Clinical profile and demographic distribution of Terrien’s marginal degeneration in a multitier ophthalmology network in India

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Purpose: To describe the clinical profile and demographic distribution of Terrien’s marginal degeneration (TMD) 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 TMD in at least one eye were included as cases. The data were collected using an electronic medical record system. Results: Overall, 184 (0.007%) new patients were diagnosed. Over half of patients were males (56.52%) with bilateral affliction (54.89%). The mean age of the patients was 38.63 ± 16.75 years. Majority (28.26%) of the patients were between 21 and 30 years of age bracket. The number of patients were from rural and urban districts were comparable (41.85% vs. 48.37%). The most common clinical signs were ectasia/thinning (50.33%), corneal scar (44.21%), and prominent nerves (5.26%). Associated ocular comorbidities included vernal keratoconjunctivitis in 6 (2.11%) eyes, meibomitis in 6 (9.7%) eyes, squamous blepharitis in 2 (3.2%) eyes, dry eye in 2 (3.2%) eyes, cataract in 46 (74.2%) eyes, and glaucoma in 6 (9.7%) eyes. Most of the eyes had mild to no visual impairment (43.86%). Two (0.7%) eyes had spontaneous perforation patients. None of patients had hydrops in the years of follow-up. Keratoplasty was performed in 3.86%. Conclusion: TMD is a rare disease affecting patients seeking eye care at the ophthalmology network. It commonly affects adult males and is predominantly bilateral. The disease progression is slow, and risk of spontaneous perforation was low. At initial presentation, visual impairment was mild to moderate in majority and the most common surgical intervention was cataract surgery during the study period.

Key words: Electronic medical records, India, Terrien’s marginal degeneration

Terrien’s marginal degeneration (TMD) is a slowly progressive peripheral ectatic corneal disorder that more commonly involves the superior cornea and characterized by the development of discrete faint subepithelial opacities in the peripheral cornea that progress circumferentially resulting in peripheral furrow formation, corneal ectasia, vascularization, and lipid deposition.[1,2] It is described as more common in males accounting for three-fourth of the cases and two-thirds being older than 40 years.[3] Various etiologies have been proposed that include degenerative origin, inflammatory origin, and phagocytosis of collagen by histiocytes.[4]

There is a paucity of literature on the prevalence and demographic distribution of TMD in the Indian population. The aim of the authors in this study is to present the clinical profile and frequency distribution of TMD at a large multitier ophthalmology network in India using electronic medical record (EMR) 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 4 adjacent neighboring states (Telangana, Andhra Pradesh, Odisha, and Karnataka) of India.[5] 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 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 by uniformly trained ophthalmic personnel and supervised by an ophthalmologist.[6]

Cases

A total of 2,470,793 unique 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 either: (i) corneal findings suggestive of TMD such as peripheral corneal thinning, vascularization, with or without lipid deposition (ii) suggestive corneal topography findings and (iii) final diagnosis of TMD in one or both eyes. A total of

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Received: 16-Mar-2021 Revision: 08-Jun-2021
Accepted: 08-Jul-2021 Published: 26-Nov-2021
184 patient records were identified who had symptoms, signs, visual acuity, clinical impression, and plan of management that corroborated with a diagnosis of TMD and were labeled as cases. Fig. 1 shows the clinical slit-lamp photograph and diagnostic investigations in a representative case of TMD. The methodology of determining cases using EMR database identified the patient diagnosed with TMD only once, either in the first visit or the subsequent visit within the study period.

Data retrieval and processing
The data of 285 eyes of 184 unique patients included in this study were retrieved from the electronic medical record database and segregated in 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. The visual acuity was classified according to the WHO guidelines. 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 ± 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 TMD and the overall population.

Results

Prevalence
Of the 2,470,793 unique patients who presented across the eye care network during the study period, 184 patients were diagnosed with TMD in at least one eye, translating into a period prevalence rate of 0.007% (95%CI: ±0.0001%) or 74/million unique patients seen across the network. The mean days of the patients who visited tertiary center was 864.39 ± 1903.87.

Age
The mean age of the patients with TMD was 38.63 ± 16.75 years while the median age was 37 (IQR: 25–50) years. The overall prevalence was 0.002% (7/342,035) in children (≤16 years) and 0.008% (177/2,128,758) in adults (above 16 years). The frequency distribution of TMD showed an increase between 11 and 20 years of age (n = 19; 10.33%) and peaked between 21 and 30 years of age (n = 52; 28.26%) followed by gradual decline from 41–50 years of age (n = 35; 19.02%) in the subsequent decades thereafter. The decade wise distribution of the patients is detailed in Fig. 2.

