# Pattern and Presentation of Vitreo-Retinal Diseases: Lessons from a Tertiary Eye Care Centre in Nepal

**Bhim Bahadur Rai** ( bhim.rai@anu.edu.au )
https://orcid.org/0000-0003-0748-4581
**Mohan K. Shresthra**
Tilganga Institute of Ophthalmology
**Raba Thapa**
Tilganga Institute of Ophthalmology
**Rohan W. Essex**
Canberra Hospital
**Govinda Paudyal**
Tilganga Institute of Ophthalmology
**Ted Maddess**
John Curtin School of Medical Research

**Research Article**

**Keywords:** AMD, diabetic retinopathy, retinal diseases, laterality, ocular dominance, sex differences

**Posted Date:** December 12th, 2018

**DOI:** https://doi.org/10.21203/rs.2.82/v1

# Abstract

**Background:** We examined patients presenting in a tertiary eye hospital in Nepal, focussing on information for screening and management programs for vitreo-retinal disease (VR).

**Methods:** We reviewed all patients presenting for the first time to the VR-clinic over one year. We quantified patient demography, symptoms and duration, associated systemic diseases, ophthalmological examinations, diagnostic investigations and final diagnoses.

**Results:** Of the 1905 cases 1148 were males (60.3%). The 25th-percentile of ages was 29 and 38 years for males and females respectively, indicating females presented later ($p<0.0001$). Hypertension was the commonest systemic disease (40.8%), followed by diabetes (32.5%). Macular degeneration (AMD) and diabetic retinopathy (DR) affected 447 eyes (11.8%), and 416 eyes (10.9%) respectively. Male and female AMD and DR patients did not differ in age or disease duration, which for DR was not correlated with severity. Asymmetry of disease severity between AMD and DR eyes was largest in patients with one normal eye. Presenting acuity was highly asymmetric between eyes ($p<0.0001$) with people more often reporting when their dominant eyes had acuity of 6/18 or worse.

**Conclusions:** When left to self-report patients tended to not notice visual impairment in their non-dominant eye until their disease was quite advanced, putting them at risk of serious bilateral disease. Screening of blood pressure and glucose levels combined with fundus photography could prevent many from progressing to life-changing visual impairment and blindness. Later reporting by females began at childbearing age, therefore education and ocular screening could be usefully coupled to mother and child health programs.


# Background

Vitreo-retinal (VR) diseases are common causes of visual impairment and blindness. Population-based studies have reported the overall prevalence of VR disorders to be 8.56% (range 10.4% to 21.02%) among the population aged 40 years and above [1, 2]. The 1981 Nepal Blindness Survey reported VR disorders as the third leading cause of bilateral blindness, second only to cataract and its complications [3]. A more recent Nepalese population-based study reported VR disorders to be the second commonest cause of bilateral blindness, second only to cataract, and the most common cause among pseudophakics [4].

A population-based study in Bhutan reported that 22.1% of visual impairment and blindness was due to VR pathologies amongst the population aged ≥ 50 years [5]. A similar survey in Bangladesh reported VR diseases as the second leading cause of bilateral blindness accounting for 13.3% [6], and in India 17.1% among persons aged ≥ 30 years [7]. By contrast a Nigerian study reported a prevalence of 8.1%, with AMD, DR, retinal vein occlusion (RVO) and retinal detachment (RD) as the most common retinal diseases [8]. An Ethiopian study reported RD as the commonest cause of both bilateral (59.4%) and unilateral (41.2%) blindness [9]. The Tehran study reported VR prevalence of 8.56% with acquired retinopathies and peripheral lesions as the most common retinal diseases [2].

In developed countries AMD affects nearly 10% of those over 65 years of age, and 25% over 75 years [10], including Australia [11]. In the USA, more than 8 million people have intermediate AMD and nearly 2 million have advanced AMD [12]. In the UK, the prevalence of late AMD was 2.4% among the population aged 50 years and above, 4.8% for ≥ 65 years and 12.2% for ≥ 80 years [13].

DR often affects adults of working age [14]. The American National Health and Nutritional Examination Survey 2005-2008 reported that 28.5% of diabetic patients had some degree of DR, and 4.4% had vision-threatening DR [15]. In 2012 global prevalence was 34.6% for any DR, 6.96% for proliferative DR, 6.81% for diabetic macular edema, and 10.2% for vision-threatening DR [16]. India and China are confronting a growing epidemic of diabetes and DR [17-19].

The current study focuses upon the pattern and laterality of VR diseases presenting to a tertiary eye care centre in Nepal. The study provides clear recommendations for improved care that are applicable outside Nepal, and the work provides a baseline for planned comparison studies.

## Methods

# Setting

This study was conducted at Tilganga Institute of Ophthalmology (TIO), Kathmandu, Nepal. The TIO is a tertiary eye care centre with sub-speciality clinics providing services for ophthalmological patients from all over Nepal, India and Bhutan. All sub-speciality clinics in the TIO, including the VR clinic, run from morning till afternoon and an extended paying clinic operates in the evening. Despite this availability of extended facilities 1,843 cases (96.7%) presented to the routine public VR clinic. Only 36 cases (1.9%) presented in the paying clinic, while 26 cases (1.4%) reported to the emergency department. The retrograde study collected de-identified data from patient files with approval from the TIO hospital.

# Ethics

The study has been approved by the Tilganga Institute of Ophthalmology-Institutional Review Committee (TIO-IRC) vide letter number: Ref: 10/2018. The need for consent was waived by TIO-IRC because the study was a retrograde analysis of data from the medical record.

# Study population

This study covers all cases presenting to the VR clinic for the first time over one year. Patients who presented for repeat or follow-up visits were not included here. The study ran from 01.01.2010 until 31.12.2010. A key objective for publishing this study now is to provide a baseline reference for planned follow-up studies that will use similar analyses. A further benefit of recording this hospital-based study is that there are population-based studies of disease prevalence from both Nepal [4, 20] and Bhutan [5] from

2009/2010 with which this study can be compared, adding extra value both for the region and similar countries.

# Data collection and analysis

Detailed demographic information, presenting complaints, treatment history and associated systemic diseases were noted. Best corrected visual acuity (BCVA), refractive status, Goldmann applanation tonometry, findings of slit-lamp examination, 90D bio-microscopy, fundoscopy and diagnostic investigations performed were recorded. Diagnoses were noted separately for right and left eyes. The data were analysed using SPSS (version 20.0, IBM, New York NY); and MATLAB (2016b, The MathWorks, Natick, MA). Comparisons of the expected and observed frequency of gender or eye-wise effects were done using Chi-squared tests. To compare the 10th, 25th, 50th , 75th and 90th percentiles of the distributions of Fig. 1B for male and females we applied a sampling with replacement based bootstrap analysis [21] to estimate the population means and the standard errors of the means (SE) of those percentiles. We employed 10,000 bootstrap cycles to insure the estimated means and SE converged to within 2 decimal places on 5 independent cross-validations. We then applied t-tests employing the estimated means and SE. The 1905 subjects insured that the bootstrap estimates were statistically conservative.

