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ORIGINAL PAPER

# Clinical characterization of posterior polymorphous corneal dystrophy in patients of Indian ethnicity

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**Abstract**
*Purpose* To characterize the clinical presentation of posterior polymorphous corneal dystrophy (PPCD) in eyes of Indian ethnicity.
*Design* Retrospective cohort study from January 1995 to December 2015.
*Participants* Patients with the diagnosis of posterior polymorphous corneal dystrophy.
*Methods* Medical records of the patients were reviewed for clinical presentation. Histology of corneal specimens of those that underwent keratoplasty was assessed.
*Main outcome measures* Descriptive analysis of clinical condition.
*Results* Mean age at first evaluation was 32.5 years (range 1–73 years), male:female = 35:18. Majority (44/53; 83 %) of the patients had bilateral involvement. 5/9 (44 %) patients with unilateral presentation were amblyopic in the affected eye. The clinical features documented were vesicles in 94 eyes, band-like pattern in 32 eyes, edema of varying degree in 23 eyes (12 patients, 1 patient was one eyed), and anterior segment changes in 1 eye. 8/45 (17 %) eyes had a regular astigmatism with steep axis >47 D (range 47.2–56.2 D). 16 eyes of 12 patients who had clinically evident corneal edema underwent keratoplasty. Mean age at keratoplasty was 58 years (range 1–73 years). 8 patients had penetrating keratoplasty (PK) and 8 had Descemet stripping endothelial keratoplasty (DSEK). Mean follow-up after keratoplasty was 4.2 years (1 month to 13 years). Except one, all grafts remained clear till the last follow-up. In all specimens, the Descemet membrane was grossly thickened.
*Conclusions* In our study, 12/53 (22.6 %) patients required keratoplasty for visually significant corneal edema. Except one, all were older adults. The patients who needed keratoplasty were bilaterally afflicted and had visually significant cornea edema in both eyes. With a mean follow-up duration of 4.2 years after keratoplasty, no recurrences were noted.

**Keywords** Posterior polymorphous endothelial dystrophy · Corneal endothelium · Descemet membrane · Dystrophy · Keratoplasty

Posterior polymorphous corneal dystrophy (PPCD) is a dominantly inherited corneal endothelial dystrophy that is associated with a varied phenotype, ranging from asymptomatic corneal endothelial changes to corneal edema and glaucoma [1]. The genome-wide linkage analyses on different families with PPCD have identified several gene loci responsible for this condition. These include the long arm of chromosome 20

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(20p11.2-q11.2) designated as PPCD 1, the short arm of chromosome 1 (1p34.3-p32) designated as PPCD 2, and the short arm of chromosome 10 (10p11.2) now designated as PPCD 3 [2–4].

Exact prevalence of this form of corneal dystrophy is unknown. A high prevalence of this dystrophy is reported in the Czech Republic [5]. It is possible that its prevalence is more than what is expected and reported in literature as a vast majority of the patients are asymptomatic and many cases may fail to be recognized in the clinic. The diagnosis of PPCD is recognized with slit-lamp biomicroscopic findings of corneal endothelial vesicles, bands, and geographic placoid opacities. Even with a considerable amount of clinical experience, PPCD can be confused with Fuchs endothelial dystrophy, Iridocorneal endothelial syndrome, and congenital hereditary endothelial dystrophy (CHED). The clinical findings and pathology of this entity are considerably different, and hence, an attempt must be made to characterize them to the best of the precision. A positive family history, histopathological features of multilayered endothelium with cytokeratin positivity, and genetic testing may help in making an accurate diagnosis in confusing case scenarios. Most of the cases are non progressive, asymptomatic, and corneal edema is rare to develop, and hence the condition is often diagnosed on a routine eye exam [1].. Several associations have been described such as corneal steepening, high myopia, and Alport's syndrome [6–8].

The purpose of this study was to characterize the clinical presentation of PPCD in eyes of Indian ethnicity.