Sex
There were 104 (56.52%) male and 80 (43.48%) female patients with TMD. The overall prevalence of TMD was not statistically

Figure 1: Representative slit-lamp photograph, anterior segment optical coherence tomography, and corneal tomography of a 23-year-old female, who presented with TMD in the right eye. The tomography comparison maps show a progression over a follow-up of 3 years (from 2015–2018)
significant ($P < 0.490571$) in males (0.008%; 104/1,333,946) as compared to females (0.007%; 80/1,136,847). Among the patients with TMD, the mean and median age were 36.16 ± 15.71 and 31 (IQR: 24.5 to 46) years for men and 41.85 ± 17.49 and 41 (IQR: 26 to 56) years for women, respectively. The overall mode was 46 years, 28 years for men and 46 years for women.

Rural-Urban-Metropolitan distribution
There were 89 (48.37%) patients with TMD from rural districts, 77 (41.85%) from urban districts, and 18 (9.78%) from metropolitan regions. The overall prevalence of TMD was not statistically significant ($P < 0.42262$) in rural community (0.008%; 89/1,122,384) as compared to the urban (0.007%; 77/1,051,921) or metropolitan community (0.006%; 18/296,488).

Socioeconomic status
There were 39 (21.2%) patients with TMD from the lower socioeconomic class, 132 (71.74%) from the lower-middle class, 9 (4.89%) from the upper-middle class, and 4 (2.17%) from the upper class. The overall prevalence of TMD was not statistically significant ($P < 0.199397$) in the higher socioeconomic strata (0.008%; 145/1,845,460) as compared to lower socioeconomic strata (0.006%; 39/625,333).

Occupation
Of the 184 patients with TMD, 62 (33.7%) were professionals; 43 (23.37%) were homemakers; 36 (19.57%) were students; 16 (8.7%) were agriculture related; 7 (3.8%) were manual laborers; 4 (2.17%) were currently not employed (retired or unemployed), and in the remaining 16 (8.7%), the occupational category was not available/applicable. The overall prevalence of TMD in professionals (0.014%, 62/458,611) was significantly higher ($P < 0.00001$) in comparison to other professions.

Presenting complaints
The presenting complaint was diminished vision since <1 month in 16 (14.4%), 1–6 months in 35 (31.5%), 6–12 months in 30 (27.0%), 12–16 months in 1 (0.9%), 16–20 months in 1 (0.9%), 20–24 months in 1 (0.9%), and >24 months in 27 (24.3%) patients. The median duration of symptoms of patients who visited the hospital was 90 (IQR 0–730) days.

Laterality
TMD was coded bilaterally (both right and left) in 101 (54.89%) cases and unilaterally (either in right or left eye) in 83 (45.11%) cases. The right eye was affected unilaterally in 39 (21.2%) cases and the left eye in 44 (23.91%) cases. The time difference between diagnosing the second eye was 109.78 ± 270.58 days in 83 patients.

Presenting visual acuity
In the 285 eyes, mild or no visual impairment (20/20 to 20/70) was seen in 125 (43.86%) eyes, moderate visual...
impairment (>20/70 to 20/200) in 76 (26.67%) eyes, severe visual impairment (>20/200 to 20/400) in 40 (14.04%) eyes, blindness 3 (>20/400 to 20/1200) in 40 (14.04%) eyes, blindness 4 (>20/1200 to perception of light) in 1 (0.35%) eye, blindness 5 (no perception of light) in 1 (0.10%) eye, and undetermined or unspecified in 2 (0.7%) eyes.

Spherical equivalent and astigmatism
In the 285 eyes, emmetropia (−0.50 to +0.50D) was seen in 132 (46.32%) eyes, −0.50 to −3.00D (mild myopia) in 54 (18.95%) eyes, −3.00 to −6.00D (moderate myopia) in 50 (17.54%) eyes, −6.00D (high myopia) in 20 (7.02%) eyes, >0.50 to +3.00D (mild hyperopia) in 16 (5.61%) eyes, +3.00 to +6.00D (moderate hyperopia) in 10 (3.51%) eyes, and +6.00D (high hyperopia) in 3 (1.05%) eyes. Corneal astigmatism of 0–5D was seen in 130 (45.61%) eyes, >5–10D in 26 (9.12%) eyes, and >10–15D in 6 (2.11%) eyes.

Corneal findings
In the 285 eyes, peripheral corneal thinning/ectasia was documented on clinical slit-lamp evaluation in 144 (50.53%) eyes, peripheral corneal scar in 126 (44.21%) eyes, prominent nerves in 15 (5.26%) eyes, and lipid deposition in 39 (13.79%) eyes. The other associated ocular comorbidities were vernal keratoconjunctivitis in 6 (2.11%) eyes, meibomitis in 6 (2.11%) eyes, squamous blepharitis in 2 (3.2%) eyes, dry eye in 2 (3.2%) eyes, cataract in 46 (16.18%) eyes, and glaucoma in 6 (2.11%) eyes. One (0.3%) eye developed peripheral corneal perforation without trauma, and another (0.3%) had a perforation following injury.