## Results

We will first give an overview of the general presentation of the 1,905 cases. We next present the ocular disease data as: 1) the non-retinal diseases involving posterior segment other than retina, and 2) the main analysis of the retinal diseases. Some less relevant data is presented in 4 Supplementary tables.

# General presentation

During the study year 1,905 new cases presented to the VR clinic: 1,148 males (60.3%) and 757 females (39.7%). Their ages ranged from 0.17 years to 116 years, with mean of 49.14, median of 54 and mode of 70 years (83 cases = 4.4%). Fig. 1A gives a breakdown of the presenting ages in 20-year cohorts. Fig. 1B shows that for the whole cohort the 25th percentile is 29 years for males and 38 years for females. A bootstrap analysis (Methods) revealed that the 10th, 25th, 50th and 75th percentiles were significantly older for females than males by 3.95, 9.28, 7.25, and 3.08 years: median 5.6 years. The 10th percentile difference was significant at $p<0.003$, and the others at $p = 0.0001$. Notice that the 25th percentiles for the males is generally lower in the 20-year cohorts of Fig. 1A also.

A total of 802 cases (42.1%) were from the Kathmandu valley, 1038 cases (54.5%) were from Nepal outside the Kathmandu valley, and 65 cases (3.4%) were from other countries. 1574 cases (82.6%) reported to the hospital as primary cases, while 331 cases (17.4%) were referred from other hospitals or health care centres.

# **Table 1** Symptoms

| Presenting complaints | Frequency | Percent |
|---|---|---|
| Poor vision | 1142 | 59.9 |
| Trauma | 227 | 11.9 |
| Loss of vision | 155 | 8.1 |
| Floaters | 91 | 4.8 |
| Vision not improving after cataract surgery | 44 | 2.3 |
| Sudden loss of vision | 43 | 2.3 |
| Routine eye check up | 41 | 2.2 |
| Night blindness | 34 | 1.8 |
| Foreign body sensation | 20 | 1.0 |
| Pain | 18 | .9 |
| Flashes of light | 8 | .4 |
| Black spot in visual field | 8 | .4 |
| White eye | 5 | .3 |
| Others | 69 | 3.6 |
| Total | 1905 | 100.0 |

The commonest presenting complaint was poor vision accounting for 1,142 cases (59.9%), followed by trauma in 227 (11.9%), loss of vision in 155 (8.1%), floaters in 91 (4.8%) and vision not improving after cataract surgery in 44 (2.3%). Other presenting complaints are summarised in Table 1. A total of 565 cases (30.5%) presented within a month from the onset of their symptoms, while 500 (27.0%) presented only after 12 months. In 53 cases we could not affirm the time period due to missing data (Table S1).

Hypertension was the commonest systemic disease associated in 250 cases (40.8%), followed by diabetes in 199 cases (32.5%) and combined diabetes and hypertension in 124 cases (20.2%) (Fig. 2). The other systemic diseases found in 40 cases (6.5%) are summarised in Table S2. The duration of systemic disease association was found to be less than 5 years in 42.8% of cases, 5 to 10 years in 33.2% and more than 10 years in 24.0%.

[Figure 2 about here please]

We quantified interventions done at other centres before patients reported to our clinic, including surgical, laser or ophthalmic injections. These cases included: 55 cataract surgeries (2.9%), VR surgery in 27 (1.5%), retinal laser in 27 (1.5%), and primary repair of corneo-scleral tear or eyelid lacerations in 20 (1.1%). All prior interventions are summarized in Table 2.

## **Table 2** Prior interventions (surgical / Laser)

| Intervention | Frequency | Percent |
|---|---|---|
| No Intervention | 1769 | 92.9 |
| Cataract surgery | 55 | 2.9 |
| VR surgery | 27 | 1.5 |
| Retinal laser | 27 | 1.5 |
| Primary repair: Corneo-scleral and eyelids | 20 | 1 |
| Intravitreal Avastin | 2 | 0.2 |
| Anterior chamber wash | 2 | 0.2 |
| Glaucoma surgery | 1 | 0.1 |
| Retrobulbar Methyl-prednisolone | 1 | 0.1 |
| Retinal laser + Inj. Avastin | 1 | 0.1 |
| Total | 1905 | 100 |

Haematological testing was the most commonly diagnostic test performed in 584 cases (23.1%), followed by OCT in 516 (20.4%), B-scan in 436 (17.2%), FFA in 89 (3.5%) and visual fields in 39 (1.5%). Diagnostic investigation was not indicated or not done in 687 cases (27.1%). Table S3 summarises the data.

# Non-retinal diseases

BCVA was 6/18 or better in the right eye in 660 cases (34.8%), and left eyes in 1,025 cases (54.1%). In 751 cases (39.4%) right eyes, and 355 cases (18.6%) left eyes, the BCVA was 6/18 to 6/60. Fig. 3 illustrates just how surprisingly asymmetric these values were ($p<0.0001$, see legend). These findings prompted us to explore our data to see if any other such asymmetries occurred. No such asymmetries existed among the persons with poorer acuities. Cases with BCVA <6/60 or NPL were more common on the left, but not significantly so. NPL was found in 37 (1.8%) right eyes and 44 (2.3%) left eyes. PVD was the commonest non-retinal disease with 79 cases (35 OS). There were 51 cases of endophthalmitis (24 OS): 33 (64.7%) were post-traumatic, 13 (25.5%) post-operative, and 5 (9.8%) endogenous in origin. The other common non-retinal diseases are enumerated in Table S4.

Most of the trauma related conditions involved the left eyes, but this bias did not reach statistical significance. When pooled together atrophic bulbi, phthisis and absolute eyes were more common in left eyes: 16 (0.8%) compared to only 8 right eyes (0.4%, $p=0.05$, chi-square). Dislocated cataract was similar in left eyes: 14 (0.8%) compared to 10 right eyes (0.5%, $p=0.25$, chi-square). Dislocated intra-ocular lens (IOL) into the vitreous cavity was also seen 7 left eyes (0.4%) and 3 right eyes (0.2%, $p=0.10$, chi-square). Retained intra-ocular foreign body (RIOFB) involved 7 left and 4 right eyes ($p=0.15$, chi-square). Open- and close-globe injuries affected both eyes equally. The fundus was not visible in 6 left eyes (0.3%), and 7 right eyes (0.4%).

