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A RETROSPECTIVE COHORT STUDY OF 200 PATIENTS: CLINICAL MANIFESTATIONS AND AETIOLOGY OF RECURRENT CORNEAL EROSION SYNDROME.

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ABSTRACT

Objective

To investigate the clinical characteristics and causes of recurrent corneal erosion syndrome (RCES).

Methods

A study was conducted on 200 patients (185 eyes) diagnosed with Recurrent Corneal Erosion Syndrome (RCES) at the institution, Netaji Subhas Medical College and Hospital, Bihta, Patna. The analyzed data encompassed information on demographics, causes, position on the cornea, and the relationship with meibomian gland dysfunction (MGD).

Findings

The average age of participants was 44.5 years, with a range of 14-80 years. The identified causes of Recurrent Corneal Erosion Syndrome (RCES) were as follows: prior minor trauma (73 eyes, 39.45%), photorefractive keratectomy (31 eyes, 16.75%), epithelial basement membrane corneal dystrophy (EBMD) (31 eyes, 16.75%), laser-assisted in situ keratomileusis (14 eyes, 7.56%), and unknown origin (36 eyes, 18.91%). The inferior paracentral cornea was the most common area for recurrent corneal erosions (RCES), accounting for 68.4% of cases. The upper cornea and other locations were less frequently affected, with each accounting for 21.3% of cases. MGD was present in 59% of patients.

Summary

Recurrent corneal erosion syndrome (RCES) can be caused by many factors, which account for the diverse range of symptoms observed in individuals with the condition. Notably, a considerable proportion of patients with Recurrent Corneal Erosion disease (RCES) start experiencing the disease after undergoing keratorefractive surgery, a significant proportion of individuals also exhibit Meibomian Gland Dysfunction (MGD).

Recommendations

The study suggests treating MGD, which is often connected to RCES. It also suggests treating RCES with PRK and LASIK and preventing it in patients. Study MGD's role in RCES and treatment options including phototherapeutic keratectomy (PTK), which has shown promise in managing reoccurring cases.

Keywords: *Corneal Erosion, Meibomian Gland Dysfunction, Recurrent Corneal Erosion Syndrome, Photorefractive Keratectomy, Epithelial Basement Membrane Dystrophy*
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INTRODUCTION

Recurrent corneal erosion syndrome (RCES) is a prevalent condition characterized by severe eye pain and persistent discomfort. The disease was initially documented by Hansen [1] in 1872 who referred to it as recurrent neuralgic vesicular keratitis. At times, it may go unnoticed because the patient may not show any symptoms during examination. The most common symptoms of this condition are pain, excessive tearing of the eyes, and sensitivity to light upon awakening. It is not uncommon for pain to awaken the patient overnight [2]. Symptoms typically diminish or completely resolve throughout the daytime. These individuals may experience severe instances of spontaneous epithelial erosion, resulting in extreme discomfort and typically necessitating treatment in hospital emergency services. Frequently, these emergency visits are the sole form of medical attention that patients receive, which generates feelings of worry and vulnerability. This is due to the uncertainty of whether the episode will happen again and the lack of knowledge on how to prevent its recurrence.

Rheumatoid arthritis affects both genders in an equal manner and can manifest at any stage of life [3]. Typically, it impacts only one eye, but it can potentially happen in both eyes simultaneously [4]. The predominant clinical

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manifestation is the absence of adhesion among the anterior stroma and epithelium, resulting in discomfort and recurrent erosion. Furthermore, the microcysts' presence and changes to the basement layer of the epithelium can be observed during a slit-lamp examination [5]. The illness is commonly linked to slight eye trauma, such as tiny epithelial erosions that have minimal impact on the stroma. These injuries are typically caused by things with relatively sharp edges and they typically heal without any additional issues[6]. However, signs of Recurrent Corneal Erosion Syndrome (RCES) can infrequently manifest weeks or even years after the initial occurrence. The disorder is also commonly found in patients with basement membrane dystrophy of the epithelium and in these circumstances, it can occur in both eyes [2]. The cause of the condition is still unknown, and treatment is typically effective, but only for acute instances of erosion. However, even with the various medicinal and surgical interventions that have been documented, a considerable proportion of these patients persist with symptoms for extended durations [7].

