



## EVALUATION OF SIMPLE LIMBAL EPITHELIAL TRANSPLANT IN LIMBAL STEM CELL DEFICIENCY

### Ophthalmology

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### ABSTRACT

The cornea, which is transparent and avascular structure of the eye plays crucial role in vision. However, it can be affected by Limbal Stem Cell Deficiency (LSCD), where opacity occurs along with loss of vision. Simple Limbal Epithelial Transplantation (SLET), low-cost intervention and less invasive procedure was observed being practiced to treat LSCD as it helps in restoring the corneal surface. With this view, present study aimed to determine clinical outcome of SLET among patients with LSCD. It is a prospective observational study conducted at outpatient Department of Ophthalmology, B.R.D. Medical College Gorakhpur from May 2023 to April 2024. Sample size was calculated based on total enumerations purposive sampling method after taking considering all relevant requirements into the account had led us include thirty-eight eyes who were diagnosed having LSCD after written informed consents gathered from them. It was observed that visual acuity significantly improved after subjecting patients with total unilateral LSCD to SLET with most patients achieving a stable corneal epithelial surface by the 4-month follow-up. The overall visual outcomes and corneal epithelial stability indicate an excellent response and efficacy of the simplified SLET technique for reconstruction of the ocular surface in case of LSCD. This study further validates expanding this novel indication for SLET where other forms of autografts or allografts are commonly used with added advantage of lower cost, ease of technique, and early postoperative recovery.

### KEYWORDS

Limbal Stem Cell Deficiency, Simple Limbal Epithelial Transplantation (SLET), Visual acuity

### INTRODUCTION

Blindness remains an important public health problem that affects not only the physical quality of life but also the social, economic, and mental health of the afflicted person.<sup>(1)</sup> Corneal opacity is the second most common cause of blindness in India. The corneal opacity though can be treated by corneal transplantation. Due to paucity of the donor cornea, each year around 20,000 new cases are added to the backlog.<sup>(2)</sup>

Limbal stem cells (LSCs) are the adult stem cells of the corneal epithelium; the transparent, multilayered, and avascular superficial layer of the cornea, the window at the front of the eye. They reside in an anatomically distinct stem cell niche within the limbus, which borders the circumference of the cornea.<sup>(3)</sup> Within the limbal niche and its microenvironment, complex signaling pathways mediate cell-to-cell interactions that promote wound healing and ensure adequate corneal epithelial cell turnover.<sup>(4,5)</sup> When these cellular processes are disrupted, there may be clinical manifestations that may result in severe ocular complications. In limbal stem cell deficiency (LSCD), the limbal stem cell reserve is depleted and/or becomes dysfunctional, leading to a loss of corneal epithelial replenishment.<sup>(6)</sup> Recent advances in limbal stem cell transplantation have improved the surgical approach to differing severities of LSCD. Limbal stem cell deficiency (LSCD) can stem from numerous etiologies, resulting in serious visual morbidity. And so, early diagnosis of this entity is essential in order to institute the appropriate therapy in a timely manner.<sup>(7)</sup>

Dr. Sangwan initially presented the surgical procedure known as Simple Limbal Epithelial Transplantation (SLET) in 2012 as a means of treating limbal stem cell deficit (LSCD).<sup>(8,9)</sup> SLET is a single-stage, repeatable procedure that doesn't require a unique lab setup. Compared to CLAU, it is more donor eye conservative and enables us to harvest a smaller limbal transplant. The transplant is autologous, hence systemic immunosuppression is not required. Because there is no additional setup required, this one-stage process is affordable for smaller centers.<sup>(9)</sup>

By directly transplanting limbal stem cells onto the damaged cornea, Simple Limbal Epithelial Transplant (SLET) offers a novel treatment technique that attempts to restore a healthy corneal surface.<sup>(6)</sup> Notwithstanding the encouraging initial results, thorough assessments of SLET's effectiveness, safety, and long-term consequences are still necessary. By carefully assessing the results of SLET in patients with LSCD, this study aims to close this gap.<sup>(9)</sup>

### MATERIAL AND METHODS

#### Study Design

The Prospective observational study was conducted on patients visiting the outpatient Department of Ophthalmology, B.R.D. Medical College, Gorakhpur. Written informed consent was obtained from either the patients or their guardians. The study duration was 12 months (May 2023 to April 2024).