# **Table 3** Diseases involving retina

| | Right Eye | | | Left Eye | | |
|---|---|---|---|---|---|---|
| Diagnosis | N | Percent across retinal diseases | Percent across all diseases | N | Percent across retinal diseases | Percent across all diseases |
| AMD | 223 | 13.5 | 11.7 | 224 | 13.6 | 11.8 |
| Diabetic retinopathy | 208 | 12.6 | 10.9 | 208 | 12.6 | 10.9 |
| Retinal Detachment | 112 | 6.8 | 5.9 | 126 | 7.6 | 6.6 |
| BRVO | 80 | 4.8 | 4.2 | 70 | 4.2 | 3.7 |
| Myopic degeneration | 63 | 3.8 | 3.3 | 54 | 3.3 | 2.8 |
| Retinitis pigmentosa | 56 | 3.4 | 2.9 | 57 | 3.5 | 3 |
| Hypertensive retinopathy | 45 | 2.7 | 2.4 | 42 | 2.5 | 2.2 |
| CSCR | 44 | 2.7 | 2.3 | 33 | 2 | 1.7 |
| CRVO | 33 | 2 | 1.7 | 32 | 1.9 | 1.7 |
| Macular scar | 31 | 1.9 | 1.6 | 22 | 1.3 | 1.2 |
| Macular hole | 30 | 1.8 | 1.6 | 25 | 1.5 | 1.3 |
| Retinal vasculitis | 23 | 1.4 | 1.2 | 23 | 1.4 | 1.2 |
| Chorio-retinal scar | 22 | 1.3 | 1.2 | 20 | 1.2 | 1 |
| ERM | 20 | 1.2 | 1 | 19 | 1.2 | 1 |
| Macular dystrophy | 16 | 1 | 0.8 | 15 | 0.9 | 0.8 |
| Irido-chorio-retinal coloboma | 15 | 0.9 | 0.8 | 18 | 1.1 | 0.9 |
| Retinal Hole / HST | 13 | 0.8 | 0.7 | 12 | 0.7 | 0.6 |
| S/P RD surgery | 9 | 0.5 | 0.5 | 4 | 0.2 | 0.2 |
| CRAO | 8 | 0.5 | 0.4 | 5 | 0.3 | 0.3 |
| Stargardt’s disease | 5 | 0.3 | 0.3 | 8 | 0.5 | 0.5 |
| Retinal haemorrhage | 4 | 0.2 | 0.2 | 10 | 0.6 | 0.5 |
| Cone dystrophy | 3 | 0.2 | 0.2 | 3 | 0.2 | 0.2 |
| Normal fundus | 593 | 35.8 | 31.1 | 622 | 37.7 | 32.6 |
| Total | 1656 | 100.1 | 86.9 | 1652 | 100 | 86.7 |

# Retinal diseases

The commonest retinal disease was AMD affecting 223 right eyes (11.7%) and 224 left eyes (11.8%), followed by DR involving 208 left, and 208 right eyes (10.9%). RD was the third commonest affecting 112 right eyes (5.9%) and 126 left eyes (6.6%), of which 71.0% were rhegmatogenous, 17.2% exudative, and 11.8% tractional RD. There were 150 cases of branch retinal vein occlusion (BRVO), 80 in right and 70 in left eyes. Myopic degeneration affected 63 right and 54 left eyes and retinitis pigmentosa (RP) was seen in 56 right and 57 left eyes. Other retinal diseases diagnosed were hypertensive retinopathy in total of 87

eyes, central serous chorio-retinopathy (CSCR) in 77 eyes, central retinal vein occlusion (CRVO) in 65 eyes, macular scar in 53 eyes, macular hole in 55 eyes, retinal vasculitis in 46 eyes, and others are detailed in Table 3. 94.8% of full-thickness macular hole and 84.6% lamellar macular hole were unilateral. The fundus was found to be normal in 623 left eyes (32.7%) and 593 right eyes (31.1%).The types of AMD and the severity of DR are shown in Table 4.

Among the AMD patients dry AMD was the commonest type (79.2%), followed by wet AMD (15.9%), retinal pigment (RPE) change (4%), and familial drusen (0.9%). In contrast to the results for all patients (Fig. 1) there was no statistical difference in the number of male (122) and female (100) AMD patients. The male and female AMD patients also did not differ significantly in age: males 71.0 ± 9.48, females 68.8 ± 10.3 (mean ± SD years). Across these patients 81.7% of the AMD was bilateral and 18.3% unilateral. As might be expected, patients with unilateral disease were significantly younger than those with bilateral disease: 67.0 ± 13.1 cf. 70.7 ± 8.93 years (p=0.031, t-test).

In part because of the higher rate of smoking by males in Nepal [22], we decided to examine wet AMD eyes relative to fellow eyes. Two patients had familial drusen bilaterally, and for this analysis they were classed as having dry AMD. Four patients had a non-visible fundus (mainly due to cataract) and were eliminated from the analysis. The ages of males whose worst eye had wet AMD was not different to females: 66.0 ± 15.3 vs. 65.8 ± 13.7 years. There were 40 males whose worst eye had wet AMD, vs. 15 females, which was marginally significant (p=0.063, t-test, correcting for the relative abundance on males in the study population). Interestingly, patients whose worst eye had dry AMD were older than those with a worst eye that was wet AMD, 69.5 ± 14.8 vs. 65.9 ± 10.5 years (p=0.045). Overall there was a suggestion of males developing wet AMD earlier, and in relatively greater numbers relative to females. This might have been an effect of smoking, but needs further investigation. We also examined laterality by scoring normal fundus to wet AMD on a scale from 1 to 3 (normal, dry, wet) and then examining the absolute value of the difference in scores between eyes. Six patients had wet AMD OU. For the 186 patients whose best eye had dry AMD, only 30 had a worst eye with wet AMD. Patients whose best eye was normal were even more heterogeneous. Of those 36 patients 17 had a fellow eye that was dry, and 19 had a fellow eye that was wet. Thus the pattern of progression seemed to be relative heterogeneity early, progressing to ever more bilateral disease, rather than simple bilaterally at each stage.