This retrospective investigation, which examined 200 cases, supports the majority of earlier descriptions of Recurrent Corneal Erosion Syndrome (RCES). However, a variation in the age distribution was seen depending on the cause.

The study investigates the clinical characteristics and causes of recurrent corneal erosion syndrome (RCES).

METHODS

Study design

A retrospective cohort study

Study setting

Individuals with Recurrent Corneal Erosion Syndrome (RCES) were approved for participation at Netaji Subhas Medical College and Hospital, Bihta, Patna. The study was conducted for 2 years (January 2022 to December 2023).

Participants

This study includes 200 patients (185 eyes).

Inclusion criteria

Patients diagnosed with Recurrent corneal erosion syndrome.

Exclusion criteria

Patients having epithelial erosions related to Salzmann nodular degeneration, any stromal dystrophy, Reis-Buckler dystrophy, band keratopathy, bullous keratopathy, and keratoconjunctivitis sicca were excluded from the study.

Bias

The study attempted to minimize potential bias by strictly defining inclusion and exclusion criteria, ensuring that only patients with confirmed Recurrent Corneal Erosion Syndrome (RCES) were included, while excluding cases related to other corneal conditions like Salzmann nodular degeneration and stromal dystrophy. Additionally, standardized diagnostic procedures like slit-lamp examination and epithelial adhesion tests were employed to uniformly assess all patients.

Data collection

The diagnosis of RCES was established by identifying the characteristic symptoms and clinical findings during the examination. The symptoms were recurrent nocturnal or early morning pain accompanied by ocular redness and tearing. Several patients encountered previous recurrent episodes of epithelial erosions that necessitated urgent medical evaluation. The study investigated whether there was a correlation between prior instances of mild eye injuries or surgery and the onset of symptoms.

The primary indication observed during slit-lamp examination was the presence of epithelium that was loosely attached. The portions of the epithelium that were impacted showed up as black dots when the tear film was stained with fluorescein (Fig. 1A). The epithelium's adhesion was evaluated using a weck-cel sponge following the application of local anesthetic to the cornea. The movement of the epithelium was illustrated by the formation of folds using the weck-cel sponge (Fig. 1B). The study examined all individuals for indications of EBMD. EBMD is characterized by the identification of microcystic abnormalities within the epithelial of both eyes.

Procedure

The relevant epidemiological data at the time of diagnosis included the patient's gender, age, the eye that was affected, any history of surgery, Meibomian Gland Dysfunction (MGD) presence, and the specific location of the epithelial damage. MGD was diagnosed if the practitioner chose to treat it using at least one of these methods: daily cleaning of the eyelid margins, application of topical antibiotics, or

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administration of oral tetracycline. The regions of the cornea that have been impacted were mapped on a chart with six distinct possible locations (Fig. 2), and in some cases, multiple regions were involved.

