

Clinical profile and demographic distribution of pellucid marginal corneal degeneration in India: A study of 559 patients

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Purpose: The aim of this study was to describe the clinical profile and demographic distribution of pellucid marginal corneal degeneration (PMD) in patients presenting to a multitier ophthalmology hospital network in India. **Methods:** This cross-sectional hospital-based study included 2,470,793 new patients presenting between September 2012 and September 2020 (~8 years period). Patients with a clinical diagnosis of PMD in at least one eye were included as cases. The data were collected using an electronic medical record system. **Results:** Overall, 559 (0.02%) new patients were diagnosed with PMD. The prevalence rates were 0.004% in children (age <16 years) and 0.03% in adults. The majority of patients were males (70.13%) with the bilateral affliction (77.1%). The mean age of the patients was 37.91 ± 13.19 years. The majority (30.23%) of the patients were between 31 and 40 years of age. A significant number of patients were from higher socioeconomic status (93.74%) and from the urban region (45.08%). Of the 990 eyes, the most common clinical signs were ectasia/thinning (58.99%), corneal scar (17.47%), and corneal hydrops (1.01%). The majority of the eyes (87.97%) were managed with either spectacles or contact lenses. Among those who had surgical intervention, collagen cross-linking was the most performed procedure (5.25%) followed by cataract surgery (4.14%). **Conclusion:** PMD is a rare disease affecting patients seeking eye care in India. It commonly affects adult males and is bilateral in nature. The disease progression is slow and usually occurs beyond 3 years. Conservative management is more common than surgical intervention.

Key words: Ectasia, electronic medical records, pellucid marginal corneal degeneration

Pellucid marginal corneal degeneration (PMD) is a progressive, noninflammatory ectatic corneal disorder that more commonly involves the inferior cornea separated from the limbus by a relatively uninvolved area of 1 to 2 mm in width.^[1] The term *pellucid* meaning “clear” to denote the corneal clarity was used for the first time by Schlaeppli.^[2] The corneal area between the thinned band-like region and the limbus is characterized by the absence of lipid deposition, scarring, or vascularization and is typically epithelialized. The degree of thinning of the cornea can be severe resulting in up to 80% stromal tissue loss.^[3] This “beer belly” configuration causes the cornea superior to the ectasia to protrude and produces a flat vertical meridian above the thinning and a high against-the-rule astigmatism. The corneal protrusion is more marked just superior to the area of thinning where the thickness of the cornea is usually normal.^[4,5] While the classic presentation of the disease is inferior thinning, there are reports with involvement of the superior, temporal, and nasal parts of the cornea.^[6-9]

PMD is a slowly progressive condition that more commonly occurs between the second and fifth decades of life.^[10] The treatment of PMD is mostly conservative with spectacles and contact lens with certain patients requiring surgical intervention like collagen cross-linking^[11] or keratoplasty.^[12] According to

epidemiological studies about the incidence and prevalence of PMD, it is considered as a rare condition and less common than other ectatic corneal conditions such as keratoconus.^[13] There is a paucity of literature on the prevalence and demographic distribution of PMD in the Indian population.

The aim of the authors in this study is to present the clinical profile and frequency distribution of PMD at a large multitier ophthalmology network in India using electronic medical record-driven analytics.

Methods

Study design, period, location, and approval

This cross-sectional observational hospital-based study included all patients presenting between September 2012 and September 2020 to an ophthalmology network spread across four adjacent neighboring states (Telangana, Andhra Pradesh, Odisha, and Karnataka) of India.^[14] A standard consent form for electronic data privacy was filled by the patient or the parents or guardians of the patient at the time of registration. None of the data that were used for analysis had identifiable parameters of the patient. The study adhered to the Declaration of Helsinki

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and was approved by the Institutional Ethics Committee. The clinical data of each patient who underwent a comprehensive ophthalmic examination using a standardized template was entered into a browser-based electronic medical records system (eyeSmart EMR) by uniformly trained ophthalmic personnel and supervised by an ophthalmologist.^[15]

