equal to 6/12. Amongst eyes having Grade III injuries 53 % final visual outcome better than or equal to 6/12 had final BCVA more than or equal to 6/12 and 44% patients had BCVA between 6/12 to 6/60. There were 10 patients with Grade IV injury.4 had final BCVA between 6/12 to 6/60 and 6 had vision ≤6/60. More than 90 % patients with Grade V and Grade VI injury had poor final visual outcome (less than 6/60).

Similar results were observed according to the Ropper Hall classification.100 % patients having Grade I injury had vision better than or equal to 6/12.97.77% eyes with Grade II injury he had final BCVA of more than 6/12. While Grade III injury patients, 54% had vision equal to or more than 6/12 and 44 % patient s had vision between 6/12 to 6/60. While out of 24 patients presenting with Grade IV injury about 75 % had poor visual outcome. Their final BCVA was less than 6/60.


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Thus, according to Dua's classification, Grade I and II have good prognosis. Grade III, IV injuries have moderate and Grade V and VI have poor prognosis. According to Ropper Hall classification, grades I and II have good prognosis, grade III has good to moderate and grade IV injuries have poor prognosis despite of treatment.

**Table 6:** Distribution of final visual outcomes of study subjects based on Dua's Grading

| s grading | ≥6/12 (good) | | <6/12 to >6/60 (fair) | | ≤6/60 to LP (poor) | | Total number |
|---|---|---|---|---|---|---|---|
| | No[r] | % | No[r] | % | No[r] | % | |
| Grade I | 13 | 100 | 0 | 0 | 0 | 0 | 13 |
| rade II | 44 | 97.77 | 1 | 2.23 | 0 | 0 | 45 |
| rade III | 22 | 53.66 | 18 | 43.91 | 1 | 2.43 | 41 |
| rade IV | 0 | 0 | 4 | 40 | 6 | 60 | 10 |
| rade V | 0 | 0 | 1 | 25 | 3 | 75 | 4 |
| rade VI | 0 | 0 | 1 | 10 | 9 | 90 | 10 |

## 6.Conclusion

From the present study, it can be concluded that according to Dua's classification, Grade I and II have good prognosis. Grade III, IV injuries have moderate and Grade V and VI have poor prognosis. According to Ropper Hall classification, grades I and II have good prognosis, grade III has good to moderate and grade IV injuries have poor prognosis despite of treatment.

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