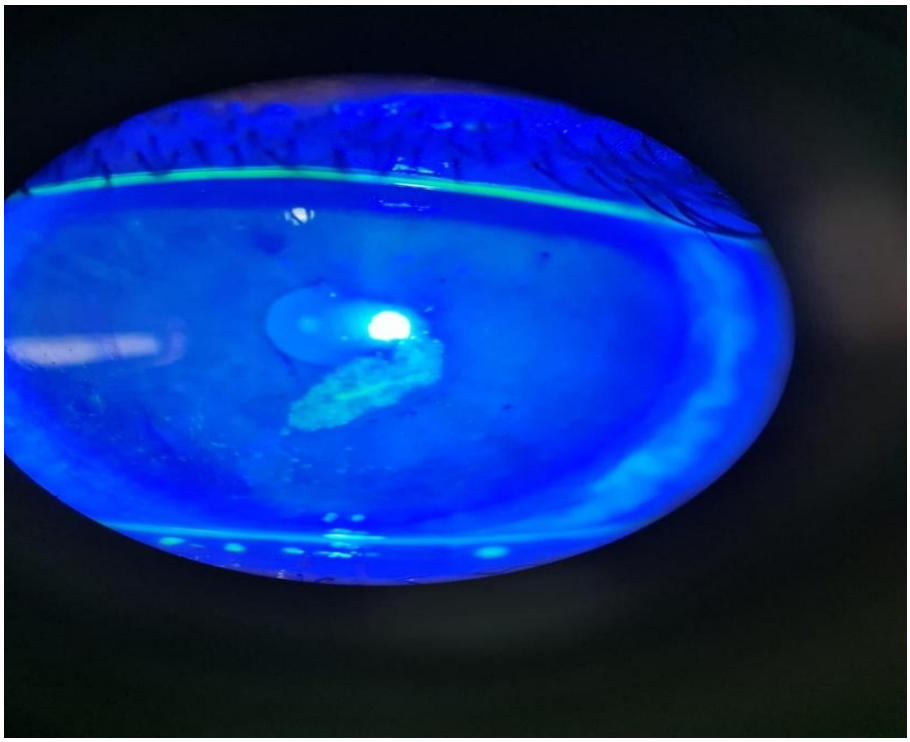

Fig.1: The corneal surface image displays fluorescein staining of the loosely adherent epithelium and black spots of tear film abnormalities. The epithelium lossely peeled off easily when tested with a weck-cel sponge.

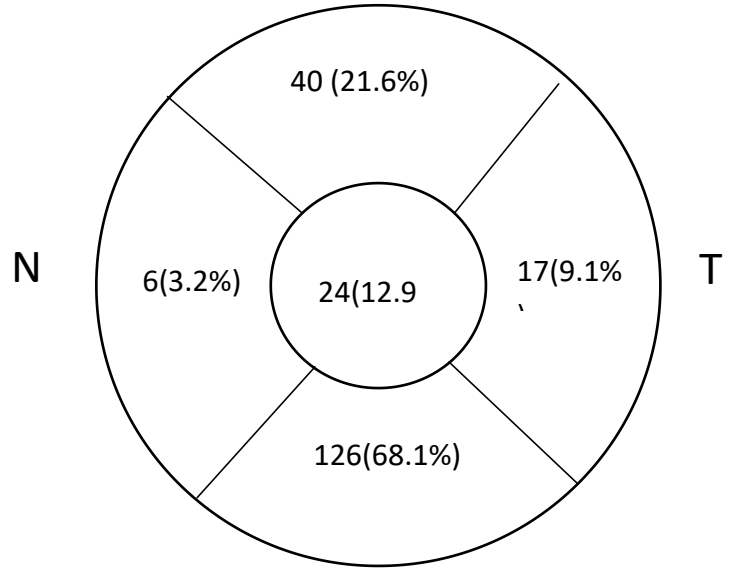

Fig.2: Epithelial mapping chart used to document the precise location of the afflicted epithelium. The study identified six distinct locations: upper, central, lower, nasal (N), temporal (T), and widespread. Multiple locations

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were potentially viable in any scenario. The values represent the average number of eyeballs and the matching percentage of instances.