## Methods

A retrospective analysis of 98 patients with a diagnosis of PPCD from 1995 to 2015 was done. As the study spanned over a period of 20-year retrospective data analysis, those medical records which were illegible (old scanned records), or where the diagnosis was questionable or documentation of clinical lesions incomplete or had a confounding event such as a prior intraocular surgery were excluded (Total added up to 45) from the analysis. This was to avoid ambiguity and uncertainties in the diagnosis of the condition.

A total of 53 medical charts were identified and reviewed for the clinical presentation, systemic history, familial history, and management plan. Of these 53 patients, 16 eyes of 12 patients underwent keratoplasty for endothelial dysfunction. The histology of the corneal specimens was reviewed.

**Table 1** Clinical features of the study population

| Parameters | Observations |
|---|---|
| Mean age at presentation | 32.5 years (range 1–73 years) |
| Male:female | 35:18 (66 %:34 %) |
| Laterality | 44(83 %)—bilateral, 9(17 %)—unilateral |
| | Meridional amblyopia—5/9 unilateral |
| Cornea and anterior segment features | Vesicles—94 eyes |
| | Bands—32 eyes |
| | Corneal edema of varying degree—23 eyes |
| | Anterior segment changes(corectopia, ectropion uvea, peripheral anterior synechiae)—1 eye |
| Topographic features ($N = 45$ eyes of 25 patients) | Steep cornea—8 eyes |
| | Mean K in keratoplasty eyes—43.2 D (range 40–46) |
| Keratoplasty | Performed in 16 eyes of 12 patients |
| | (DSEK—8 eyes, PK—8 eyes) |
| | Mean age of keratoplasty patients—52 years (1–73 years) |
| | Mean follow-up—4.2 years (1 month–13 years) |

## Results

### Demographics

Mean age at first evaluation was 32.5 years (range 1–73 years), male:female ratio was 35:18. 6/12 (50 %) patients that needed keratoplasty gave a definite history of an affected family member (either a parent or sibling) who had undergone keratoplasty in at least one of the eyes for a corneal pathology similar to that in the patient; remaining five patients were either unsure or unaware. 4/12 (44 %) patients that had a keratoplasty done had diabetes. The patients in whom keratoplasty was required had bilateral progression of corneal edema and needed surgery in both eyes for endothelial dysfunction (Table 1).

### Clinical features

The clinical features documented were vesicles in 94 eyes, band-like pattern in 32 eyes, edema of varying degree in 23 eyes (12 patients, 1 patient was one-eyed), and anterior segment changes in 1 eye. 2 patients had esotropia, 1 had an absolute eye secondary to lens-induced glaucoma, and 1 patient had extensive myopic chorioretinal degeneration with a neovascular membrane.

Majority (44/53; 83 %) of the patients had bilateral involvement. 5/9 (44 %) patients with unilateral presentation had meridional amblyopia in the affected eye. Table 2 shows the clinical characterization of the unilateral cases. Figures 1 and 2 illustrate the representative cases that had a unilateral involvement.

12 patients had presented to the clinic with complaints of gradually decreasing vision due to corneal edema, 4 patients complained of noticing poor vision in one eye; the remaining visited the clinic either for a routine eye check, consideration of laser refractive surgery, or for diminished vision attributed to causes other than the corneal pathology.

Corneal topography (either Orbscan II/Oculyzer/Galilei) was documented in 45 eyes of 25 patients. 8/45 (17 %) eyes had a symmetric astigmatism with steep axis >47 D (range 47.2–56.2 D). Mean keratometry in patients ($n = 12$ eyes, 7 patients) that underwent keratoplasty was 43.92 D (range 42.5–46). Mean keratometry in eyes that did not require keratoplasty was 45.75 D (range 41.3–55.15).