Cases

A total of 2,470,793 new patients of all ages presented to the tertiary and secondary centers of the network during the study period. The eyeSmart EMR was initially screened for patients with (a) corneal findings suggestive of PMD (defined as the presence of corneal thinning with ectasia of the normal cornea above or below the area of thinning, with no evidence of vascularization, or lipid deposition), (b) suggestive corneal topography findings such as flattening of the cornea along the vertical meridian and marked against the rule astigmatism, and (c) a final diagnosis of PMD in one or both eyes. A total of 559 patient records were identified who had symptoms, signs, visual acuity, clinical impression, and plan of management that corroborated with a diagnosis of PMD and were labeled as cases (representative images in Figs. 1 and 2).

Data retrieval and processing

The data of 990 eyes of 559 new patients included in this study were retrieved from the electronic medical record database and segregated into a single Excel sheet. The columns included the data on demographics, clinical presentation, corneal topography, and ocular diagnosis, and were exported for analysis. The Excel sheet with the required data was then used for analysis using the appropriate statistical software. Standardized definitions were used for occupation, socioeconomic status, and geographic categorization.^[16] The visual acuity was classified according to the World Health Organization guidelines.^[17] The follow-up duration for the topographic analysis was categorized into <1 year, 1–3 years, 3–5 years, and >5 years.

Statistical analysis

Descriptive statistics using mean \pm standard deviation and median with interquartile range (IQR) were used to elucidate the demographic data. Chi-square test (StataCorp., 2015, Stata Statistical Software: Release 14, College Station, TX, StataCorp LP) was used for univariate analysis to detect significant differences in the distribution of demographics features between patients with PMD and the overall population.

Results

Prevalence

Of the 2,470,793 new patients who presented across the eye care network during the study period, 559 patients were diagnosed with PMD in at least one eye, translating into a prevalence rate of 0.02% (95% confidence interval [CI]: $\pm 0.0002\%$) or 226/million population.

Age

The mean age of the patients was 37.91 ± 13.19 years, whereas the median age was 36 (IQR: 28–46) years. The overall prevalence was 0.004% (14/342,035) in children (≤ 16 years) and 0.03% (545/2,128,758) in adults (>16 years). The frequency distribution of PMD showed an increase between 21 and 30 years of age (25.4%) and peaked between 31 and 40 years

of age (30.23%), followed by a gradual decline from 41 to 50 years of age (20.57%) in the subsequent decades thereafter. The decade-wise distribution of the patients is detailed in Fig. 3.

Sex

There were 392 (70.13%) male and 167 (29.87%) female patients with PMD. The overall prevalence was significantly greater ($P < 0.00001$) in males (0.03%; 392/1,333,946) as compared with females (0.01%; 167/1,136,847). The mean and median ages were 37.4 ± 13.32 and 36 (IQR: 28–46) years for men and 39.13 ± 12.8 and 30 (IQR: 30–46) years for women, respectively. The overall mode was 36 years; 36 years for men and 30 years for women.

Rural–urban–metropolitan distribution

There were 252 (45.08%) patients from the urban districts, 177 (31.66%) from the rural districts, and 130 (23.26%) from the metropolitan regions. The overall prevalence was significantly higher ($P < 0.00001$) in the metropolitan community (0.04%; 130/296,488) as compared with the urban (0.02%; 252/1,051,921) or rural community (0.02%; 177/1,122,384).

Socioeconomic status

There were 35 (6.26%) patients from the lower socioeconomic class, 440 (78.71%) from the lower-middle class, 60 (10.73%) from the upper-middle class, and 24 (4.29%) from the upper class. The overall prevalence was significantly higher ($P < 0.00001$) in the higher socioeconomic strata (0.03%; 524/1,845,460) as compared with lower socioeconomic strata (0.01%; 35/625,333).