#### Study Population

In this study, 40 eyes of patients with partial stem cell deficiency underwent Simple Limbal Epithelial Transplantation (SLET). Inclusion criteria included patients over 10 years old, who provided written consent and committed to follow-up. Patients attended the ophthalmology OPD at BRD Medical College with signs of limbal stem cell deficiency and corneal neovascularization. Exclusion criteria involved patients who didn't consent, had medication hypersensitivity, no visual potential in a blind eye, scleral ischemia due to chemical injuries, uncorrected adnexal pathologies (lagophthalmos, ectropion, trichiasis, entropion), previous SLET, other ocular pathologies (glaucoma, retinal disorders), and pregnant or lactating women.

#### Methodology

Patients meeting the study criteria provided written consent, after which data on their profiles, medical history, symptoms, and treatment history were recorded. A comprehensive history and baseline evaluation involving general and local examinations, as well as various investigations, were conducted. The study involved patients with primary corneal neovascularization due to limbal stem cell deficiency at BRD Medical College from May 2023 to April 2024. Follow-up visits at 1 week, 1 month, and 4 months post-SLET included slit lamp biomicroscopy and visual acuity testing. The surgical technique involved donor limbal tissue transplantation, and post-operative care included eye examinations, BCL removal after 72 hours, and prescription of topical antibiotics and lubricants. Success criteria were stable corneal epithelium, improved visual acuity, and reduced corneal neovascularization, with materials including AMG, BCL, and fibrin glue.

#### Statistical Analysis

The collected data was analyzed using the software SPSS (Statistical Package for Social Sciences, version 22, SPSS Inc, Chicago, IL). Statistical tests were applied, and the obtained results were saved in document format.

### RESULTS

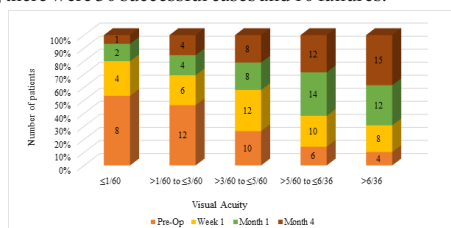
Analysing demographic data helps in ensuring that the study results are applicable to a diverse population and aids in stratifying results based on demographic factors. This study represents the demographic details of 40 patients, illustrating the age and gender distribution within the study. The mean age is noted as 34.7 years with a standard deviation of 12.5, indicating a middle-aged patient group with some variability in age range. It was observed that among the sample size of 40 patients, 16 patients were lying in the group between 10-to-25-year age group. The aetiology of Limbal Stem Cell Deficiency, showcasing various causes was observed in this study.

The Outcome according to etiology demonstrate that a post op eye was considered to have undergone a failed operation when after 4 month follow up, the operated eye cornea showed signs of significant neovascularisation.

**Table 1: Outcome On The Basis Of Presence Or Absence Of Symblepharon**

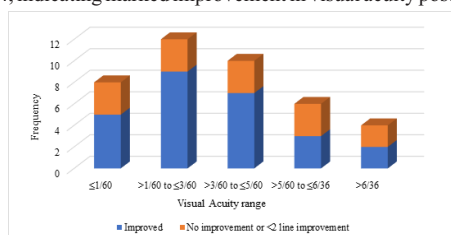
| Symblepharon | Success | Failure |
|--------------|---------|---------|
| Present      | 9       | 8       |
| Absent       | 21      | 2       |
| Total        | 30      | 10      |

The table displays the success and failure rates of the procedure based on the presence or absence of symblepharon. Among the patients with symblepharon, 9 cases were successful, and 8 were failures. For those without symblepharon, 21 cases were successful, and 2 were failures. In total, there were 30 successful cases and 10 failures.