**Table 2** Clinical characteristics of patients with unilateral involvement (Unilateral PPCD)

| Case | Age (years) | Sex | Clinical features OD | Clinical features OS | BCVA OD | BCVA OS | Manifest refraction OD | Manifest refraction OS | Mean K OD (D) | Mean K OS (D) | ECD OD | ECD OS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 17 | M | Vesicles, bands | – | 20/50 | 20/16 | +1.5/+2.5 × 100 | plano | – | – | – | – |
| 2 | 21 | M | – | Bands | 20/20 | 20/200 | −2.5 | +3.5/−6 × 180 | 43 | 47.5 | – | – |
| 3 | 32 | F | Vesicles, bands | – | 20/30 | 20/20 | −2.5 × 10 | plano | – | – | – | – |
| 4 | 24 | F | Bands, vesicles | – | 20/20 | 20/20 | −5 | −5 | 46 | 46.5 | – | – |
| 5 | 27 | M | – | Bands | 20/20 | 20/20 | −4.5 | −4 | 48.2 | 47.9 | – | – |
| 6 | 23 | F | – | Bands | 20/20 | 20/20 | −7/−1.75 × 10 | −9/−1.75 × 180 | 45 | 45.8 | 2360 | 2006 |
| 7 | 7 | F | – | Bands, vesicles | 20/20 | 20/60 | +1/−1 × 90 | +1.75/−2 × 140 | 43.2 | 44.6 | 3133 | 764 |
| 8 | 25 | M | Bands, vesicles in peripheral cornea | – | 20/30 | 20/20 | −2.5 × 170 | Plano | 47.5 | 44.2 | 1546 | 3126 |
| 9 | 26 | M | Bands involving the central cornea | – | 20/20 | 20/20 | −0.75 | −1.5 | 42.3 | 41.3 | 1176 | 2641 |

*BCVA* best corrected visual acuity, *K* keratometry, *ECD* endothelial cell density)