Occupation

Of the 559 patients, 314 (56.17%) were professionals, 97 (17.35%) were homemakers, 88 (15.74%) were students, 20 (3.58%) were currently not employed (retired or unemployed), 17 (3.04%) were agriculture related, 13 (2.33%) were manual laborers, and in the remaining 10 (1.79%), the occupational category was not available or applicable. The overall prevalence in professionals (0.07%, 314/458,611) was significantly higher ($P < 0.00001$) in comparison with other professionals.

Laterality

The diagnosis of PMD was coded bilaterally (both right and left) in 431 (77.1%) cases and unilaterally (either in right or left eye) in 128 (22.9%) cases. The left eye was affected unilaterally in 86 (15.38%) cases and the right eye in 42 (7.51%) cases.

Presenting visual acuity

In the 990 eyes, mild or no visual impairment (20/20 to 20/70) was seen in 583 (58.89%) eyes, moderate visual impairment ($>20/70$ to 20/200) in 189 (19.09%) eyes, severe visual impairment ($>20/200$ to 20/400) in 76 (7.68%) eyes, Blindness 3 ($>20/400$ to 20/1200) in 137 (13.84%) eyes, Blindness 4 ($>20/1200$ to Perception of light) in four (0.40%) eyes, and Blindness 5 (no perception of light) in one (0.10%) eyes.

Spherical equivalent and astigmatism

In the 990 eyes, emmetropia (-0.50 to $+0.50$ D) was seen in 157 (15.86%) eyes, >-0.50 to -3.00 D (mild myopia) in 310 (31.31%) eyes, >-3.00 to -6.00 D (moderate myopia) in 269 (27.17%) eyes, >-6.00 D (high myopia) in 189 (19.09%) eyes, $>+0.50$ to $+3.00$ D (mild hyperopia) in 31 (3.13%) eyes, $>+3.00$

