

# FREQUENCY AND RISK FACTORS OF PERSISTENT CORNEAL EPITHELIAL DEFECT IN DIABETIC PATIENTS UNDERGOING PARS PLANA VITRECTOMY

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## Abstract

**Background:** Persistent corneal epithelial defect (PCED) is a significant postoperative complication that can occur after pars plana vitrectomy (PPV), particularly in diabetic patients. It may delay corneal healing, impair visual recovery, and increase the risk of ocular morbidity.

**Objective:** To estimate the frequency and risk factors of persistent corneal epithelial defects (PCED) among diabetic patients undergoing pars plana vitrectomy (PPV).

**Material and Methods:** This Retrospective study was carried out in the outpatient department of ophthalmology at Hayatabad HMC Peshawar Medical Complex from January 2017 to December 2018. The sample of 437 (511 eyes) that underwent PPV from 2017 to 2018 was studied. If the patient had epithelial defects in cornea, edematous cornea or superficial punctate keratopathy within first week after PPV, was labeled as complications of the cornea. However, if the complications of the cornea persist for more than 14 days after conservative treatment, the patient was labeled as a persistent corneal epithelial defect (PCED). The diabetic patients were grouped in two i.e. PCED and non-PCED. The sociodemographic and clinical/ surgical data were analyzed and outcomes were assessed. For statistical analysis, SPSS version 24 was used. P value was calculated and considered significant if it was less than 0.05.

**Results:** After PPV corneal complications were developed among 114 eyes of 437 subjects (22%), while PCED was developed among 38 eyes out of 114 eyes (33%). The chi square P value of PCED, SPK and Corneal Edema were (0.032), (0.003) and (0.936) respectively. Among those eyes that developed complications, 22 eyes progressed to PCED. Poor visual acuity was observed among eyes with PCED with (P = 0.035). After most suitable statistic tests applied to the data, the results showed that among the risk factors of PCED after PPV, diabetes mellitus has significant association.

**Conclusion:** There was an association of diabetes and PCED with p value of (p=0.03). Diabetes mellitus, perfluoropropane intravitreal tamponade, and assistance of first-year resident were among the risk factors. Poor visual acuity was observed among these patients. Initially aggressive treatment is required for patients with corneal epithelial defects after surgery to avoid unfavorable results.

**Keywords:** Diabetes Mellitus, Pars Plana Vitrectomy, Corneal Epithelial Defect.

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## Introduction:

It is estimated that the prevalence of blindness worldwide is 45 million. Among these numbers, many of the people suffered from diseases that could be treated or prevented.<sup>1</sup> Globally among preventable causes of blindness is cataract and among the 2020 vision goals it was placed at the top of the list for the

accomplishment of the vision 2020 initiative,<sup>2</sup> diabetes is among the risk factors of cataract development.<sup>3</sup> The global figure of diabetes is more than 285 million. The International Diabetes Federation states that these statistics will increase to 439 million by 2030.<sup>3</sup> We live in a world where chronic diseases take over and the world faces epidemics of chronic diseases of which

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diabetes is the largest contributor. Diabetic patients who suffer hyperglycemia causes metabolic stress that decreases corneal layers cell density.<sup>4</sup>

The outer coat of the eye ball is constituting by cornea and sclera. It serves as the protective shield of the structures inside the eye. The Avascular part of the eye, cornea provides the structural barrier and protection against infections. The two third of the refractive power is provided by the cornea.

The nonkeratinized stratified squamous epithelium is smooth surface.<sup>5</sup> The optical transparency of cornea is due to its a vascularity regular mosaic model of the layers of the cornea furthermore crystalline play structural role to protect light scattering in the corneal layers.<sup>6</sup>

Slit lamp examination can be performed on subjects to examine corneal surface for any corneal epithelial defects enrolled in clinical trials.<sup>7</sup> Damage to the pumping mechanism of the endothelial layer leads to corneal edema that must be properly analyzed with specular microscopy for any corneal haziness attributed by endothelial damage.<sup>8</sup>

To address this important vision problem postoperatively, it is of immense importance to assess the constancy and susceptibility of the corneal epithelium to prevent damage to the cornea after surgery and minimize edema of the cornea to maintain normal corneal function. Therefore, the study aimed to investigate the clinical presentation and incidence of PCED.