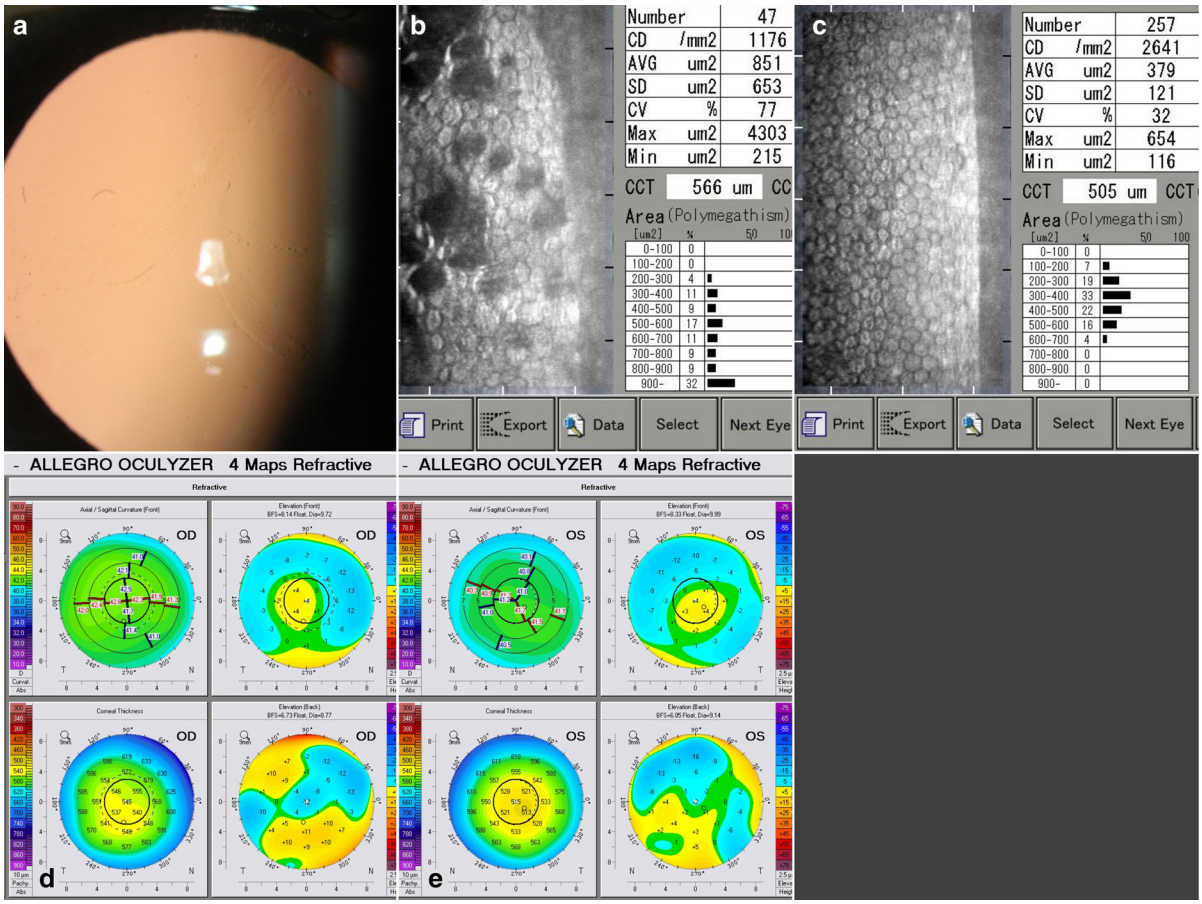


**Fig. 1** (**a**–**e**) Representative case (case no 9 in Table 2) that had endothelial abnormalities in one eye (right eye); **a** slit-lamp photograph in retroillumination showing the band-like pattern at the level of Descemet membrane endothelial complex; **b** specular microscopy of the involved eye showing the endothelial morphological abnormality and reduced endothelial cell density(=1176 cells/mm$^{2)}$ in the right eye; **c** specular microscopy of the normal left eye(endothelial cell density = 2641 cells/mm$^2$); (**d**, **e**) tomography maps showing $K_m$ of 42.3 and 41.3 D in the right and the left eye, respectively

## Keratoplasty

16 eyes of 12 patients who had clinically evident corneal edema underwent keratoplasty at the institute. Mean age at keratoplasty was 58 years (range 1–73 years). One patient had bilateral symmetrical corneal edema at the time of birth and was initially diagnosed with CHED. However, the corneal specimen had histological features and cytokeratin study consistent with PPCD. 8 patients had PK and 8 had DSEK. Mean follow-up after keratoplasty was 4.2 years (1 month to 13 years). Except one, all grafts remained clear till the last follow-up. One eye developed persistent graft edema when cataract surgery was performed 13 years after keratoplasty. 5/16 eyes had transient episode of raised intraocular pressures after keratoplasty which was controlled with a single anti glaucoma medication. There were no recurrences of the primary pathology in the graft.

## Histology

Histology was available for 13 specimens. In all specimens, the Descemet membrane was grossly thickened but without any evidences of guttae as is characteristic of Fuchs Endothelial dystrophy; multilayering of endothelial cells was seen in 9 and pan-Cytokeratin positivity was seen in 8 specimens. Figure 3a and b shows the histology of representative case that underwent DSEK. Figure 3c and d shows the

