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Clinical profile and demographic distribution of pigment dispersion syndrome: An electronic medical record-driven big data analytics from an eye care network in India

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ABSTRACT

Objectives: The purpose of this study was to describe the demographics and clinical profile of pigment dispersion syndrome (PDS) in patients presenting to a multi-tier ophthalmology hospital network in India.

Material and Methods: This cross-sectional hospital-based study included 2,961,706 new patients presenting between August 2010 and September 2021. Patients with a clinical diagnosis of PDS in at least one eye were included as cases. The data were collected using an electronic medical record system.

Results: Overall, 403 (0.014%) patients were diagnosed with PDS. Three fourth of the patients were male (75.43%) and 91.81% had bilateral affliction. The most common age group at presentation was during the fourth decade of life with 100 (24.81%) patients. In the 773 eyes, 443 (57.31%) eyes had mild or no visual impairment (<20/70) and blindness (>20/400) in 81 (10.48%) eyes. Krukenberg spindle was seen in 445 (57.57%) eyes and iris transillumination defects in 33 (4.27%) eyes. About a third of the eyes, 241 (31.18%) eyes had an intraocular pressure (IOP) >21 mm of Hg at presentation. Three hundred and twenty-eight (42.43%) eyes were on more than one anti-glaucoma medication. YAG peripheral iridotomy was documented in 100 (12.94%) eyes. In the 46 (5.95%) eyes that required a glaucoma related surgical intervention, combined surgery was performed in 30 (3.88%) eyes and trabeculectomy in 16 (2.07%) eyes.

Conclusion: PDS is more common in males presenting during the fourth decade of life and is predominantly bilateral. A third of the eyes have raised IOP and a tenth of them are affected with blindness at presentation.

Keywords: Pigment dispersion syndrome, Electronic medical records, Big data, India

INTRODUCTION

Pigment dispersion syndrome (PDS) has features of iris pigment dispersion all over the eye with or without raised intraocular pressure (IOP).^[1] The first case of PDS was described in 1940 by Sugar.^[2] He went on to further report the features of PDS and pigmentary glaucoma (PG), in two cases and further strengthened the association of the risk for glaucoma in the presence of dense pigmentation in the trabecular meshwork,^[3] with the origin of the pigment being the iris.^[4] The features of Krukenberg's spindle on the corneal endothelium, mid peripheral iris

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transillumination defects, deep anterior chamber, dense pigmentation of the trabecular meshwork on gonioscopy and increase in IOP (especially post mydriatic use), with associated myopia were first described here.[3] The added features are the concave configuration of the peripheral iris on gonioscopy^[5] and the more posterior insertion of the iris, confirmed on ultrasound biomicroscopy (UBM).^[6] Zentmayer first described a ring of pigments on the posterior capsule of the lens, later known as Zentmayer's line^[7] or Scheie's and Cameron stripe^[8] and the pigmentation of the Schwalbe's line is known as Sampaolesi line.^[9] Initially thought to be a very rare disease, the prevalence of PDS has increased, due to better diagnostic capabilities and increased awareness, with demographic studies helping us to understand it's distribution. There is, however, a paucity of literature on the prevalence and demographic distribution of PDS in the Indian population. The purpose of the study is to present the clinical and demographic profile of PDS at a large multi-tier ophthalmology network in India using electronic medical record-driven analytics.

MATERIAL AND METHODS

Study design, period, location and approval

This cross-sectional observational hospital-based study included all patients presenting between August 2010 and September 2021 to a multi-tier ophthalmology network located in India.^[10] The patient or the parents or guardians of the patient filled out a standard consent form for electronic data privacy at the time of registration. None of the identifiable parameters of the patient were used for analysis of the data. The clinical data of each patient who underwent a comprehensive ophthalmic examination were entered into a browser-based electronic medical records system (eyeSmart EMR) by uniformly trained ophthalmic personnel and supervised by an ophthalmologist using a standardised template.^[11] The study adhered to the Declaration of Helsinki and was approved by the Institutional Ethics Committee.

Cases

A total of 2,961,706 new patients presented to the tertiary and secondary centres of the multi-tier ophthalmology network during the study period. The eyeSmart EMR was screened for patients with a documented ocular diagnosis of PDS in one or both eyes. A total of 403 patient records were identified using this search strategy and were labelled as cases. A diagnosis of PDS was made based on the findings of a deep anterior chamber, with dense pigmentation of the trabecular meshwork and/or the presence of Krukenberg's spindle, iris transillumination defects, concave iris configuration^[12] with or without raised IOP and/or glaucomatous optic nerve changes.^[13] Secondary PG was ruled out in the unilateral

cases by looking for keratic precipitates, corneal ulcers, sectoral iris atrophy, anterior and posterior synechiae. A total of 773 eyes diagnosed with PDS in the above patients were further analysed for clinical information.