## Material and Method:

**Study Design:** Retrospective study.

**Study Duration:** Two years carried out in the outpatient department of ophthalmology at Hayatabad HMC Peshawar Medical Complex.

**Ethical Consideration:** Ethical approval was obtained from the Ethical Council of the Pakistan Community Ophthalmology Institute HMC Peshawar.

**Inclusion criteria:** All those diabetic patients who required pars plana vitrectomy due to diabetic eye complications like vitreous hemorrhage, tractional retinal detachment macular hole or advance diabetic eye disease at the tertiary level hospital during January 2017 to December 2018 were taken were included.

**Exclusion criteria:** Those patients who did not fill out a consent form or those patients who could affect the statistical analysis as a confounding factor, such as those who suffered from other ocular morbidities like keratitis or keratopathies were excluded.

**Sample size and Sampling:** A total of 437 diabetic subjects were taken as sample from January 2017 to December 2018. These subjects underwent 20 and 23 gauge three ports vitrectomy. The type of silicone gas or oil and other intra operative medicine solution, fluid air exchange, and intra ocular tamponade used depended on the individual clinical situation.

If the patient had corneal epithelial blemishes or corneal edema at least 1 week after vitrectomy, it was labeled as corneal complications like corneal epithelial layer loss. If complications last for more than 2 weeks, the patient was labeled as a persistent corneal epithelial defect (PCED), the criterion was proposed by Hiraoka et al, (5). The diabetic patients were grouped in two categories PCED and NON-PCED.

**Statistical analysis:** SPSS version 24 was used. The data were presented in the form of tables in an organized way. To assess the categorical variables among the two groups in term corneal complications, the chi-square test was used. The logistic regression was used for the analysis of continuous variables. The value of P value was calculated and considered significant if it was less than 0.05.

## Results:

Corneal complications were found in 114 eyes out of 511 eyes among 437 patients who underwent PPV. The frequency of corneal complications like corneal epithelial layer loss after PPV was 22% while PCED occurred among 33% of the eyes out of 114 eyes that had developed corneal epithelial loss. Table 1 shows demographic data and characteristics of the study patients.

|                | Number of Eyes that developed corneal complications | Patients NON-PCED (eyes) | Patient with PCED (eyes) | Predictive Value |
|----------------|-----------------------------------------------------|--------------------------|--------------------------|------------------|
| Number of Eyes | 114                                                 | 76                       | 38                       |                  |
| Gender M/F     | 56/58                                               | 28/28                    | 38/20                    | .73              |
| Mean Age       | 59.19                                               | 58.94 ± 14.65 SD         | 59.73 ± 13.60 SD         | 0.84             |

Clinical features of the subjects under the study are discussed in table 2. Predictive values were calculated using multi variant logistic regression for excepted risk factors for DM, I/VitTemponade, 1st Year Residents were ( $p = 0.035$ ), ( $p = 0.012$ ), ( $p = 0.048$ ) respectively. However, among these risk factors, the most common factors were postoperative ocular hypertension within 2 weeks and was only marginally insignificantly associated with a PCED P value of ( $P = 0.051$ ). Thirty eyes resulted PCED among 114 eyes with corneal complications.