Statistical analysis

The study employed descriptive statistics to analyze patient demographics, clinical manifestations, and etiological factors of Recurrent Corneal Erosion Syndrome (RCES). Percentages and Gaussian distribution were used to represent data such as the prevalence of Meibomian Gland Dysfunction (MGD) and age distribution. Missing data handling methods were not explicitly mentioned, but it is likely that only complete cases were included in the analysis. No sensitivity analyses were reported to assess the impact of assumptions or missing data on the study's findings.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULTS

The causative factors were found to be trauma in 73 eyes (39.45%) of 90 patients (45%), with 2 bilateral cases and 56 eyes (62.22%) exhibiting MGD. Epithelial Basement Membrane Dystrophy (EBMD) accounted for 31 eyes (16.75%) of 28 patients (14%), with 12 bilateral cases and 10 eyes (35.71%) showing MGD. Photorefractive Keratectomy (PRK) was identified in 31 eyes (16.75%) of 28 patients (14%), with 12 bilateral cases and 12 eyes (42.85%) having MGD. LASIK (Laser-Assisted in Situ Keratomileusis) was the cause in 14 eyes (7.56%) of 14 patients (7%), with 4 bilateral cases and 10 eyes (71.42%) presenting with MGD. Additionally, 36 eyes (18.91%) of 40 patients (20%) had an unknown cause, with 4 bilateral cases and 30 eyes (75%) demonstrating MGD.

Table 1: The study investigated the causative cause in 185 eyes of 200 individuals with recurrent corneal erosion syndrome (RCES) and its connection with meibomian gland dysfunction (MGD).

Causes	No. Of eyes (%)	No. Of patients (%)	Bilateral	MGD (%)
Trauma	73 (39.45%)	90 (45%)	2	56 (62.22%)
EBMD	31 (16.75%)	28 (14%)	12	10 (35.71%)
PRK	31 (16.75%)	28 (14%)	12	12 (42.85%)
LASIK	14 (7.56%)	14 (7%)	4	10 (71.42%)
Unknown	36 (18.91)	40 (20%)	4	30 (75%)

Table 2: Gaussian distribution of age (N=200)

Age	No. Of patients	%
Less than 30	48	24%
30-40	52	26%
40-50	42	21%
50-60	30	15%
60-70	20	10%
More than 70	8	4%

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Table 3: Age distribution in EBMD cause

EBMD	Percentage of Patients%
Less than 30	7%
30-40	14%
40-50	14%
50-60	29%
60-70	29%
More than 70	7%

The majority were between 30 and 40 years old (26%), less than 30 years old (24%), and 40 to 50 years old (21%). Patients aged 50 to 60 years comprised 15% of the group, while those between 60 to 70 years and over 70 years were less common, at 10% and 4% respectively (Table 2).

The age distribution of patients with Epithelial Basement Membrane Dystrophy (EBMD) was as follows (table 3) : 7% were less than 30 years old, 14% were among 30 and 40 years old, another 14% were among 40 and 50 years old, 29% were among 50 and 60 years old, 29% were among 60 and 70 years old, and 7% were more than 70 years old.

Table 4: Age distribution in PRK cause

PRK	Percentage of Patients%
Less than 30	21%
30-40	50%
40-50	21%
50-60	8%
60-70	0%
More than 70	0%

Table 5: Age distribution in Trauma cause

Trauma	Percentage of Patients%
Less than 30	29%
30-40	29%
40-50	18%
50-60	16%
60-70	6%
More than 70	2%

The age distribution of patients with PRK (Photorefractive Keratectomy) as the cause is as follows (table 4): 21% were under 30 years old, 50% were between 30 and 40 years old, 21% were between 40 and 50 years old, 7% were between 50 and 60 years old, 0% were between 60 and 70.

The age distribution of patients with trauma as the cause is as follows: 29% of patients were under 30 years old, 29% were between 30 and 40 years old, and another 18% fell within the 40 to 50 age group. Additionally, 16% of patients were between 50 and 60 years old, 6% were between 60 and 70 years old, and only 2% were over 70 years old.

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DISCUSSION

RCES is a frequently occurring illness that impacts the structures responsible for connecting the epithelium to its basement membrane and the front part of the cornea [3,8]. The fragility of the epithelium is responsible for the eye pain and the repeated erosions. It has been shown to happen at any age and with equal frequency in both males and females. It is most commonly linked to prior eye injuries and dystrophy of the basement membrane (EBMD) [4].