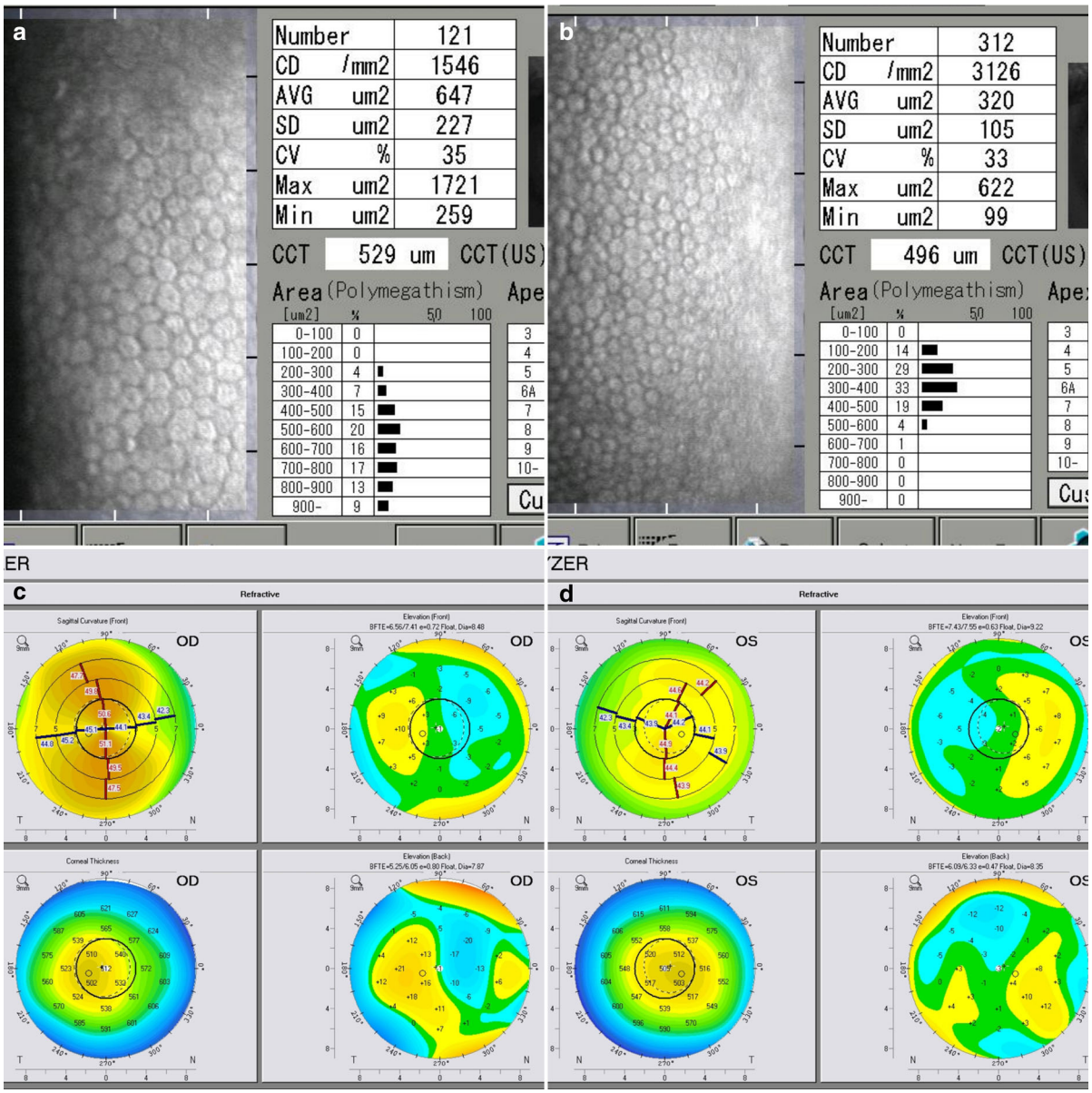


**Fig. 2** (**a**–**d**) Representative case (case no 8 in Table 2) showing a unilateral involvement (right eye); **a**, **b** specular microscopy image of the right eye showing reduced endothelial cell density (=1546 cells/mm$^2$) and increased mean cell area compared to the normal left eye (endothelial cell density = 3126 cells/mm$^2$); **c**, **d** tomography maps showing the with-the-rule astigmatism in the affected right eye, $K_m$ of 47.5 D in the right eye and 44.2 D in the left eye

histology of the 1-year-old child who underwent penetrating keratoplasty.

