Axial Myopia and its Influence on Diabetic Retinopathy

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ABSTRACT

Objective: To evaluate the correlation between axial myopia and diabetic retinopathy.

Study Design: Cross-sectional study.

Place and Duration of Study: Eye Department of Postgraduate Medical Institute, Lahore General Hospital, from August 2012 to February 2013.

Methodology: A total of 258 participants suffering from type-2 diabetic retinopathy were included. Axial length was measured by two optometrists using contact type ultrasound biometer. Colored retinal photographs, red free retinal photographs and Fundus Fluorescein Angiography (FFA) were performed on all patients using standard fundus camera. All fundus photographs and angiograms were independently reviewed and graded by two qualified vitreoretinal fellows.

Results: Out of 258 patients, 163 were males (63.2%) and 95 (36.8%) were females. Average age of patients was 56.30 ± 7.57 years. Average axial length of right and left eyes were 23.16 mm and 23.15 mm respectively. There was statistically significant negative correlation between axial length and severity of diabetic retinopathy in the right eye, (Spearman correlation = -0.511, p = 0.0001) as well as the left eye (Spearman correlation = -0.522, p = 0.0001).

Conclusion: There is a protective influence of longer axial length of globe on the stage and severity of diabetic retinopathy. This study may help in modifying the screening protocol for diabetic retinopathy amongst patients of differing axial lengths.

Key Words: Myopia. Diabetic retinopathy. Axial length. Clinically significant macular edema.

INTRODUCTION

Diabetes Mellitus (DM) is one of the major causes of morbidity and mortality in the world and its occurrence in middle age population is on constant incline. In one study, conducted in the province of Punjab (Pakistan), prevalence of type-2 DM was found to be 13.14%. The cause of this chronic disease is multifactorial and it results in a myriad of cardiac and vascular accidents that result in long-term morbidity.

Diabetic Retinopathy (DR) is one of the most common and devastating microvascular complications of DM. According to Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR), in Northern America, DR is the most common factor responsible for new cases of blindness between the ages 25 - 74 years. The occurrence of DR was found to be 29.1% in self reported diabetics. There have been many clinical and epidemiological studies that have looked into the possible risk factors in diabetics that lead to visual impairment. After a careful evaluation, it has been postulated that neuropathy, microalbuminuria, age more than 60 years and presence of nuclear sclerosis are risk factors for visual impairment in diabetic retinopathy.

Likewise, recent trials have shown the influence of certain modifying factors, which are protective towards development and progression of diabetic retinopathy. Optic atrophy and myopia are few of such factors that have shown trend of having a protective influence.

Recently, researchers have started to focus on the pathophysiology of myopia that is in play towards having a protective effect on DR. Meanwhile, the researchers try to find the pathophysiologic relationship between myopia and diabetic retinopathy, there have been many studies that have shown the progression of DR is slowed in the presence of myopia, but the evidence still remains to be inconclusive as the myopia could have been axial or non-axial in most of these studies.

The rationale of this study was to demonstrate a statistically conclusive relationship between axial myopia and its effects on the development and progression of DR. This study can further help the clinicians to modify the screening and therapeutic protocols of DR in patients with differing Axial Length (AL).

The objective of this study was to evaluate the correlation between axial myopia and diabetic retinopathy.

METHODOLOGY

This cross-sectional study was conducted in Eye Department of Postgraduate Medical Institute, Lahore General Hospital, from August 2012 to February 2013. A total of 516 eyes of 258 participants suffering from
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type-2 DM were included in this study from the Outdoor Patient Department. All participants aged 35 years and above were physician diagnosed cases of type-2 DM under treatment of Diabetic Clinic of Lahore General Hospital. Self reported cases of diabetes and those who had undergone cataract extraction were excluded from the study.

Informed consent was taken from all participants of the study. Approval for this study was obtained from Ethical Committee of Postgraduate Medical Institute, Lahore General Hospital. There were no conflict of interests in this study.

Axial Length (AL) was measured by two independent trained optometrists using contact type Axis-II PR A Scan ultrasound Biometer (Quantel Medical, Cedex, France). Ten readings by each optometrist were recorded and the average AL was finally documented for analysis. AL was categorized in 4 quartiles. First quartile had AL equal to or less than 19.5 mm. Second quartile had AL more than 19.5 mm and equal to or less than 22 mm. Third quartile had AL more than 22 mm and equal to or less than 24.5 mm. Fourth quartile had AL more than 24.5 mm.

Autorefraction was performed using Topcon RM 8000B Autorefractor Keratometer (Topcon Medical Systems, Oakland, NJ, USA). Five consecutive readings were recorded. After this, subjective refraction was performed by certified optometrist. Spherical equivalent was defined as the sum of sphere and half of cylinder and was documented for final analysis.