Data retrieval and processing

The data of 403 patients included in this study were retrieved from the electronic medical record database and segregated into an excel sheet. The columns included the data on patient demographics, clinical presentation, ocular diagnosis and treatment information and were exported for analysis. The excel sheet with the required data was then used for analysis using the appropriate statistical software. Standardised definitions were used for occupation and socio-economic (SE) status.^[14] The visual acuity was classified according to the WHO guidelines.^[15] The grade of pigmentation on gonioscopy was classified as with the Shaffer scheme.^[16]

Statistical analysis

Descriptive statistics using mean \pm standard deviation and median with interquartile range (IQR) were used to elucidate the demographic data. All tables for age, gender, visual acuity and clinical features were drawn using Microsoft Excel (Microsoft Corporation 2018. Redmond, USA). 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 PG and the overall population.

RESULTS

Prevalence

Of the 2,961,706 new patients who presented across the eye care network during the study period, 403 patients were diagnosed with PDS in at least one eye, translating into a prevalence rate of 0.014% (95% CI: $\pm 0.0001\%$) or 136/million population.

Age

The mean age of the patients was 46.92 ± 14.23 years, while the median age was 46 (IQR: 36-56) years. The most common age group of the patients were distributed between 31 and 40 years (n = 100; 24.81%) followed by 41 and 50 years (n = 94; 23.33%). The distribution of patients in each age-decade is presented in [Figure 1].

Sex

There were 304 (75.43%) male and 99 (24.57%) female patients of PDS. The overall distribution was greater

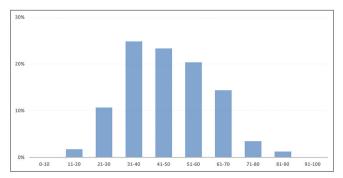


Figure 1: Decade-wise distribution of patients with pigment dispersion syndrome.

(P < 0.00001) in males (0.019%; 304/1,594,915) as compared to females (0.007%; 99/1,366,791). The mean and median age were 45.6 ± 14.03 and 44 (IQR: 35-56) years for men and 50.81 ± 14.16 and 52 (IQR: 39-61) years for women, respectively. The overall mode was 56 years; and was 35 years for men and 65 years in women.

Urban-rural distribution

Of the 403 patients, 196 (48.64%) were from an urban locality, 149 (36.97%) were from a rural locality and 58 (14.39%) patients presented from the metropolitan region. The overall prevalence of PDS in metropolitan community (0.017%; 58/345,180) was higher as compared to the urban (0.015%; 196/1,287,025) or rural community (0.011%; 149/1,329,501) and was not statistically significant (P = 0.08).

SE status

Of the 403 patients, there were 54 (13.4%) patients from the lower SE strata, 308 (76.43%) from the lower middle SE strata, 26 (6.45%) from the upper middle SE strata and 15 (3.72%) from the upper SE strata. The overall prevalence of PDS was significantly higher in the higher SE strata (0.015%; 349/2,262,273) as compared to lower SE strata (0.008%; 54/699,433) which was statistically significant (P < 0.00001).

Laterality

Of the 403 patients, 19 (4.71%) were affected in the right eye and 14 (3.47%) were affected in the left eye. In the majority of the cases in 370 (91.81%), the affliction was bilateral. There were 8 (1.98%) patients who were one eyed.

Presenting visual acuity

 Perception of Light; PL), 8 (1.03%) eyes had blindness no perception of light (NPL) and, in 139 (17.98%) eyes, the visual acuity was undetermined or unspecified. Of the patients who had blindness (>20/400–NPL), the ocular comorbidities present were 19 eyes with cataract, three eyes with vein occlusion, one eye with retinal detachment and one eye with a corneal scar.

Grade of pigmentation on gonioscopy

Among the 773 eyes, the most common type of pigmentation was grade 4 in 296 (38.29%) eyes, grade 3 in 208 (26.91%) eyes and grade 2 in 46 (5.95%) eyes and not available in 223 (28.85%) eyes. One hundred and three eyes (34.8%) of grade 4 pigmentation had IOP >21 mmHg and 65 eyes (31.25%) of grade 3 pigmentation had IOP >21 mmHg. One hundred and forty-two eyes (47.97%) of grade 4 pigmentation had a cup disc ratio (CDR) of >0.7:1 and 80 eyes (38.46%) of grade 3 pigmentation had a CDR of >0.7:1.