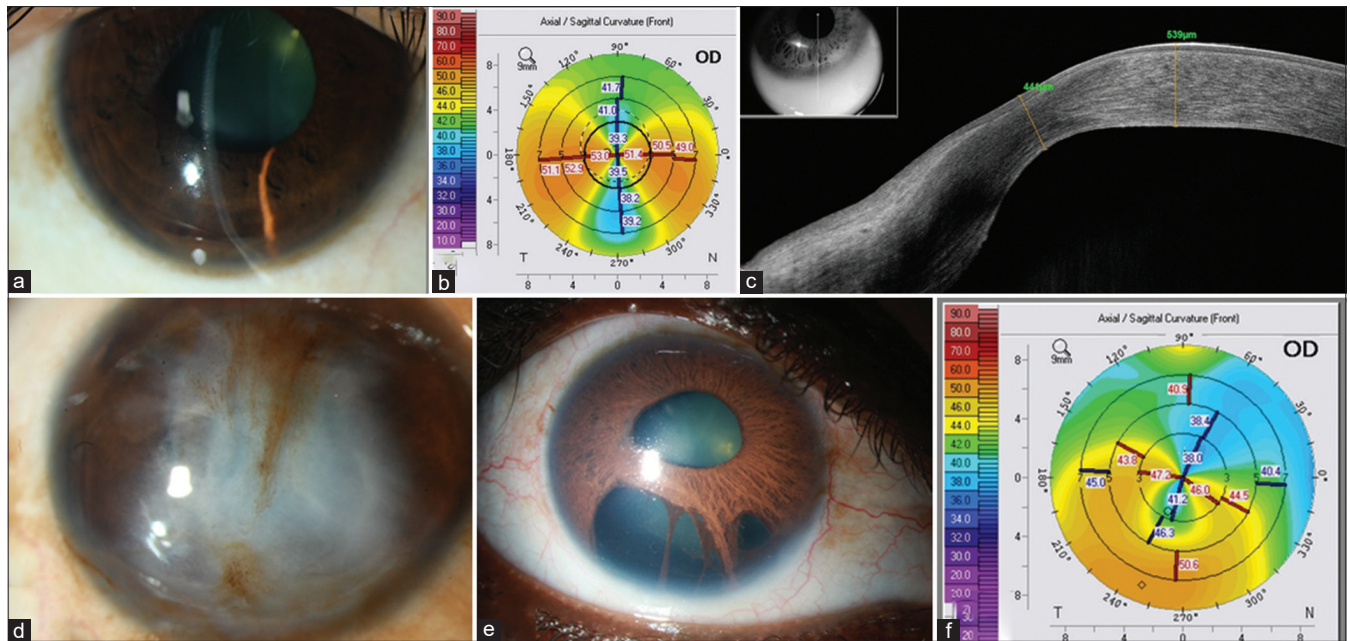


Figure 1: (a-f) Clinical features of pellucid marginal corneal degeneration (PMD) (a): Slit-lamp photograph showing a classic inferior peripheral thinning; (b): corneal topography showing the against-the-rule astigmatism; (c): anterior segment optical coherence tomography showing the area of the peripheral thinning; (d): clinical picture showing scarring following healed hydrops in PMD; (e and f): Slit-lamp photograph (e) and topography (f) of a patient who had Axenfeld–Rieger anomaly associated with PMD