Colored retinal photographs, red free retinal photographs and fundus fluorescein angiography were performed on all patients using standard fundus camera (Topcon TRC 50DX, Topcon Medical Systems, Oakland, NJ, USA). All fundus photographs and angiographs were independently reviewed and graded by two qualified vitreoretinal fellows. In case of any difference of opinion regarding DR grading, a third independent opinion was sought by qualified personnel. We used modified Airlie House classification for staging of DR and categorized patients in following 5 groups in order of increasing severity. Group-1 had mild diabetic retinopathy [no signs of non-Proliferative Diabetic Retinopathy (NPDR), very mild NPDR, mild NPDR]. Group-2 had moderate diabetic retinopathy (Moderate NPDR). Group-3 had severe diabetic retinopathy (severe NPDR, very severe NPDR), Group-4 had proliferative diabetic retinopathy [mild-moderate Proliferative Diabetic Retinopathy (PDR), high risk PDR]. Group-5 had advanced diabetic eye disease. Group-5 did not include patients with tractional retinal detachment involving macula, severe vitreous hemorrhage obscuring fundus details and subhyaloid hemorrhage covering entire macula to ensure accurate biometry findings.

The presence of Clinically Significant Macular Oedema (CSMO) was documented according to recommen-
dations of ETDRS. CSMO was found to be present when there was retinal thickening within 500 microns of macula, exudation within 500 microns of macula, if associated with retinal thickening which may be outside 500 microns of macula and retinal thickening 1500 microns or larger, any part of which may be within 1500 microns of center of macula.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 12. For qualitative data like gender and severity of diabetic retinopathy, the data was presented in the form of frequency (%). Histogram was made for age of the patients. To see correlation in severity of diabetic retinopathy, CSMO and axial length, Spearman rank correlation was calculated and was considered statistically significant at p ≤ 0.05.

RESULTS

Out of a total 258 patient (516 eyes) recruited in the study, 163 were males (63.2%) whereas rest of 95 (36.8%) were females. Average age of patients was 56.30 ± 7.57 years with minimum age observed as 38 years and maximum of 76 years. Average axial length of eyes was 23.15 mm (average right eye axial length = 23.16 mm, left eye axial length = 23.15 mm).

Clinically Significant Macular Oedema (CSMO) was present in majority (318 eyes; 61.62%) of patients (right eye 161; 50.62% and left eye 157; 49.31%). Two hundred and forty seven (47.9%) eyes had mild diabetic retinopathy (right eye in 125; 50.6% and left eye in 122; 49.3%). Sixty two (12%) eyes had moderate diabetic retinopathy (right eye in 32; 51.6% and left eye in 30; 48.3%). Twenty two (4.2%) eyes had severe diabetic retinopathy (right eye in 9; 40.91% and left eye in 13; 59%). One hundred and thirty three (25.8%) eyes had proliferative diabetic retinopathy (right eye in 67; 50.3% and left eye in 66; 49.6%). Fifty two (10.1%) eyes had advanced disease (right eye in 25; 48.1% and left eye in 27; 51.9%).

Regarding axial length in both eyes, 10 (2%) eyes were in first quartile (right eye in 5; 50% and left eye in 5; 50% each). (28.5%) eyes were in second quartile (right eye in 74; 50.3% and left eye in 73; 49.6%). Two hundred and sixteen (41.9%) eyes were in third quartile [whose axial length 22.1 - 24.5 mm] (right eye in 107; 49.5% and left eye in 109; 50.4%). One hundred forty three (27.8%) eyes were in 4th quartile [whose axial length > 24.5 mm] (right eye in 72; 50.3% and left eye in 71; 49.6%).

The average duration of disease in recruited patients was 8.56 ± 4.31 years with a minimum of 2 years and maximum of 23 years. There was significant negative correlation between AL and severity of DR in both eyes, with Spearman correlation of -0.511 and p < 0.0001 (right eye Spearman correlation = -0.469, p < 0.0001 and left eye Spearman correlation = -0.552, p < 0.0001, Table I).
Correlation of axial length and severity of diabetic retinopathy.

Quigley inferred that increasing AL results in stretching of vessel walls.\textsuperscript{17} This result in reduced blood flow in the resultant leakage from retinal vessels in diabetics. Increased blood flow is associated with increasing severity of DR.\textsuperscript{12-15} This elongation of globe. It has been shown that retinal blood flow increases with increasing severity of DR.\textsuperscript{12-15} This finding further stresses on the need of a longitudinal study with controlled variables. Nevertheless, we were able to further strengthen the clinical belief that myopic patients are protected against the onset and progression of DR regardless of the pathogenic mechanisms responsible for this observation.