# **Table 4** Types of AMD and severity of DR

| | Right eye | | Left eye | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Dry | 175 | 78.5 | 179 | 79.9 | 354 | 79.2 |
| Wet | 37 | 16.6 | 34 | 15.2 | 71 | 15.9 |
| RPE Change | 9 | 4 | 9 | 4 | 18 | 4 |
| Familial drusen | 2 | 0.9 | 2 | 0.9 | 4 | 0.9 |
| Total | 223 | 100 | 224 | 100 | 447 | 100 |
| | | | | | | |
| Mild | 33 | 15.9 | 25 | 12 | 58 | 13.9 |
| Moderate | 68 | 32.7 | 76 | 36.5 | 144 | 34.6 |
| Severe | 57 | 27.4 | 52 | 25 | 109 | 26.2 |
| PDR | 50 | 24 | 55 | 26.4 | 105 | 25.2 |
| Total | 208 | 100 | 208 | 100 | 416 | 100 |

DR was classified according to the modified Airlie House Classification system except that all proliferative DR (PDR) was classified together, providing five diagnostic categories. Of these five moderate non-proliferative diabetic retinopathy (NPDR) was the commonest (34.6%), followed by severe NPDR (26.2%), PDR (25.2%) and mild NPDR (13.9%). A total of 230 eyes had clinically significant macular edema (CSME): 50.9% involving left eyes and 49.1% right eyes.

Like the AMD patients the DR group contained more males (123) than females (91), but this was not significant. Their ages also did not differ at 58.7 ± 9.91 years for males, and 58.3 ± 11.21 years for females. Their durations of diabetes (DM) did not differ at 11.5 ± 6.79 and 10.4 ± 6.96 years respectively. Nine patients had a non-visible fundus in one eye and were removed from further analysis. We examined the laterality of DR in the remaining 205 patients. We scored the five DR diagnostic categories from normal fundus to PDR as 1 to 5. We then binned subjects according to the diagnosis in their least affected eye. To quantify the degree of laterality we took the absolute value of the difference of these severity steps in each pair of eyes. A boxplot of the results is shown in Fig. 4A. Basically, as with AMD, eyes tended to become more similar as severity of the best eye increased. As shown in Fig. 4B severity of DR was not correlated with duration of disease.

## Discussion

The visual handicap experienced by individuals suffering from unilateral eye disease, like macular hole, is strongly influenced by ocular dominance [23]. Ocular-dominance and handedness are associated, with about 65% of right-handers, and 43% of left-handers, being right eye-dominant [24]. Some of our data (Fig. 3) suggested eye dominance played a role in patient reporting to the hospital: with the predominantly right-handed subjects only reporting once their right eye had BCVA worse than 6/18. AMD and DR were very homogenous with respect to age and sex, however when the best eye was normal the range of severity in the fellow eye was surprisingly broad (e.g. Fig. 4). Taken together the results mean that if that eye was a dominant eye then patients tended not to notice their sight threatening disease in

their fellow eye, an excellent argument for more screening. Given the results on presenting BCVA (Fig. 3) we subsequently analysed other data by eye (Tables 3, 4, S4) in order to elucidate any eye-wise biases, however few were found.

The preponderance of males in the total group was 60.3%, and for AMD and DR patients combined was 56.5%, which was marginally more than females ($p=0.052$). This agrees with the findings of some hospital-based studies on VR diseases [9, 25], but differs from a Nepalese population-based study, in which only 45.5% were males [20], and one in India with only 45% males [1]. Our results could be due to women being reserved due to social norms and therefore do not come forward for medical check-ups. Here the 25th percentile of ages reporting was nearly 10 years higher for females ($p<0.0001$, t-test 9.27 years; 95% CL 6.05 and 12.5 years). The mean and median age of 49 and 54 years for males and females tally well with other studies of VR diseases [1, 9]. Overall ages ranged from 2 months to 116 years. Considering the life expectancy at birth for Nepal is 68.3 years for men and 71.5 years for women [26], the oldest patient in the study, a man aged 116 years, was unexpected.

Only 41 cases (2.2%) presented for routine check-up. Chronic retinal diseases like AMD, DR, RD, RVO, RP, etc., ranked high in the diagnostic list but only 2.2% of cases were found to present for routine check-up indicating that there is a need to emphasize patient education and counselling about the importance of regular check-ups and follow ups.

In 53 cases the interval between the onset of symptoms and presentation to the hospital could not be confirmed due to the lack of recorded data. 565 cases (30.5%) presented within a month, 507 cases (27.1%) between 1 to 6 months, 280 cases (15.1%) between 6 to 12 months, and 500 cases (27.0%) presented after 12 months from the onset of the symptoms. The delayed presentation time might be because of: illiteracy and ignorance (the overall literacy rate of Nepal for population aged 5 years and above was 65.9% in 2011, 75.1% for males and 57.4% for females [27]. Remote areas and associated difficulty in accessing medical attention, mean people initially rely on traditional methods of healing.

Systemic disease association was not found in 1,292 of the 1,905 cases. As shown in Fig. 2 (and Table S2) among the 613 remaining cases the commonest associated diseases were hypertension (40.8%), diabetes (32.5%), and both (20.2%). This agrees with the Tehran eye study which reported hypertension (21.14%), followed by diabetes (15.99%) [2]. By contrast, a Nigerian study found diabetes to be more common (14.6%) than hypertension (13.2%) [25]. Other systemic diseases were found in 40 of our cases (6.5%, Table S2). The duration of systemic disease association was less than 5 years in 210 cases (42.8%), 5 to 10 years in 163 cases (33.2%) and more than 10 years in 118 cases (24.0%).

The commonest VR disease was AMD affecting 11.8%, followed by DR at 10.9%; matching another Nepalese study reported that AMD was the commonest VR disease at 28.3%, followed by DR at 17.9% [20]. They do not match a Nigerian hospital study, which reported DR (24.9%) as the commonest VR disease, followed by hypertensive retinopathy (13.3%) and AMD (24.9%) [25]. In our case 208 of 324 (64.2%) confirmed diabetic cases had some form of DR, which did not tally with population-based studies reporting only 10.5% [1]. In our study 117 left eyes and 113 right eyes of 323 patients had CSME but a

population-based study in Nepal found it in only 2 of 305 diabetic cases [20]. This disparity could be explained by the early onset of macular edema causing a high percentage of patients of CSME to present to the TIO.

RD was the third commonest VR disease in our study affecting 112 right eyes (5.9%) and 126 left eyes (6.6%), while a the Nepalese population-based study reported population prevalence of only 0.10% [20]. A hospital-based study in Ethiopia reported RD as the second commonest VR disease at 24.5% [9]. Of 65 cases of FTMH in our study 33 cases (50.8%) affected right eyes, while others have reported only 48% involving right eyes in one study [23]. In our study 94.8% of the FTMH and 84.6% of the LMH were unilateral, which are similarly reported in other studies as macular holes (full thickness or lamellar) and are basically the consequence of factors affecting the macula locally. When such unilateral macular diseases affect the dominant eyes of the individuals they cause greater functional visual impairment [23].