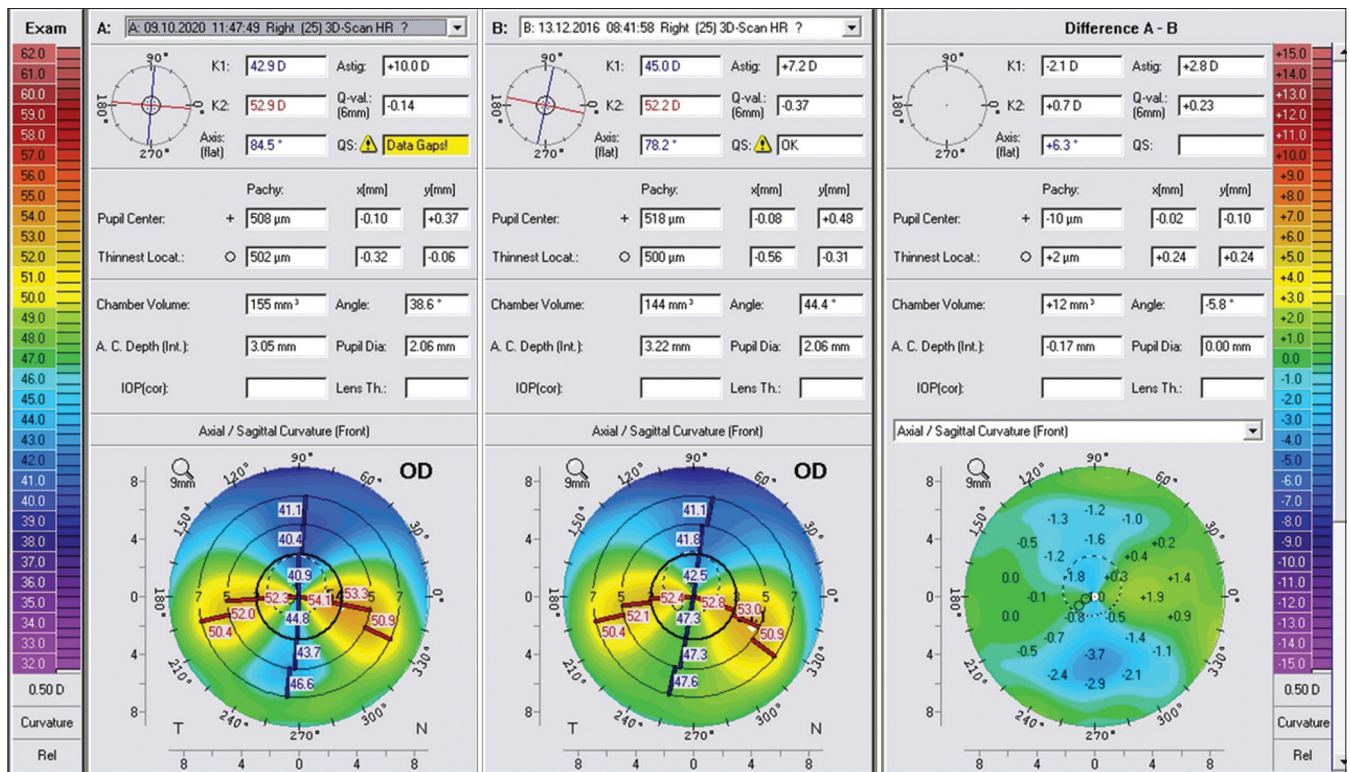


Figure 2: Corneal topography of a 31-year-old female who underwent collagen cross-linking for pellucid marginal corneal degeneration, the 4 years follow-up shows a stable course

to +6.00 D (moderate hyperopia) in six (0.61%) eyes, and >+6.00 D (high hyperopia) in five (0.51%) eyes. The refractive error was not available in 23 (2.32%) eyes. Corneal astigmatism of 0

to 5 D was seen in 522 (52.73%) eyes, >5 to 10 D in 291 (29.39%) eyes, >10 to 15 D in 40 (4.04%) eyes, >15 to 20 D in 10 (1.01%) eyes, and >20 D in five (0.51%) eyes.

Corneal findings

In the 990 eyes, corneal thinning/ectasia was documented on clinical slit-lamp evaluation in 651 (65.76%) eyes, peripheral corneal scar in 173 (17.47%) eyes, and acute corneal hydrops in 27 (2.73%) eyes. The location of thinning was documented as inferior in 392 (39.6%) eyes, superior in 69 (6.97%) eyes, central/paracentral in 52 (5.25%) eyes, peripheral in 28 (2.83%) eyes, and circumferential in two (0.2%) eyes. The associated comorbid conditions were keratoconus in 147 (14.85%) eyes, keratoglobus in 10 (1.01%) eyes, vernal keratoconjunctivitis in six (0.6%) eyes, and Axenfeld–Rieger anomaly in three (0.3%) eyes.

Corneal topography

In the 990 eyes, corneal topography data (via Oculyser/Orbscan II) were available in 842 eyes. The keratometry and

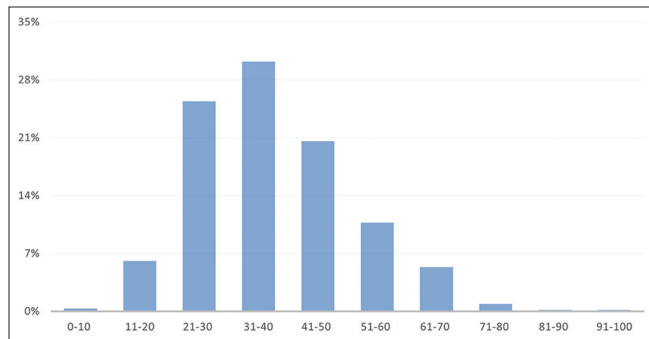


Figure 3: Decade-wise age distribution of pellucid marginal corneal degeneration

pachymetry changes categorized by the duration of follow-up are described in detail in Fig. 4. The average K1 values for a baseline visit and last visit were 43.97 ± 6.36 and 43.92 ± 6 , respectively. The average K2 values for a baseline visit and last visit were 50.87 ± 6.57 and 50.76 ± 5.57 , respectively. The average pachymetry at apex values for a baseline visit and last visit were 488.61 ± 72.89 and 486.56 ± 92.16 microns, respectively. The average thinnest location values for baseline visit and last visit were 459.98 ± 65.54 and 453.8 ± 72.05 , respectively.