Clinical findings

Among the 773 eyes, Krukenberg's spindle was documented in 445 (57.57%) eyes and more commonly in males 322 (72.36%), iris transillumination defects in 33 (4.27%) eyes, concave iris in 80 (10.35%) eyes, Sampaolesi line in 13 (1.68%) eyes, Zentmayer line in 6 (0.78%) eyes, cataract in 176 (22.77%) eyes, pseudo exfoliation in 9 (1.16%) eyes, lattice degeneration in 4 (0.52%) eyes and retinal detachment in 3 (0.39%) eyes. YAG peripheral iridotomy was documented in 100 eyes (12.94%).

Optic disc findings

Among the 773 eyes, a cup-disc ratio of between 0.1 and 0.4 was documented in 101 (13.07%) eyes, 0.5-0.7 in 130 (16.82%) eyes and >0.7 in 310 (40.10%) eyes. Notching of the disc was documented in 135 (17.46%) eyes, disc excavation in 36 (4.66%) eyes, rim thinning in 88 (11.38%) eyes, retinal nerve fibre layer loss in 36 (4.66%) eyes and disc damage in 252 (32.6%) eyes.

IOP

Among the 773 eyes, an IOP of between 1 and 9 mm of Hg was documented in 15 (1.94%) eyes, 10-21 mm of Hg in 501 (64.81%) eyes, 22–30 mm of Hg in 163 (21.09%) eyes and >30 mm of Hg in 78 (10.09%) eyes. The mean IOP was 20.15 ± 8.5 mmHg.

Refractive error

In the eyes where refractive error was documented, hypermetropia was found in 22 (3.06%) eyes and myopia was found in 208 (26.91%) eyes, which was classified as mild myopia (<0.5D--3.00D) in 110 eyes (52.88%), moderate

myopia (-3.00D--6.00D) in 52 (25%) eyes and high myopia (>-6.00D) in 15 (7.12%) eyes.

Treatment

Most patients were prescribed anti glaucoma medications in the first visit 547 eyes (70.76%), with prostaglandin analogues being the most prescribed medication, in 375 eyes. Pilocarpine was prescribed in 15 eyes. Just under half of the 328 (42.43%) eyes were on more than one anti-glaucoma medication. In the 105 (13.58%) eyes that required a surgical intervention, cataract surgery was performed in 46 (5.95%) eyes, combined surgery in 30 (3.88%) eyes, trabeculectomy in 16 (2.07%) eyes and vitreo-retinal surgery in 7 (0.91%) eyes. The detailed list of interventions performed is described in [Table 1].

DISCUSSION

This study sought to describe the clinical profile and demographic distribution of PDS in a large cohort of patients presenting to a multi-tier hospital network in India using electronic medical records-driven big data analytics. The primary purpose of the study was to determine the relative proportion and demographic profile of PDS in the clinical care setup. The diagnosis of PDS is most often clinical with the clinical findings having wide variations, making PDS an underdiagnosed and misdiagnosed condition.^[17] In challenging cases with a high degree of doubt, the diagnosis can be clenched with the use of UBM^[18] or anterior segment optical coherence tomography.^[19] The overall prevalence of PDS was 0.014% of all eye diseases diagnosed between 2010 and 2021 (11-year period). In other studies, a prevalence of 2-4%^[1,20] shows that PDS has a higher prevalence among Caucasians as compared to non-Caucasians.^[21,22] The most probable reason being the denser pigmentation of the irides which may conceal iris transillumination defects in non-Caucasians. In the US, the prevalence is 2.5% and the incidence is 4.8/100000 population/year.[23] A study involving subjects who were consulting for refractive surgery showed a higher prevalence of 25.9%, although the bias here may be due to the higher number of myopic subjects.^[24]

The "Burn out phase" is the phase which is said to occur approximately 10 years after the onset of the disease and is

 Table 1: Type of surgical interventions in eyes affected with pigment dispersion syndrome.