In eastern Asia pathological myopia is a major issue found in 80-90% of school-leavers, and 10-20% of those completing secondary school [28], and contributes to RD numbers. The prevalence of myopia varies from 0.8% to 53.4%, depending on geographical area, age, occupation and ethnicity [29-31]. In Nepal, Sherpa children had a prevalence of 2.9% as compared to 21.7% for Tibetan children [32]. A myriad of myopic complications like atrophic retinal holes and RD, choroidal neo-vascular membranes, degeneration, cataract and glaucoma cause visual loss warranting attention [33]. Thapa et al.[20] reported the population prevalence of macular hole as 0.20% in Nepal. Asymptomatic macular holes occur at a prevalence of 6.26% among high myopes with more than -20D [34].

# Limitations

Nineteen patients were excluded due to incomplete data. AMD was not classified as per the AREDS classification system. Only the final diagnoses, and not ocular comorbidities, have been considered for analysis which might have altered the reported disease patterns.

## Conclusion

This study indicates that low cost screening and management programs for retinal disease could be of immense value in developing countries. We found that without screening programs patients tend to not notice developing visual impairment in their non-dominant eye, often until it is too late. In Nepal, and perhaps in similar countries, females report later for care than men. That was true from child baring age, so education and screening could be usefully coupled to child health programs. The high prevalence of hypertension and diabetes amongst retinal disease patients suggest that a simple screening of blood pressure and glucose levels combined with fundus photography could prevent many from progressing to life-changing visual impairment and blindness.

## Declarations

# Ethical approval and consent to participate

The study has been approved and the need for consent was waived by the Tilganga Institute of Ophthalmology-Institutional Review Committee (TIO-IRC) vide letter number: Ref: 10/2018.

# Consent for publication

The publication of the study has been approved by the Tilganga Institute of Ophthalmology-Institutional Review Committee (TIO-IRC) vide letter number: Ref: 10/2018.

# Availability of data and materials

The data have not been placed in any online data storage. The datasets generated and analysed during the study are available upon request from the first author.

# Funding

None

# Authors' contributions

BBR conceived of the study, collected data, did analysis partly and drafted the manuscript. MKS helped in collecting data and did the initial analysis. RT guided BBR and reviewed the manuscript. RWE advised on analytical part and reviewed the manuscript. GP guided and reviewed the manuscript. TM did the analysis, reviewed the manuscript and guided BBR closely. All authors read, reviewed and approved the final manuscript.

# Acknowledgements

We gratefully acknowledge the Himalayan Cataract Project for sponsoring BB Rai's Retinal Fellowship training at the John A. Moran Eye Centre, University of Utah, SLC, Utah, USA; and the Tilganga Institute of Ophthalmology, Kathmandu, Nepal. The data for the study was collected during the training period. We also thank the co-directors of the project, Dr Ruit Sanduk and Dr. Geoffrey Tabin, all the consultants and staff of the institutions for their support and cooperation. We acknowledge the TIO-IRC for granting approval for the study.

# Competing interests

None

## References


1. Nirmalan PK, Katz J, Robin AL *et al*. Prevalence of vitreoretinal disorders in a rural population of southern India: the Aravind Comprehensive Eye Study. Arch Ophthalmol 2004; 122(4):581-586.

2. Hatef E, Fotouhi A, Hashemi H, Mohammad K, Jalali KH. Prevalence of retinal diseases and their pattern in Tehran: the Tehran eye study. Retina 2008; 28(5):755-762.

3. Brilliant GEP, R. P.; Grasset, N. C.; Lepkowski, J. M.; Shrestha, S. R.; Konyama, K.; et al. The Epidemiology of blindness in Nepal: report of the 1981 Nepal Blindness survey In: *The Sewa Foundation.* Edited by Chelsea MI. Nepal; 1981.

4. Thapa SS, Berg RVD, Khanal S *et al*. Prevalence of visual impairment, cataract surgery and awareness of cataract and glaucoma in Bhaktapur district of Nepal: The Bhaktapur Glaucoma Study. BMC Ophthalmology 2011; 11:(2) 1-9.

5. Lepcha NT, Chettri CK, Getshen K *et al*. Rapid assessment of avoidable blindness in Bhutan. Ophthal Epidemiol 2013; 20(4):212-219.

6. Wadud Z, Kuper H, Polack S *et al*. Rapid assessment of avoidable blindness and needs assessment of cataract surgical services in Satkhira District, Bangladesh. Br J Ophthalmol 2006; 90(10):1225-1229.

7. Dandona L, Dandona R, Naduvilath TJ *et al*. Is current eye-care-policy focus almost exclusively on cataract adequate to deal with blindness in India? Lancet 1998; 351(9112):1312-1316.

8. Nwosu SNN. Prevalence and pattern of retinal diseases at the Guinness Eye Hospital, Onitsha, Nigeria. Ophthal Epidemiol 2000; 7(1):41-48.

9. Teshome T, Melaku S, Bayu S. Pattern of retinal diseases at a teaching eye department, Addis Ababa, Ethiopia. Ethiop Med J 2004; 42(3):185-193.

10. Smith W, Assink J, Klein R *et al*. Risk factors for age-related macular degeneration: Pooled findings from three continents. Ophthalmology 2001; 108(4):697-704.

11. Mitchell P, Bressler N, Doan QV *et al*. Estimated Cases of Blindness and Visual Impairment from Neovascular Age-Related Macular Degeneration Avoided in Australia by Ranibizumab Treatment. PLOS ONE 2014; 9(6):e101072.

12. Ratnapriya R, Chew EY. Age-related macular degeneration – clinical review and genetics update. Clin Genet 2013; 84(2):160-166.

13. Owen CG, Jarrar Z, Wormald R *et al*. The estimated prevalence and incidence of late stage age related macular degeneration in the UK. Br J Ophthalmol 2012; 96(5):752-756.

14. Zheng Y, He M, Congdon N. The worldwide epidemic of diabetic retinopathy. IJO 2012; 60(5):428-431.

15. Zhang X, Saaddine JB, Chou C-F *et al*. Prevalence of Diabetic Retinopathy in the United States, 2005–2008. JAMA Ophthalmol 2010; 304(6):649-656.

16. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski ea. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care 2012; 35(3):556-564.

17. Wang FH, Liang YB, Zhang F *et al*. Prevalence of diabetic retinopathy in rural China: the Handan Eye Study. Ophthalmology 2009; 116(3):461-467.

18. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. IJO 2016; 64(1):38-44.

19. Raman R, Ganesan S, Pal SS, Kulothungan V, Sharma T. Prevalence and risk factors for diabetic retinopathy in rural India. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study III (SN-DREAMS III), report no 2. BMJ Open Diabetes Res Care 2014; 2(1).

20. Thapa SS, Thapa R, Paudyal I *et al*. Prevalence and pattern of vitreo-retinal diseases in Nepal: the Bhaktapur glaucoma study. BMC Ophthalmol 2013; 13:(9) 1-8.

21. Efron B. Bootstrap methods: Another look at the jackknife. Ann Statist 1979; Number 1:1-26.

22. Sreeramareddy CT, Ramakrishnareddy N, Harsha Kumar H, Sathian B, Arokiasamy JT. Prevalence, distribution and correlates of tobacco smoking and chewing in Nepal: a secondary data analysis of Nepal Demographic and Health Survey-2006. Subst Abuse Treat 2011; 6(1):33.

23. Waheed K, Laidlaw DAH. Disease laterality, eye dominance, and visual handicap in patients with unilateral full thickness macular holes. Br J Ophthalmol 2003; 87(5):626-628.

24. McManus IC, Porac C, Bryden MP, Boucher R. Eye-dominance, writing hand, and throwing hand. Laterality 1999; 4(2):173-192.

25. Eze BI, Uche JN, Shiweobi JO. The Burden and Spectrum of Vitreo-Retinal Diseases Among Ophthalmic Outpatients in a Resource-Deficient Tertiary Eye Care Setting in South-Eastern Nigeria. Middle East African J Ophthalmol 2010; 17(3):246-249.

26. WHO. WHO report on Life Expectancy/Nepal. In.; 2015.

27. NPHC. National Population and Housing Census 2011 (National Report). In. Edited by Commission NP, vol. 01. Kathmandu, Nepal; 2012.

28. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. Lancet 2012; 379(9827):1739-1748.

29. Saw SMK, J.; Schein, O. D.; Chew, S. J.; Chan, T. K. Epidemiology of Myopia. Epidemiol Rev 1996; 18(2):175-187.

30. Nepal BP, Koirala S, Adhikary S, Sharma AK. Ocular morbidity in schoolchildren in Kathmandu. Br J Ophthalmol 2003; 87(5):531-534.

31. Adhikari S, Nepal BP, Shrestha JK, Khandekar R. Magnitude and determinants of refractive error among school children of two districts of Kathmandu, Nepal. Oman J Ophthalmol 2013; 6(3):175-178.

32. Garner LF, Owens H, Kinnear RF, Frith MJ. Prevalence of myopia in Sherpa and Tibetan children in Nepal. Optom Vis Sci 1999; 76(5):282-285.

33. Tano Y. Pathologic myopia: where are we now? AJO 2002; 134(5):645-660.

34. Coppé AM, Ripandelli G, Parisi V, Varano M, Stirpe M. Prevalence of Asymptomatic Macular Holes in Highly Myopic Eyes. Ophthalmology 2005; 112(12):2103-2109.

## Figures

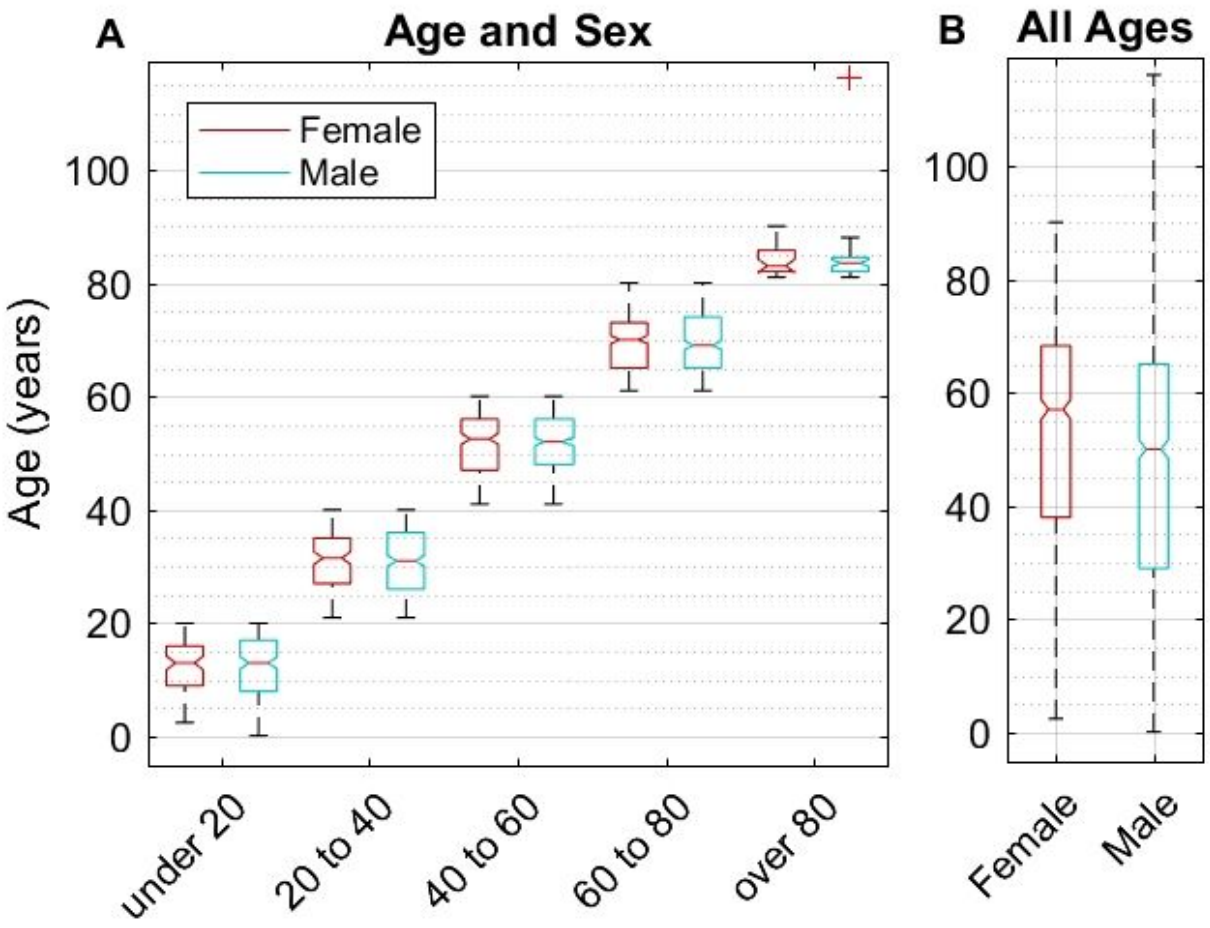


Figure 1

Age and Sex Boxplot: (A) Presenting ages of the 1905 patients in cohorts of 20 years. The boxes indicate 25th, 50th and 75th percentile of the age distributions. The red + represents a 116 year old male outlier. (B) The overall distribution of ages. A bootstrap analysis showed that the 10th, 25th, 50th and 75th percentiles for females were all significantly older than for males (Text).