**Figure 1:** Comparison of results of improved visual acuity (Pre-Op, week 1, month 1 and month 4)

Figure 1 presents the comparison of visual acuity improvement over time (Pre-Op, Week 1, Month 1, and Month 4). Initially, 8 patients had a visual acuity of  $\leq 1/60$ , which reduced to 1 patient by Month 4. For visual acuity  $> 1/60$  to  $\leq 3/60$ , the number decreased from 12 Pre-Op to 4 by Month 4. The count for visual acuity  $> 3/60$  to  $\leq 5/60$  increased from 10 Pre-Op to 12 at Week 1, stabilizing at 8 from Month 1 onwards. Patients with visual acuity  $> 5/60$  to  $\leq 6/36$  increased from 6 Pre-Op to 14 at Month 1, slightly reducing to 12 by Month 4. Lastly, those with visual acuity  $> 6/36$  increased significantly from 4 Pre-Op to 15 by Month 4, indicating marked improvement in visual acuity post-SLET.



**Figure 2:** Improvement in Visual Acuity (Snellen's visual acuity) from Baseline to 4 Months

This diagram categorizes the improvements in visual acuity from baseline to 4 months into five different groups, capturing a detailed spectrum of patient outcomes. It shows that the largest percentage of patients (75%) experienced improvements, highlighting significant visual recovery. Smaller proportions of patients had either less or more substantial improvements, illustrating the variability in patient responses to treatment. Detailed categorization helps in understanding the different degrees of improvement, assisting clinicians in predicting patient prognosis and tailoring individualized care plans based on initial visual acuity measurements.

**Table 2: Stability Of Corneal Epithelial Surface At 1 Week**

| Stability | Frequency | Percentage |
|-----------|-----------|------------|
| Stable    | 15        | 37.5%      |

|          |    |         |
|----------|----|---------|
| Unstable | 25 | 62.5%   |
| Total    | 40 | 100.00% |

The above table assesses the stability of the corneal epithelial surface one-week post-surgery in 40 patients. A total of 37.5% of patients demonstrated a stable epithelial surface (on slit lamp examination) based on tear film maintenance, which is a positive early indicator of successful treatment adherence and minimal postoperative complications. Conversely, 62.5% of the patients exhibited unstable corneal epithelial surface on slit lamp examination. This early evaluation is critical for determining the immediate postoperative recovery and can help in early identification of patients who might require additional care to ensure optimal outcomes.

**Table 3: Stability of Corneal Epithelial Surface at 1 Month**

| Stability | Frequency | Percentage |
|-----------|-----------|------------|
| Stable    | 17        | 42.50%     |
| Unstable  | 23        | 57.50%     |
| Total     | 40        | 100.00%    |

The above table presents data on the stability of the corneal epithelial surface one month after treatment, indicating an increase in stability with 42.50% of patients showing a stable surface. This improvement from the one-week postoperative data suggests effective healing and adaptation of the epithelium following surgical intervention. Monitoring such progress is essential for understanding the healing dynamics and for planning any necessary adjustments in patient management to enhance recovery and prevent long-term complications.

**Table 4: Stability of Corneal Epithelial Surface at 4 Months**

| Stability | Frequency | Percentage |
|-----------|-----------|------------|
| Stable    | 22        | 55.00%     |
| Unstable  | 18        | 45.00%     |
| Total     | 40        | 100.00%    |

This table presents the stability of the corneal epithelial surface at 4 months following medical intervention, displaying that 55% of the cases were noted as stable, which signifies a significant positive outcome in the management of the corneal condition. On the other hand, 45% remained unstable, reflecting the challenges in achieving complete stability for all patients. The total number of cases reviewed was 40, indicating a comprehensive study scale that provides a solid basis for statistical reliability. This data is crucial for clinicians as it offers insights into the effectiveness of treatment methods applied within the first few months of recovery.

## DISCUSSION

The present study consists of the 40 patients of mean age with SD 12.5, which gives an idea about middle aged group of patients with variability in the age distribution. Male majority was seen as 22(55%) and 18(45%) were females,<sup>(1)</sup> also found the similar result as mean age in their study of 731 eyes of LSCD patients Eastern India was found to be  $35.0 \pm 19.4$  years and higher incidence of LSCD among young male population.