Surgical profile	Eyes	%
Cataract surgery	46	5.95
Combined (Cataract surgery+Trabeculectomy)	30	3.88
Trabeculectomy	16	2.07
Vitreo-retinal surgery	7	0.91
Others	6	0.78
Total eyes	105	13.58

characterised by a lowering of IOP and stabilisation of the glaucomatous damage. The hypothesis behind this being the enlargement of the anteroposterior diameter of the lens with an increase of distance between the iris and zonular fibres and reduction in pigment release.^[1] This finding seems to be true in the Indian population as well, as seen by the decreasing incidence with age in our data. Mean age at diagnosis of PDS for Caucasian men is 40-50 years.^[1] Males were seen to be diagnosed with PDS about 3 times more than females and at younger age correlating with the findings in this present study,^[3,25] although some studies state equal prevalence in both.^[5,8] Possible protective effect of sex hormones, progesterone and oestrogen, in increasing outflow facility have been implicated in this difference, but further studies have not been conducted.^[26,27] Krukenberg's spindle was however found more in males in our study, contradicting the findings by Duncan.^[26]

The disease is predominantly bilateral asymmetry which is often noted, with the worse affected eye having more pigment deposition.^[1,28] A higher incidence in the higher SE strata and urban population in our study may be attributed to better awareness about the need for frequent ophthalmic checkups in this section of society.

Myopia >-1.00 D has been noted in almost 38–100% of cases in other studies.^[8,28] In our study, myopia was present in 208 eyes, (28.93%). Lattice degeneration was frequently found in PDS at the rate of $20\%^{[29]}$ and $33.3\%^{[30]}$ and retinal breaks were found at an incidence of $12\%.^{[29,31]}$ Retinal detachments occur at a rate of 6.6% irrespective of pilocarpine use, although most clinicians caution against its use.^[8,32] In our set of patients, lattice degeneration and retinal detachment were however found to be lower as compared to the previous studies. Some authors have hypothesised that a genetic link exists between myopia, pigment dispersion and dystrophic retinal changes in patients having all these manifestations.^[8] Further studies would be required to confirm or refute this.

Iris transillumination defects have been reported in about 86% of cases,^[23] more so in Caucasian eyes. It has also been noted that the more the pigment dispersion, the more the magnitude of iris transillumination and Krukenberg's spindle size.^[33] The comparatively less incidence of iris transillumination defects in our patients could be attributed to the thick highly pigmented irides in Indian eyes. Detection can however be improved in patients with thick and highly pigmented irides by the use of infrared imaging.^[34]

The grade of pigmentation of the trabecular meshwork is said to be higher in cases with higher IOP and more severe glaucoma.^[35,36]

Prostaglandin analogues do not have any particular anti-PDS effects per se but their mechanism of action of increased uveoscleral outflow seem to be advantageous in such patients with studies showing it to be more efficacious than timolol.^[37] There is no evidence that they can increase pigment dispersion.^[38] They were the most prescribed medication in our set of patients. In terms of mechanism of action, pilocarpine would seem to be the ultimate management strategy for PDS and PG as it reduces the posterior bowing of the iris, checks pupil dilatation and diminishes the exercise induced rise in IOP.^[12,39,40] Its poor tolerability among patients, in the form of the general side effects, along with ocular effects such as accommodative spasm, risk of cataract and retinal detachment, however, has limited its use.^[41]

Laser peripheral iridotomy (LPI) is still a controversial mode of treatment for PDS and PG. It was first advocated by Campbell^[12] after the concept of reverse pupillary block gained momentum.^[42] LPI is not the mainstay in the management of PDS and PG as it is not successful in all eyes,^[43] especially in those eyes that have advanced and permanent damage to the trabecular meshwork.^[44] A few randomised trials have failed to show any benefit of LPI in preventing progression of PDS with high IOP to PG.^[45,46] YAG peripheral iridotomy was documented in 100 eyes (12.94%) in our study.

Selective laser trabeculoplasty (SLT) as a treatment modality can be tried in PDS and PG, but cases of considerable increase in IOP requiring trabeculectomy have been reported.^[47] Hence, awareness of this possible sustained IOP spike is needed and close follow-up required. No SLT was performed in our patients.

CONCLUSION

This study aimed to describe the epidemiology and clinical presentation of PDS and PG in 2.9 million new patients presenting to a multi-tier ophthalmology hospital network in India. The findings show that PG is more common in males presenting during the fourth decade of life and is predominantly bilateral. A third of the eyes have raised IOP and a tenth of them are affected with blindness at presentation.

Authors' contributions

Conceptualisation: AVD contributed to the conceptualisation of the article. Methodology: AVD, GBW and SS contributed to the design of the article. Statistical analysis: AVD contributed to the statistical analysis of the article. Original draft preparation: AVD and GBW contributed to the preparation and writing of the draft. Review and editing: AVD, GBW and SS contributed to the reviewing and editing of the draft.

Declaration of patient consent

The Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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