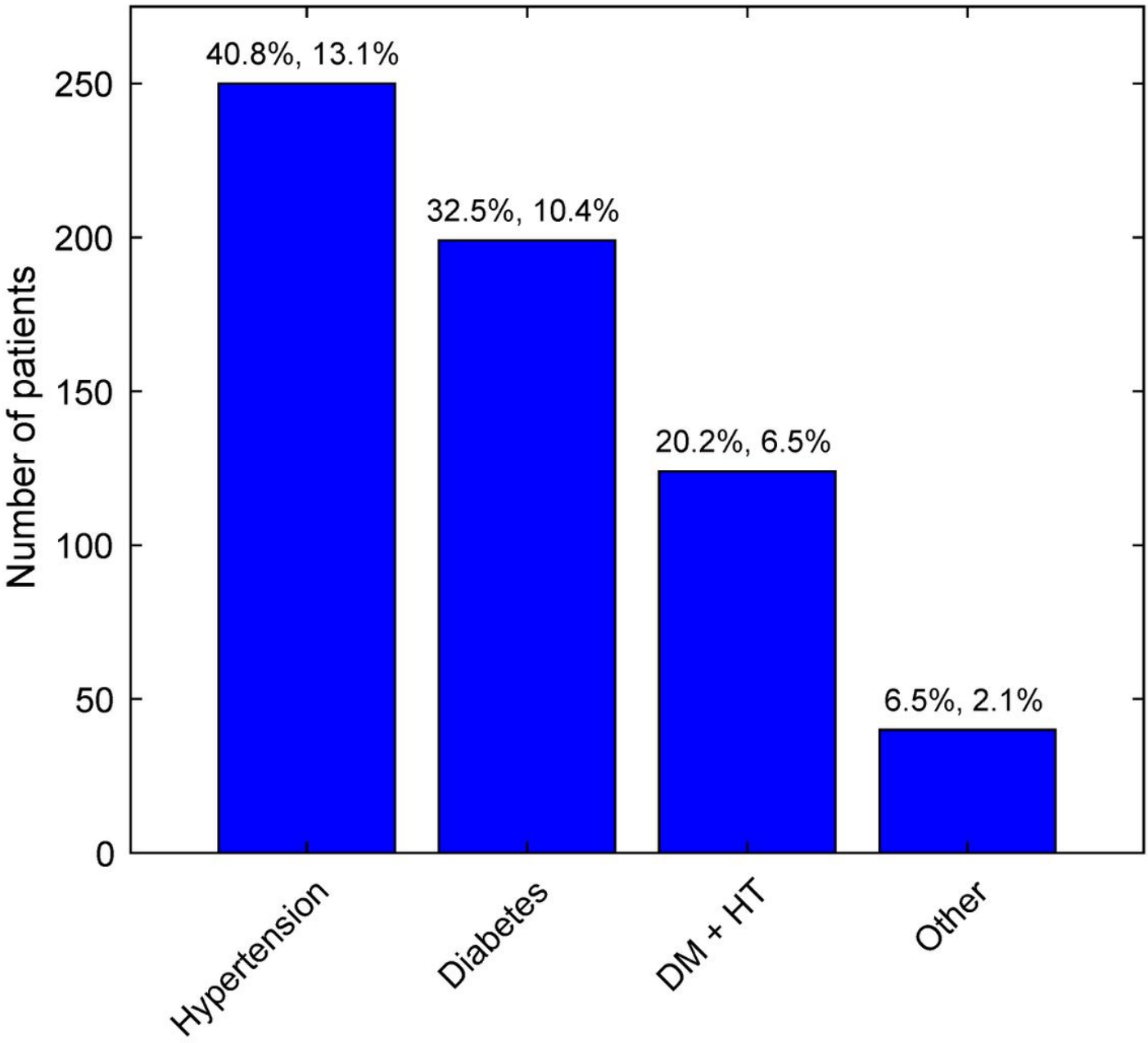


Figure 2

Systemic Disease Prevalence: The breakdown of the commonest systemic diseases found in 613 (32.2%) of the 1,905 patients. The values at the top of the columns give the percentages of the systemic disease patients (left), and the percentage of all patients (right).