Preoperative visual acuity among the 40 participants varied widely, with the most common ranges being  $> 1/60$  to  $\leq 3/60$  (30%) and  $> 3/60$  to  $\leq 5/60$  (25%). Visual acuity better than  $> 6/36$  was noted in 10% of the patients, indicating a significant portion had relatively better vision before treatment for limbal stem cell deficiency (LSCD). This finding aligns with the results of Basu et al., who reported a two-line improvement in visual acuity in 75.2% of cases post-SLET, with 67% achieving 20/60 or better vision.<sup>(10)</sup> The present study found that postoperative visual acuity at 1 week varied among the 40 participants. The most common visual acuity range was  $> 6/36$  to  $\leq 5/60$ , observed in 30.00% of the patients. At one-month post-treatment, the present study found that 42.5% (17 out of 40) of the patients demonstrated a stable corneal epithelial surface. Also at four months post-treatment, 55% (22 out of 40) of the patients had a stable corneal epithelial surface. This finding is consistent with the results of Basu et al.<sup>(10)</sup>

## CONCLUSION

The study results prove that the efficacy of SLET as an effective, and a promising method for treating LSCD. Thorough analysis of 40 patients' revealed significant improvements in visual acuity and corneal epithelial stability over a 4-month post-operative follow-up indicating that the procedure has promising potential to restore corneal integrity and function thus mitigating the morbidity associated with LSCD. The demographic profile showed a marginal male

preponderance with middle age being the most common age group in our cohort. Similar observations had been noted by other workers too in their publications further establishing the robustness of data on the effectiveness of SLET across varied etiologies. This study highlights the need for developing standard protocols to minimize the inter surgeon variability and formulate guidelines that will help improve the success rate and have a better therapeutic effect. The evidence presented demonstrates that SLET can be used more extensively especially in resource poor settings as it is cost effective, less invasive and requires less dependency on donor tissue. More such studies with larger number of patients and longer follow-up would be needed to further substantiate this finding as well as develop newer modification for improving its long-term efficacy. This study consists of existing data toward applications within regenerative ophthalmology creating scope for better LSCD management in near future.

## REFERENCES

1. Singh VK, Kumari N, Kusumesh R Sinha BP. Limbal stem cell deficiency: Demography, aetiology, and clinical presentation in Eastern India. *Journal of Family Medicine and Primary Care*. 2024; 13(1):48-53.
2. Sharma N, Arora T, Singhal D, Maharana PK, Garg P, Nagpal R, et al. Procurement, storage and utilization trends of eye banks in India. *Indian Journal of Ophthalmology*. 2019; 67(7):1056-9.
3. Ghareeb AE, Lako M, Figueiredo FC. Recent advances in stem cell therapy for limbal stem cell deficiency: a narrative review. *Ophthalmology and Therapy*. 2020; 9(4):809-31.
4. Zhang Y, Sun H, Liu Y, Chen S, Cai S, Zhu Y, Guo P. The limbal epithelial progenitors in the limbal niche environment. *International Journal of medical sciences*. 2016; 13(11):835.
5. Yeh SI, Chu TW, Cheng HC, Wu CH, Tsao YP. The use of autologous serum to reverse severe contact lens-induced limbal stem cell deficiency. *Cornea*. 2020; 39(6):736-41.
6. Lee YF, Yong DWW, Manotosh R. A Review of Contact Lens-Induced Limbal Stem Cell Deficiency. *Biology*. 2023; 12(12):1490.
7. Kate A, Basu S. A review of the diagnosis and treatment of limbal stem cell deficiency. *Frontiers in Medicine*. 2022; 9:836009.
8. Sangwan VS, Basu S, MacNeil S, Balasubramanian D. Simple limbal epithelial transplantation (SLET): a novel surgical technique for the treatment of unilateral limbal stem cell deficiency. *British Journal of Ophthalmology*. 2012; 96(7):931-4.
9. Thokala P, Singh A, Singh VK, et al. Economic, clinical and social impact of simple limbal epithelial transplantation for limbal stem cell deficiency. *British Journal of Ophthalmology*. 2022; 106(7): 923-8.
10. Basu S, Sureka SP, Shanbhag SS, Kethiri AR, Singh V, Sangwan VS. Simple limbal epithelial transplantation: long-term clinical outcomes in 125 cases of unilateral chronic ocular surface burns. *Ophthalmology*. 2016; 123(5):1000-10.