## Discussion

PPCD is a genetically heterogenous condition with extremely variable expression. Lesions generally develop in early childhood and are mostly bilateral but may be asymmetrical or unilateral in some cases. Most patients are asymptomatic with no corneal edema, but progressive visual impairment due to stromal clouding may occur later in life. Rarely, corneal edema may be seen right at the time of birth [9]. In the largest series of PPCD cases reported (120 individuals), thirteen (10.8 %) patients required

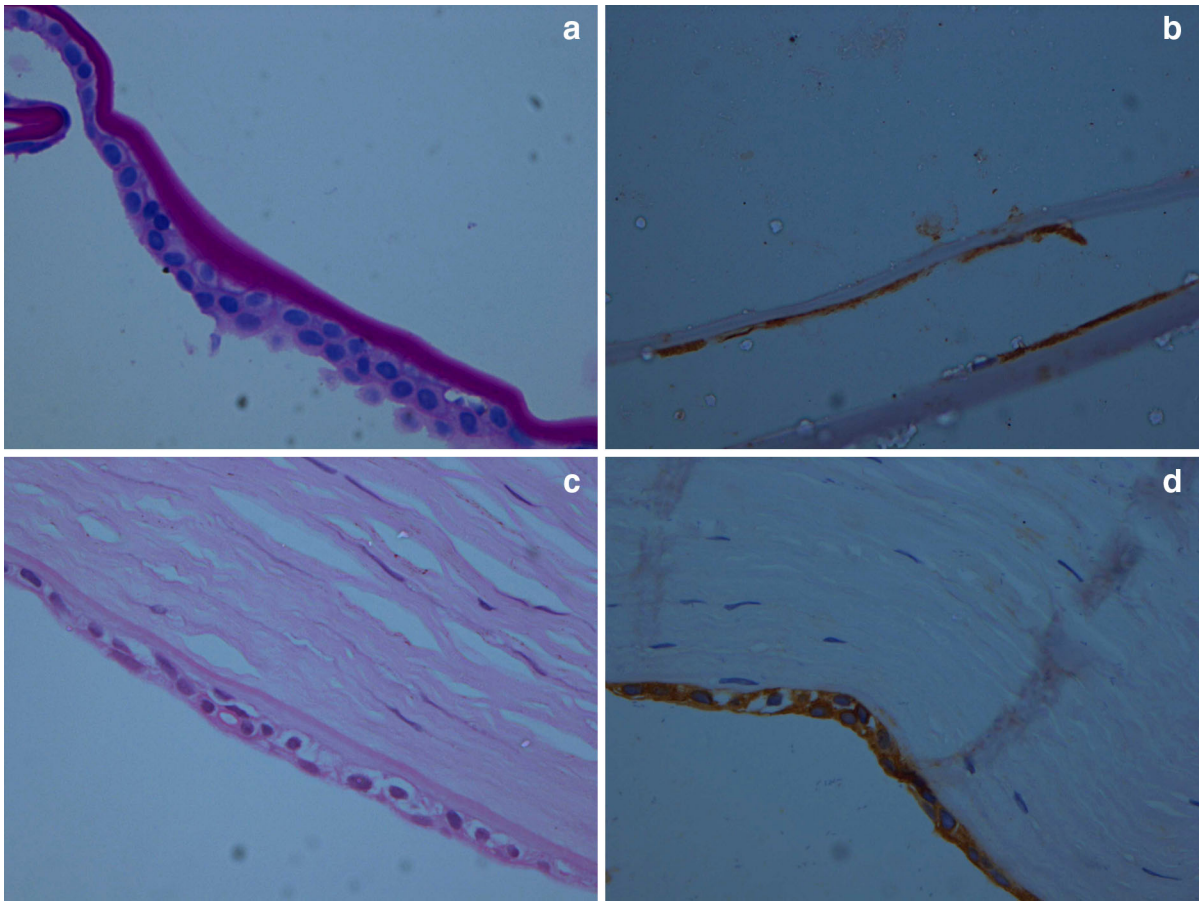


**Fig. 3** **a** Histology of the stripped Descemet membrane of 59-year-old male patient who underwent DSEK, 40×; **b** the same specimen showing positivity for cytokeratin marker; **c** histology of full-thickness corneal button of 1-year-old child who underwent PK. Note the multilayering of the cells and thickened Descemet membrane, 40×; **d** cytokeratin positivity seen in the corneal specimen

corneal transplantation [10]. In our study 12/53 (22.6 %), patients required keratoplasty. All were bilaterally afflicted and had visually significant cornea edema in both eyes. All of these were older adults except one case who had bilateral edematous corneas right at birth. This child was referred to us at the age of 1 year for a congenital glaucoma. 50 % of the patients with corneal edema had a definite positive family history of one affected family member. The parents of the child who had congenital corneal edema were, however, normal. These are relevant clinical associations and should be asked for in these subjects to understand the likely course of the disease when seen in the early stages. A positive family history and a corneal edema in one eye at the time of presentation put the patient at a risk of developing corneal edema in future, necessitating a keratoplasty. Keratoplasty in PPCD has a good success rate [1]. There are reports of recurrences of the condition in the graft. In this study, within a mean follow-up duration of 4.2 years, no recurrences were noted.

Aldave et al. have observed corneal steepening in some patients with PPCD and suggested that the eyes with corneal steepening may be at higher risk of endothelial dysfunction. In this study, there was, however, no difference in the mean keratometry of patients that required keratoplasty versus those who did not. More studies with a long-term follow-up are needed to investigate this association. It has been observed that in bilateral cases of PPCD, the more affected eye has a greater degree of astigmatic error, presumably causing amblyopia in that eye [11]. Also,