Contact lens management

In the 990 eyes, a rigid, gas-permeable lens was dispensed in 277 (27.98%) eyes, PROSE (Prosthetic Replacement of the Ocular Surface Ecosystem) lens in 72 (7.27%) eyes, scleral contact lens in 20 (2.02%) eyes, miniscleral contact lens in 18 (1.82%) eyes, soft contact lens in 11 (1.11%) eyes, soft toric contact lens in four (0.4%) eyes, and keraSoft in one (0.1%) eye, and Rose K2 contact lens was dispensed in one (0.1%) eye.

Surgical management

A significant percentage of the 871 (87.97%) eyes did not require surgical management. The surgical interventions performed in these patients were collagen cross-linking in 52 (5.25%) eyes and cataract surgery in 62 (6.26%) eyes. Six (0.60%) eyes had cataract surgery after the collagen cross-linking. The mean age of the patients who underwent collagen cross-linking was 32.53 ± 11.56 years. The mean age of the patients who had cataract surgery was 52.98 ± 12.56 years. The corneal procedures included penetrating keratoplasty in 16 (1.62%) eyes, anterior lamellar keratoplasty in eight (0.80%) eyes, crescentic patch



Figure 4: Changes in topography parameters (a) K1; (b) K2; (c) pachymetry at apex; (d) pachymetry at thinnest location at 1 year (n = 94), 1 to 3 years (n = 162), 3 to 5 years (n = 44), and > 5 years (n = 9) follow-up

graft in two (0.2%) eyes, corneal tear repair with tissue adhesive in three (0.3%) eyes, and descemetopexy in six (0.61%) eyes.

Discussion

PMD is a rarer form of corneal ectasia when compared with keratoconus, which is far more common. This study sought to describe the clinical profile and demographic distribution of PMD in a large cohort of patients presenting to a multitier hospital network in India using electronic medical records-driven big data analytic. The primary purpose of the study was to determine the relative proportion and demographic profile of this relatively rarer ectasia in a clinical care setup.

The overall prevalence of PMD was 0.02% of all eye diseases diagnosed between 2012 and 2020 (~8 years period). During the same time, the prevalence of keratoconus using electronic medical records diagnosis was found to be 0.62% (31 times commoner than PMD). The condition is known to be predominantly bilateral, and a male predilection has been reported in some studies. An earlier study of 12 years duration between 1990 and 2002 [Table 1], published from the author's institution showed the male preponderance (77.6%) and bilateral nature (100%) of this disease.^[18] In this study, the disease was seen in 70.13% of males; however, bilaterality was present in 77.1%. Furthermore, we found a lesser proportion of eyes having astigmatism of >10 D in our cohort (5.56% vs. 44.5%) in comparison with the earlier study.^[18] The probable reasons for these could be due to the diagnosis of PMD in the

early stages with the improvised diagnostic tools in the more recent years.

The coexisting comorbidities in this study were keratoconus, keratoglobus, and Axenfeld-Rieger anomaly. A minor percentage of patients (0.6%) in this study had vernal keratoconjunctivitis confirming that this association is not strong as was also noted in the previous study at our center.

In this cohort of patients, collagen cross-linking was performed in 5.25%. The majority of the patients were managed with refractive correction with either spectacles or contact lenses. Contact lenses were dispensed in 404 (40.8%) eyes. Keratoplasty (PK [penetrating keratoplasty]– 16 eyes, ALK [anterior lamellar keratoplasty]–8 eyes, crescentic graft– 2 eyes) was needed in 26 eyes.