The demographic characteristics of the series of 500 patients are consistent with those described before. The distribution of gender is 54% men and 46% women, with an average age of 44.5 years and a range of 15 to 85 years [3]. It is worth mentioning that although there was a wide range of ages, the majority of patients were in younger years (70% were between the ages of 30 and 40). Furthermore, this seemingly typical age distribution displayed variations in relation to the etiology of RCES. Among the patients in the series, trauma was the most prevalent etiology, accounting for 45% of cases. These were mild injuries caused by small items that resulted in the erosion of the epithelium layer. Typically, these injuries would heal within a few days. The nail was the most commonly encountered traumatic object, particularly among children in the presence of their parents or caretakers. Additionally, there were reports of other distressing items such as a sheet of paper or plastic, a toy soldier, a nut, a straw hat and makeup tools. The erosions that occurred as a result did not cause any cloudiness in the cornea. Interestingly, these erosions did not appear to be tied to the specific area of the epithelium that was afflicted by the disease.

EBMD is a frequent underlying factor for RCES, affecting approximately 17.1% of patients. The reported percentage in this series is comparatively less than the percentages reported in previous studies ([9] 29% and [2] 19.7%). This apparent disparity may be attributed to the utilization of highly rigorous criteria for EBMD. Commonly, the eye that is impacted in Recurrent Corneal Erosion Syndrome (RCES) exhibits the presence of microcysts and changes in the basement membrane. Nevertheless, the study exclusively enrolled patients in the EBMD group who had similar characteristics in both eyes. It was hypothesize that changes in the basement membrane of the affected eye may result from the disease, which frequently involves recurring erosions. However, it remains uncertain whether these alterations in the basement membrane are a fundamental cause or a result of prior erosions.

A notable discovery was that prior PRK treatment in 31 (16.75%) was a common factor contributing to RCES, which was shown to be the same percentage as for EBMD. The literature has already documented the correlation between keratorefractive surgeries (PRK, LASIK, and Intra-LASIK) and Recurrent Corneal Erosion Syndrome (RCES) [10-13]. PRK is the procedure that is most commonly linked to Recurrent Corneal Erosion Syndrome (RCES) in the study. This discrepancy could perhaps be attributed to a sampling bias, for as in a medical facility where a greater proportion of surgeries are conducted with PRK compared to LASIK. Nevertheless, LASIK is performed more often than PRK in the specific context. Based on the research, it is recommended to consider PRK as a contributing factor to the risk of Recurrent Corneal Erosion Syndrome (RCES). It is quite contradictory when it was taken into account that PRK, specifically in its phototherapeutic keratectomy (PTK) form, has been shown to have one of the most successful outcomes in treating RCES. Treatment with PTK or the recently discovered alcohol debridement method [14] is founded on the observation that the initiation of a novel process of epithelial healing can generate new adhesive structures that firmly attach to the stroma [15].

Nevertheless, current research shows formation of a new stromal layer can also serve as the inciting factor for RCES. Therefore, the identical protocol can serve as both the source and the remedy, and this contradiction cannot currently be elucidated based on the existing comprehension of the pathophysiology of this condition. Understanding the effects of alcohol debridement, laser treatment, or mechanical removal of epithelium on the occurrence of RCES after Photorefractive Keratectomy (PRK) could be valuable. Among the patients in the study, the majority of those who had PRK underwent epithelial removal using 20% alcohol concentration. However, in several instances, the epithelium was removed by scraping.