|              | Patients Eyes who have Non PCED | Patients Eyes who have PCED | Predictive Value |
|--------------|---------------------------------|-----------------------------|------------------|
| F/U Duration | 13 ± 12                         | 14 ± 10                     | .97              |

|                                                      |         |          |     |
|------------------------------------------------------|---------|----------|-----|
| Eyes of Patients who had DM (n=114) eyes             | 76      | 38       | .03 |
| During Surgery data                                  |         |          |     |
| MeanTime                                             | 121± 52 | 135 ± 50 | .34 |
| 20G                                                  | 67      | 30       | .65 |
| 23G                                                  | 9       | 8        | .64 |
| Air, Gas, Oil used, (n=114 eyes)                     |         |          |     |
| Room air                                             | 15      | 7        | .48 |
| C3F8                                                 | 26      | 19       | .00 |
| SF6                                                  | 10      | 0        | .45 |
| Silicon Oil                                          | 25      | 12       | .23 |
| <b>Fellows Assisted the surgery among n=114 eyes</b> |         |          |     |
| 1st Year                                             | 21      | 11       | .04 |
| 2nd Year                                             | 30      | 9        | .50 |
| 3rd Year                                             | 20      | 6        | .34 |
| 4th Year                                             | 5       | 12       | 2   |

There were several risk factors that contributed in development of PCED, among which some are listed in table 3. However, ocular hyper tension and time taken in surgery were insignificantly associated.

| <b>Table 3. Predictive P values for risk factors</b> |                |
|------------------------------------------------------|----------------|
| <b>Variables</b>                                     | <b>P Value</b> |
| Diabetes                                             | .03            |
| Surgeon Assistant                                    | .07            |
| C3F8                                                 | .08            |
| Glaucomatous                                         | .13            |
| Time taken in surgery                                | .77            |

It was observed that the PCED progressed to vision-threatening complications. One of the eyes suffered from phthisisbulbi that was the result of endophthalmitis secondary to infectious keratitis.

However, compared to the group without PCED, the PCED group had a visual outcome (77% vs 23%, P = 0.035).

| <b>Table 4. Visual Outcome among the two Groups</b> |                       |                 |                 |                        |                   |                  |
|-----------------------------------------------------|-----------------------|-----------------|-----------------|------------------------|-------------------|------------------|
|                                                     | <b>Pre Surgery VA</b> |                 |                 | <b>Post-surgery VA</b> |                   |                  |
|                                                     | Non-PCED, n 76 eyes   | PCED, n 38 eyes | Predictive alue | Non-PCED, n 76 eyes    | PCED, n = 38 eyes | Predictive Value |
| 6/6-6/12                                            | 6                     | 0               | 0.64            | 4                      | 1                 | 1                |
| 6/18-6/60                                           | 20                    | 8               | 0.82            | 30                     | 7                 | 0.00             |
| <6/60                                               | 50                    | 28              | 2               | 42                     | 30                | 0.035            |

## Discussion:

Among many other retinal diseases from which visual benefit could be obtained by pars plana vitrectomy, diabetic eye disease is one of them. However, there are some comorbidities like diabetes with this procedure which affects the final visual outcome. In diabetic patients occurs diabetic neuropathy damage to corneal nerves layers and prevent healing that further delays the corneal epithelial regrowth and causes endothelium layer of the cornea damage and dysfunction the pump mechanism due to this reason diabetes is a major risk factor for the development of corneal complications and persistent corneal epithelial

defects after PPV.<sup>20</sup> In the current study, cumulative corneal complications were developed among 22% of eyes and PCED occurred among 33% of the eyes. However, it was also noted that complications could be reversed if treated in a timely and early manner, however past literature shows 5 to 11% incidence.<sup>1,6,7</sup> For the associated risk factors, a multivariate analysis of PCED was performed, which showed an association with diabetes. In previous studies, intraoperative debridement was necessary for visual clarity during the procedure in approximately 2.3% to 32% of patients, however our study shows lower rate of <2% of patient.<sup>1,6-8</sup> This could be due to the high professional techniques of our Vitreo Retinal surgeons and the high standard instruments used in the procedure.