there are a few reports of unilateral PPCD with an astigmatic error in the affected eye and hence leading to anisometric/ meridional amblyopia [12]. We found that 5/9 cases of unilateral PPCD had meridional amblyopia in the affected eye. An important difference in this study population was a relatively low frequency of iris and angle anomalies. The good prognosis following keratoplasty can be attributed to the absence of anterior segment lesions in this study population. Although one patient had unilateral involvement of the anterior segment and underwent keratoplasty (DSEK) in both eyes, there was no evidence of raised intraocular pressure and disc changes in the follow-up period of 8 years.

The literature on PPCD from different geographical areas reports a wide and variable range of phenotypic parameters. Most of the clinical studies are limited to case reports and a few large series. Apart from the endothelial morphological abnormalities, reduced endothelial cell densities have been shown in most studies [1, 10]. The association with steep corneas and glaucoma is variably reported [6, 7, 12–14]. Some studies have also reported an association with extraocular abnormalities [15, 16]. In our study population, all proposed features were noted except for glaucoma and associated extraocular abnormalities.

This study was a retrospective analysis, and hence, the genetic characterization was not ascertained in the patient population. Genetic analysis is in way for the some of the subjects included in this study. Utmost care was taken to include the subjects in the study. Only those records where a proper documentation was available and/or histology was corroborative were included in the analysis.

The variability in the clinical presentation and the course of this condition needs a continued investigation. Considering the variable phenotypes in this relative rare endothelial dystrophy and paucity of literature on its prevalence, it would be useful to have collaborative multicenter studies to ascertain its true prevalence and genotype–phenotype clinical correlation from various parts of the world.

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**Author's Contribution** Design and conduct of the study: SCH; collection, management, analysis, and interpretation of the data: SCH, RM, BG; preparation of the manuscript: SCH; review of the manuscript: SCH, MDR; final approval of the manuscript: SCH, MDR, RM, BG, DM, SIM.

**Compliance with ethical standards**

**Conflict of interests** None.

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