Corneal topography
In the 285 eyes, corneal topography data (via Oculyser/Orbscan) was available in 170 eyes. The average K1 values for baseline visit and last visit were 44.59 ± 5.91 and 43.29 ± 5.65, respectively. The average K2 values for baseline visit and last visit were 52.24 ± 54.87 µm and 53.16 ± 58.09 µm, respectively. The average thinnest location values for baseline visit and last visit were 480.11 ± 93.99 and 468.43 ± 92.87, respectively. The keratometry changes on topography categorized by duration of follow-up are described in detail in Fig. 3.

Contact lens management
In the 285 eyes, a rigid gas permeable lens was dispensed in 25 (8.77%) eyes, scleral lens in 10 (3.51%) eyes, and miniscular contact lens/KeraSoft contact lens/soft contact lens in 1 (0.35%) eye each.

Surgical management
A significant percentage of the 256 (89.82%) eyes did not require surgical management. The most common surgical interventions performed in these patients were cataract surgery in 17 (5.96%) eyes. Corneal procedures included penetrating keratoplasty in 4 (1.4%) eyes, lamellar keratoplasty in 4 (1.4%) eyes, corneal patch graft in 2 (0.78%) eyes, and collagen crosslinking in 1 (0.35%) eye.

Discussion
TMD is a rare form of corneal ectatic condition with an uncertain etiopathogenesis. In this study, we sought to describe the clinical profile and demographic distribution of TMD in a large cohort of patients presenting at a tertiary care network. The overall prevalence of TMD was 0.007% of all eye diseases diagnosed between 2012 and 2020 (~8 years period). During the same time, the prevalence of keratoconus and pellucid marginal degeneration was 0.62% (88 times commoner) and 0.02% (27.28 times commoner), respectively.

In this cohort, the mean age of patients was 38.63 years with a male preponderance in 56.52%, which is comparable to that reported in literature. Bilaterality was seen in 54.89% in comparison to 72% in the study by Chan et al. in a period of 10 years. The rate of progression of TMD is slow over several years. In this study, the mean dioptric change in K1 and K2 values was 1.36, 0.83, and 1.55; and 1.57, 0.60, and 3.50 at <1 year, 1–3 years, and 3–5 years follow-up period [Fig. 2]. The maximum change in thinnest pachymetry (128 µm) was seen at 3–5 years follow-up, compared to 5 and 22 µm at <1 year and 1–3 years. This is corroborative with the slow nature of the progression of this condition. When compared to earlier reports,[10,11] the proportion of eyes with perforation was smaller in our patients (0.7% versus 11.62–15%). None of patients in our study had hydrops in the years of follow-up.

An association between meibomian gland dysfunction and TMD (40%) has been reported.[10,11] In contrast, the association with other ocular surface comorbidities such as vernal keratoconjunctivitis, meibomitis, blepharitis, and dry eyes were seen in only 5.6% eyes in this study, suggesting a weaker association in this cohort.

The majority of patients were managed conservatively, and surgical intervention was required in 3.8% eyes, which included penetrating keratoplasty in 4 eyes, lamellar keratoplasty in 4 eyes, crescentic patch graft in 2 eyes (for perforation), and collagen crosslinking in 1 eye.

This study is based on data obtained from the electronic medical records and has both inherent limitations and advantages. In view of several confounding factors such as user variabilities on EMR and patients’ initial visit to various specialty clinics other than cornea, we could not perform a period-wise analysis of those with bilateral disease, who were initially diagnosed with unilateral disease. The other drawback of electronic medical record system is the completeness of data entry with respect to clinical findings, which may account for some errors. While periodic auditing of electronic records can reduce these errors, these cannot be eliminated. Despite these limitations, the EMR system has several advantages over manual records in generating data for research studies from a large sample size, which can be challenging with manual data entry and likely to have human errors.[12]

Conclusion
In conclusion, this study aimed to describe the epidemiology and clinical presentation of TMD in 2.4 million new patients presenting to a multiter ophthalmology hospital network in India. The findings show that TMD is a rare disease affecting patients seeking care at our network of eye centers. It predominantly affected adult males and was bilateral in majority and slow to progress. Complications such as perforation were low. At initial presentation, visual impairment was mild to moderate in a vast majority of the patients and the most common surgical intervention was cataract surgery during the study period.
Acknowledgement
The authors wish to acknowledge the support of our Department of eyeSmart EMR and AEye team specially Mr. Ranganath Vadapalli and Mr. Mohammad Pasha.

Financial support and sponsorship
Hyderabad Eye Research Foundation, Hyderabad, India.

Conflicts of interest
There are no conflicts of interest.

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