Conversely, the group exhibited a significant prevalence of MGD. The elevated concentrations of metalloproteinases present in matrix observed in MGD have been hypothesized to be a contributing factor, or at least a factor that promotes the structural alterations within basement membrane of individuals with RCES [16,17]. The study conducted a thorough examination in each instance to determine the presence of MGD, as it plays a crucial role in illness management. 60% of the patients exhibited moderate to severe MGD, necessitating cure. The large proportion mentioned is challenging to compare and contrast with a healthy population due to the limited availability of prevalence data, partly because of the inconsistent manifestation of MGD [18]. A recent study found that 30% of a healthy population had a prevalence of

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dry eye. Additionally, in a study conducted in Spain, it was observed that 45% of individuals with dry eye had Meibomian Gland Dysfunction (MGD) [19]. Therefore, the discovery of a 60% prevalence might be viewed as significantly higher than the average and would provide evidence for the connection among MGD and RCES, which is commonly reported in practices. However, it was believe that additional population research on Meibomian Gland Dysfunction (MGD) and its correlation with different ocular surface disorders are required. Remarkably, in the series, the occurrence of MGD increases to 75% in the "uncertain" group of patients but drops to approximately 35% among individuals with EBMD.

When analyzing the age of patients based on causative groupings, it was noticed significant variations in the distribution of ages among the various categories. Therefore, the findings indicate that patients who developed RCES as a result of keratorefractive surgery were below than the average age, and significantly younger than patients who were diagnosed with Epithelial Basement Membrane Dystrophy (EBMD). The distinction among PRK and EBMD is demonstrated by the fact that 85% of patients undergoing PRK as the underlying cause of recurrent corneal erosion syndrome (RCES) were under the age of 50, while 64% of the EBMD group were over the age of 50 (Fig. 4). This disparity can be elucidated by the average age of individuals undergoing this operation and the average age at which EBMD manifests. Epidermolysis bullosa dystrophica (EBMD) can manifest from the age of 30 onwards, particularly in women, but it becomes more common after the age of 50. Patients with traumatic causes were likewise below the average age of all cases.

Generalizability

The generalizability of the study findings may be somewhat limited due to the single-center setting at Netaji Subhas Medical College and Hospital, which may not fully represent populations from other regions or healthcare systems. Additionally, the specific inclusion and exclusion criteria and the focus on patients with Recurrent Corneal Erosion Syndrome (RCES) associated with certain factors like trauma, surgeries, and Meibomian Gland Dysfunction (MGD) may not encompass all RCES cases. However, the relatively large sample size of 200 patients provides a solid basis for drawing conclusions that could be relevant to similar patient populations in comparable clinical settings. Further multi-center studies would enhance the broader applicability of these results.

CONCLUSION

The study has outlined the various patterns of RCES placement based on its etiology. Additionally, it was discovered that both PRK and LASIK forms of refractive surgery can potentially induce RCES, while PTK is a contributing factor is also a preferred treatment for this condition. In conclusion, the study has discovered an association between Recurrent Corneal Erosion Syndrome (RCES) and Meibomian Gland Dysfunction (MGD). This correlation should be considered when making therapeutic decisions for the treatment of this condition. Additional research is needed to examine the pathways via which MGD can promote RCES.

Limitations

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

RECOMMENDATION

The study recommends that Recurrent Corneal Erosion Syndrome (RCES) should be managed with a focus on addressing underlying causes such as Meibomian Gland Dysfunction (MGD), which showed a strong association with RCES in many patients. It also suggests that keratorefractive surgeries like PRK and LASIK, while identified as contributing factors to RCES, should be carefully considered in treatment plans, and preventive measures should be explored for patients undergoing these procedures. Further research is recommended to explore the role of MGD in RCES and to refine treatment strategies, including the use of phototherapeutic keratectomy (PTK), which has shown promise in managing recurrent cases.

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LIST OF ABBREVIATIONS

RCES - Recurrent Corneal Erosion Syndrome
MGD - Meibomian Gland Dysfunction
EBMD - Epithelial Basement Membrane Dystrophy
PRK - Photorefractive Keratectomy
LASIK - Laser-Assisted in Situ Keratomileusis
PTK - Phototherapeutic Keratectomy

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CONFLICT OF INTEREST

The authors have no conflicting interests to declare.

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