<table>
<thead>
<tr>
<th>Axial length</th>
<th>Mild diabetic retinopathy</th>
<th>Moderate diabetic retinopathy</th>
<th>Severe diabetic retinopathy</th>
<th>Proliferative diabetic retinopathy</th>
<th>Advanced disease</th>
</tr>
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<tbody>
<tr>
<td>&lt; 19.5 mm</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>19.5 - 22 mm</td>
<td>25</td>
<td>18</td>
<td>10</td>
<td>61</td>
<td>33</td>
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<tr>
<td>22.1 - 24.5 mm</td>
<td>101</td>
<td>38</td>
<td>11</td>
<td>53</td>
<td>13</td>
</tr>
<tr>
<td>&gt; 24.5 mm</td>
<td>119</td>
<td>6</td>
<td>0</td>
<td>15</td>
<td>3</td>
</tr>
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</table>

Spearman Correlation = -0.511, \( p < 0.0001 \)

Overall, a slightly positive correlation (Spearman correlation = 0.127; \( p = 0.004 \)) between CSMO and AL (both eyes) was observed which was significant statistically (right eye Spearman correlation = 0.154; \( p = 0.013 \) and left eye Spearman correlation = 0.099; \( p = 0.127 \)).

Similarly, on combined analysis, the correlation between the duration of diabetes was strongly positive with severity of DR (Spearman correlation = 0.218). All these correlations were statistically significant (\( p < 0.001 \)). The correlation between duration of diabetes was positive with severity of DR when observed individually in right and left eye (Spearman correlation regarding right eye being 0.219 and left eye being 0.217).

**DISCUSSION**

This study was conducted to investigate the influence of varying AL upon occurrence and severity of DR and CSMO. The authors were able to substantially demonstrate that people with type-2 DM and longer AL were protected from occurrence of and severe forms of DR; however, this protective relationship could not be established between longer AL and CSMO. This study showed a linear and continuous protective effect of axial myopia on DR. There have been only few studies in past to evaluate biometric parameters with DR;\textsuperscript{11} most of the studies have evaluated refractive myopia with DR. In this study, status of refractive error was not included in final analysis due to confounding effects of nuclear sclerosis on overall refraction; thereby masking the actual axial refractive error and its corresponding effects on DR. This is because nuclear sclerosis is likely to be present in patients over 50 years of age. Diabetics have earlier and more profound lenticular changes than normal population.

Although, exact mechanisms remain unclear regarding the pathophysiology of axial myopia and its protective effect on DR, most studies have attributed this effect to pathological changes occurring in retina due to elongation of globe. It has been shown that retinal blood flow increases with increasing severity of DR.\textsuperscript{12-15} This increased blood flow is associated with increasing pressure in vessel wall (Laplace's law)\textsuperscript{13,16} and the resultant leakage from retinal vessels in diabetics. Quigley inferred that increasing AL results in stretching of vessel walls.\textsuperscript{17} This result in reduced blood flow in vessels and resultant low pressure in vessels walls.\textsuperscript{18,19} With resultant decreased pressure in vessel wall, there is less profound occurrence of typical signs of DR due to decreased leakage.

It has also been shown that there is associated choriotinal thinning with increasing myopia.\textsuperscript{20} Stefansson demonstrated that choriotinal thinning is associated with decreased retinal metabolic demands which may result in protection against DR.\textsuperscript{21}

WESDR study has shown that patients with higher myopic refractive errors are protected against the progression to PDR.\textsuperscript{3} Pierro has also demonstrated that patients having NPDR and PDR had shorter AL when compared to patients with no DR.\textsuperscript{22} In a recently concluded trial (Singapore Indian Eye study), it was observed that patients with myopic refractive errors are less likely to have DR (OR, 0.68; 95% CI, 0.46 - 0.98) but are more likely to have nuclear sclerosis.\textsuperscript{23} Therefore, it is important to correlate DR with axial myopia than with overall refractive myopia (myopes are more likely to develop nuclear sclerosis which adds to overall myopic error). Man provided an elaborate review of available evidence between myopia with its AL component, corneal curvature, nuclear changes and anterior chamber depth and its association with DR.\textsuperscript{24}

He concluded that AL is the only variable contributing to protective effect of myopia on DR.

Strengths of this study lie in the standardized protocol for biometric measurements, documentation of DR through fundus photographs and fundus angiography and removal of a potential bias of nuclear sclerosis which may have added to overall myopia of participants; thus skewing the final results. The weakness of this study lies in its cross sectional design because the onset and progression of DR is dependent on multiple factors. A prospective/longitudinal trial with more controlled systemic variables will be more suitable for establishing the answer for hypothesis under question. In this study, the authors were not able to establish a protective relationship between axial myopia and CSMO. This finding further stresses on the need of a longitudinal study with controlled variables. Nevertheless, we were able to further strengthen the clinical belief that myopic patients are protected against the onset and progression of DR regardless of the pathogenic mechanisms responsible for this observation.
CONCLUSION
This study positively contributes to the clinical impression that patients with axial myopia are less likely to develop severe forms of DR. It further intrigues researchers to find exact mechanisms responsible for protection of myopic fundi against harmful effects of DR. This study may aid clinicians in improving the screening protocols in myopic diabetics and may lead to revised protocols of management of DR in such patients. The authors feel a strong need of further longitudinal studies under more controlled conditions to isolate factors leading to protection against vision threatening effects of DR.

REFERENCES