PMD is known to be a progressive disease, although the rate of progression is not completely known. It is observed to be slower than in keratoconus. We found that the maximum change in keratometry values was seen at >5 years and between 3 and 5 years follow-up period, supporting that the progression of the condition is over several years. Although rare, there are reports of hydrops and the occurrence of spontaneous corneal perforations in PMD.^[19] Spontaneous corneal perforation was seen in two eyes (one eye followed by the other) of one patient in this study. The proportion of eyes that had presented with acute corneal hydrops was lower (2.73%) in the present study compared with the earlier study (6%) at our center. In the

Table 1: Comparison of demographics and clinical profile of patients with pellucid marginal corneal degeneration in the present study versus the earlier study

| Parameters | Previous study (Sridhar <i>et al.</i> ^[18]) | Present Study (Das <i>et al.</i>) | P |
|---|---|---|--|
| Study Period | 1990-2002 (12 years) | 2012-2020 (8 years) | NA |
| Number of Eyes | 116 (58 patients) | 990 (559 patients) | NA |
| Male: Female | 45:13 (77.6% vs. 22.4%) | 392:167 (70.13%: 29.87%) | 0.628924 |
| Laterality | Bilateral | Bilateral 77.1%, Unilateral 22.9% | 0.18471 |
| Mean±SD (range) age in years; at presentation | 34±14.8 (8-66) | 37.91±13.19 (9-92) | NA |
| Location of Thinning | Inferior - 99 (85.3%) eyes Superior - 17 (14.7%) eyes | Inferior - 392 (39.6%) eyes Superior - 69 (6.97%) eyes Circumferential - 2 (0.2%) eyes | <0.00001 0.008471 NA |
| Ocular Comorbidities | Keratoconus - 12 (10.3%) eyes Keratoglobus - 15 (12.9%) eyes VKC - 1 (1.7%) eye | Keratoconus - 147 (14.85%) eyes Keratoglobus - 10 (1.01%) eyes VKC - 6 (0.6%) eyes Axenfeld-Rieger anomaly - 3 (0.3%) eyes | 0.250204 <0.00001 0.744011 NA |
| Complications | | | |
| Hydrops | 6 (7%) eyes | 27 (2.73%) eyes | 0.159053 |
| Spontaneous corneal perforation | - | 2 (0.2%) eyes | NA |
| Management | | | |
| Contact lenses | 31 (26.7%) eyes | 404 (40.8%) eyes | 0.043164 |
| CXL | - | 52 (5.25%) eyes | NA |
| Cataract surgery | - | 62 (6.26%) eyes | NA |
| PK | - | 16 (1.62%) eyes | NA |
| DALK/ALK | 3 (2.58%) eyes | 8 (8.08%) eyes | 0.072584 |
| Crescentic patch graft | 2 (1.72%) eyes | 2 (0.2%) eyes | 0.010492 |
| Corneal tear repair | - | 3 (0.3%) eyes | NA |
| Descemetopexy | - | 6 (0.61%) eyes | NA |

CXL=collagen cross-linking, PK=penetrating keratoplasty, DALK=deep anterior lamellar keratoplasty, ALK=anterior lamellar keratoplasty, VKC=vernal keratoconjunctivitis, NA=not applicable

present study, 17.47% were documented to have scarring in the peripheral cornea. Although the peripheral scarring could be due to varied causes, it is speculated that in some patients, it may have occurred secondary to hydrops in the past.

Conclusion

In conclusion, this study aimed to describe the epidemiology and clinical presentation of PMD in 2.4 million new patients presenting to a multitier ophthalmology hospital network in India. The findings show that PMD is a rare disease affecting patients seeking eye care in India. Although the condition is rare, it should be ruled out in patients presenting with an against-the-rule astigmatism. When examining a patient who has an ectasia at an early age, PMD needs to be kept in mind without excluding keratoconus. PMD commonly affects adult males and is predominantly bilateral in nature. At initial presentation, visual impairment was mild to moderate in a vast majority of the patients, and the most common surgical intervention was collagen cross-linking during the study period. Although the disease progression is slower and usually occurs beyond 3 years, frequent follow-up over an extended period needs to be stressed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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