The assistance of a first-year resident was associated with corneal complications and PCED, this association could be justified since these residents are less trained and exposed. The unit administration assigns a Fellow and a Resident to the Surgeon during surgery. These findings are consistent with that of study conducted by Chen HF, they justified the same reason that one resident would be assigned to the vitreoretinal surgeon for the whole month regardless of the duration of the surgery and would be responsible for holding the lens close to the cornea that could leads to direct corneal trauma intraoperatively.<sup>21</sup>

The operative time of the first-year resident and the senior resident was not very different, so the PCED was not associated with the operative time in a significant way (P Value = .563). In some reports, it was suggested that operative time could be associated with PCED, but in our study there was no such importance. The mean surgical time duration shows no significant differences among two groups. Therefore, this could imply that diabetic patients have association with compromised corneal disease than surgery duration.

In addition to intraoperative epithelial debridement of the cornea, direct trauma during surgery is also a risk factor that could be avoided by wearing contact lenses in acute-onset Epithelial Defect. Therefore, it is recommended in the new training for the residents to use the non-contact visualization system to better protect the corneas in high-risk patients. The high risk factor for Corneal Epithelial Defect is diabetes mellitus, which is also reported in other studies.<sup>1,6-9</sup> Since wound healing is the challenge in diabetes, this could be associated with delayed healing of corneal complications among diabetics,<sup>10,11</sup> this could be the result of deficiencies in the function of the epithelial barrier,<sup>12,13,14</sup> resulting in damage to the whole corneal layers and ultimately leads to corneal opcity.<sup>13,15,16</sup>

The results show a highly significant association of PCED with the use of C3F8 in PPV surgery. When it was analyzed further, it became known that aphakic or pseudophakic were significantly associated with

corneal complications. Corneal endothelial damage was also associated significantly with C3F8.<sup>13</sup> The present study also elaborated the strong association of PCED with intraocular C3F8 gas tamponade. Postoperative intraocular hypertension risk for developing corneal abnormalities<sup>17,18</sup> However, anti-glaucoma drugs itself can cause corneal toxicity. These findings support our results as post-operative hypertension was significantly associated with C3F8.

In the current study, patients who had PCED were not cured earlier and progress to later vision-threatening complications such as corneal opacity. These findings describe the cutoff time of more than 4 weeks for leading of PCED to opaque cornea. This study also shows positive findings of dendritic ulcer development after PPV. The use of corticosteroids topically to control the inflammation that could cause HSV geographic ulcer.<sup>19</sup>

In the current study, melted cornea that required surgical intervention was performed amniotic membrane transplants. To avoid this type of complication, it is strongly recommended to opt for aggressive antiviral treatment of HSV geographic epithelial keratitis. Ophthalmologists face some challenges when treating geographic dendritic ulcers, as they typically take longer to heal.<sup>19</sup> It is associated with inflammation of the stroma, which results in scarring of the cornea, it can also cause secondary glaucoma and cataracts. Long-term use of topical corticosteroids should be minimized after vitrectomy, as it potentially delays the healing and increases the risk of keratitis. Corticosteroid use can be used with extreme caution or can be gradually reduced in patients with corneal epithelial dysfunction over 1 week or more. To facilitate the healing of the corneal tapering of the topical corticosteroids is required.

The literature showed that PCED leads to more corneal infections and corneal opacity which greatly affects the visual outcome of surgery. The limitations of this study are that the diagnosis of geographic ulcer on slit lamp examination of few cases and not on evidence of corneal HSV infection. In addition, the data on other systemic illnesses was taken in questionnaire and was not determined by laboratory investigations. The limitation of the study includes its study design, as a case control study to identify the risk of persistent corneal epithelial defect among the diabetic and non diabetic patients would have more fruitful outcome. Furthermore, systemic comorbidities were only obtained by questionnaires without laboratory investigations for the control level of diabetes such as HbA1C levels.

## Conclusion:

In conclusion, there was an association of diabetes and corneal complications with higher incidence of PCED. The risk factors associated with PCED were Diabetes mellitus, Perfluoropropane intravitreal tamponade. and assistance of first-year resident. Poor

visual acuity was observed among these patients. Initially aggressive treatment is required for patients with corneal epithelial defects after surgery to avoid unfavorable results.

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