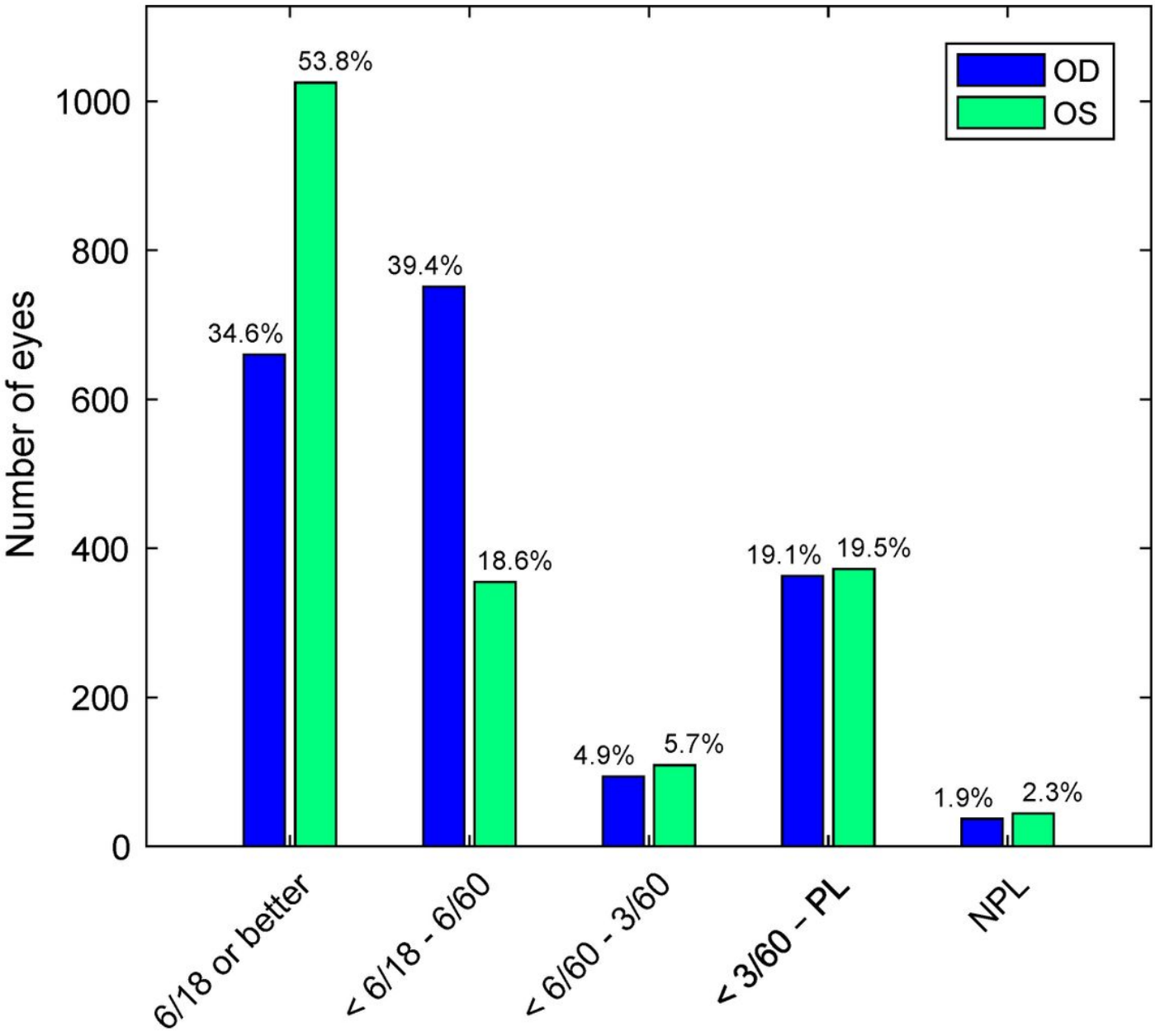


Figure 3

Presenting BCVA: The presenting BCVAs provided significant asymmetries between eyes ($p<0.0001$) in the two groups with acuities of 6/60 or better (chi-square = 158 for "6/18 or better", and 283 for "6/18 to 6/60")

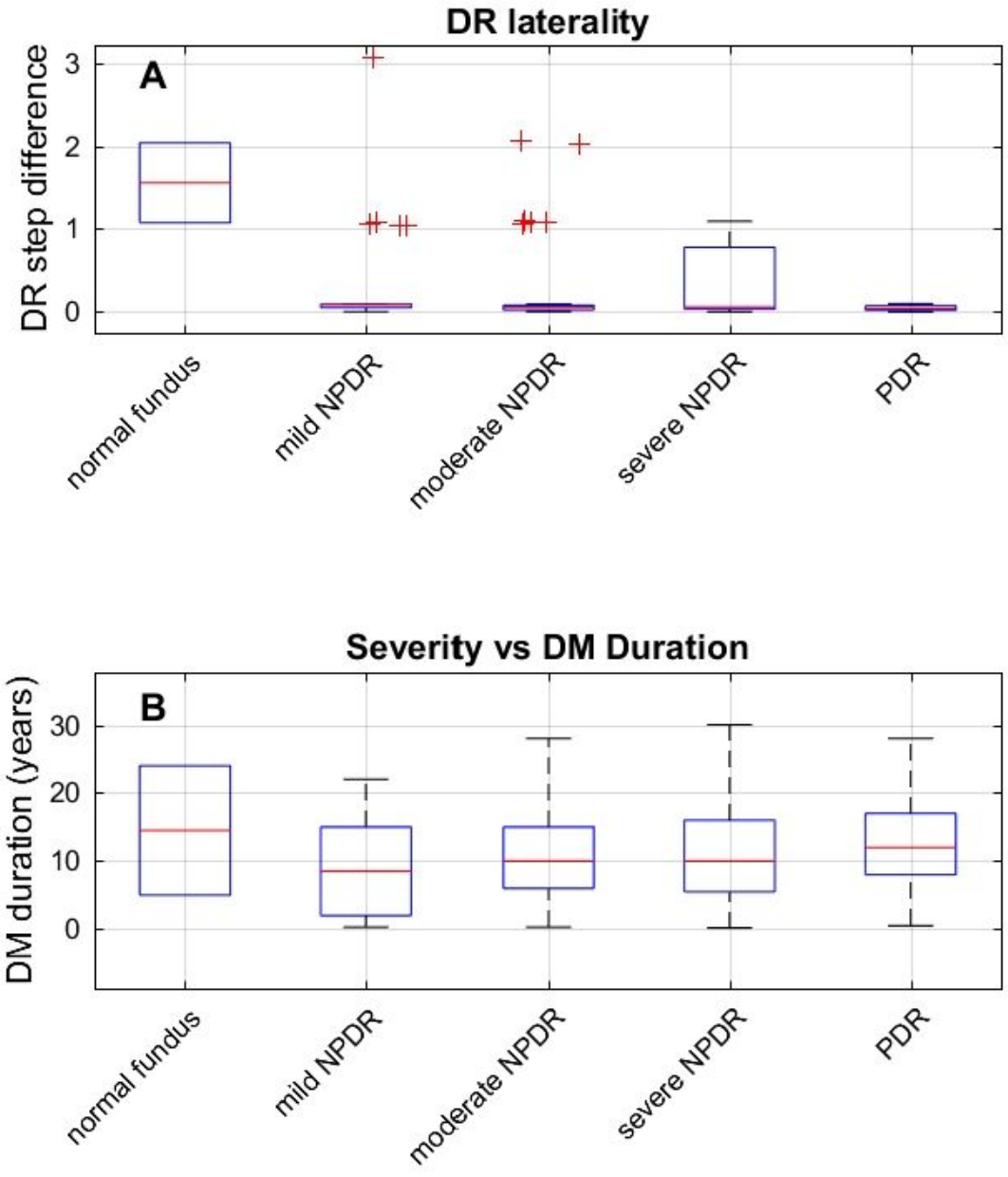


Figure 4

DR Laterality and DM Duration: Laterality and duration disease grouped by the 205 DR patients' better eye (abscissa). (A) The absolute value of the difference between DR-severity steps in the two eyes when the severity levels (normal to PDR) are scored as 1 to 5. Generally the DR became more bilaterally symmetric. A small amount of uniformly distributed noise (0 to 0.03) was added to the data to make the

outliers more distinct (red+). (B) Diabetes duration as a function of the best eye. Duration did not appear to strongly determine severity.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplement1.docx