Association between myopia and diabetic retinopathy in Saudi diabetics - A cross sectional study
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Abstract
This community based survey was held from February 2014 to May 2015 in Majmaah, Saudi Arabia. Out of the registered diabetic patients in the primary care centers of Majmaah city, a random sample was selected. An ophthalmology consultant took a detailed history and performed ophthalmic examination to determine refractive status and stage of diabetic retinopathy in each eye. Based on the spherical equivalent of refractive error, participants were grouped as having myopia, emmetropia and hyperopia. Myopia was further graded as mild (-0.75 to -3 Diopter), moderate (-3 to -6 Diopter) and severe (more than -6 Diopter). We examined 654 eyes of 327 diabetic patients. The prevalence of any stage of diabetic retinopathy in at least one eye among the study group was 35.8% (n=117). The average spherical equivalent was 0.05 with SD (+3.18). There was 112 (20.3%) eyes with myopia out of them 63 (56.3%) were mild, 27 (24.1%) were moderate and 22 (19.6%) were high. There was 194 (35.1%) eyes with hyperopia and 247 (44.7%) eyes were emmetropic. Grades of myopia seem to be negatively associated with the presence and severity of DR among the eyes of Saudi diabetics.

Keywords: Diabetes, Diabetic Retinopathy, Myopia, Proliferative diabetic retinopathy and Refractive Error

Introduction
Diabetic retinopathy (DR) is the most common complication of diabetes mellitus (DM), and is the leading cause of new cases of visual impairment and blindness among adults aged 20-74 years (Fong et al., 2004) DR is also considered to be the leading cause of blindness in the Kingdom of Saudi Arabia (Al-Rubeaan et al., 2015). The estimated prevalence of DR ranges from 20% to 30% among US adults with diabetes (Zhang et al., 2005-2008, Cynthia Owsley et al., 2015). In Saudi Arabia (SA), it is reported to be ranging from 20% to 36%. (Alwakeel et al., 2008; Ataur Rahman Khan et al., 2010; Al Ghamdi et al., 2012; Al-Rubeaan et al., 2015; Razia A. Ahmed et al., 2016).

Several factors have been identified as determinants for the development of DR and its progression, including, type and duration of DM, age, gender, glycemic control, hypertension, the body mass index (BMI), smoking, serum lipids and presence of microalbuminuria (MA) (Cai et al., 2006; Parving et al., 2006). Myopia was suggested to have a beneficial effect against DR as early as 1965 by IS (Jain et al., 1965). Subsequently, several researchers also noted this association, but the underlying cause remained debatable (Wang et al., 2016; Yu Fu et al., 2016).

Myopia is a common ocular condition affecting approximately 1.6 billion people worldwide and its prevalence is expected to reach 2.5 billion by the year
2020 (Kempen et al., 2004). However, the magnitude of myopia in adult Saudi population is not known, the prevalence of myopia in Saudi children varied from 5.8% in Qassim to 9% in the Eastern Province (Al Wadaani et al., 2012; Aldebsai, 2014). Few population-based studies have studied the association of myopia and DR (Ryan EK Man et al., 2013; Wang et al., 2016; Yu Fu et al., 2016). However, no study was conducted in Middle East to our knowledge.

Saudi Arabia, a country with high magnitude of diabetes prevalence and its eye complications has encouraged research related to non-communicable disease including diabetes and its complications and hence propose evidence based strategies to prevent such ailments (Ministry of Economy and Technology, 2017). We conducted a study in the catchment area of Majmaah Primary Health Centers (PHCs) in collaboration with our institute. We present the magnitude, grades and association of myopia to the grades of diabetic retinopathy in Saudi diabetic persons who were registered with Majmaah PHCs.

Materials and methods

This community based cross-sectional study was carried out in 2015-16. The Ethical Review Committee of our institute approved this study. A written informed consent was obtained from all participants before interview and examination. This being part of a major study, details of recruitment, population, sample size calculation and assessment methods are described in details in our previous publication (Alabdulwahhab, 2016). Briefly, the study population was 1,546 Saudi adults, enrolled in the diabetic registry of six PHCs in the Al Majmaah city of central Saudi Arabia. A representative sample of diabetics was invited for eye assessment in the eye clinic of the teaching hospital.

The participants were interviewed to collect information like age, gender, duration and mode of diabetes management. One senior ophthalmologist and two ophthalmic assistants were the field staff. They carried out comprehensive ophthalmic evaluation. Visual Acuity (VA) was measured using Snellen distance vision screen. If a person was wearing spectacles or contact lenses for distance viewing, his/her vision was noted with the visual aids. Auto refraction was performed using Reichert RK600 Auto Refractor Keratometer (Reichert ophthalmic instruments, Depew, NY, USA). Three consecutive readings were recorded and the average was registered. From them, the spherical equivalent (SE) was calculated as the sum of sphere plus half of cylinder. Myopia was defined as any SE <-0.75 D (Diopter) and hyperopia as any SE >+0.75D. Mild myopia was considered if -0.75 ≥ SE > -3.0, moderate myopia if -3.0 ≥ SE > -6.0 and high myopia if SE < -6.0. The anterior segment of each eye was assessed using the Haag Streit Slit lamp bio-microscope (Haag Streit, Germany). The pupils were dilated using 0.5% tropicamide and posterior segment was evaluated with indirect ophthalmoscope (Keeler, UK) as well as using slit-lamp bio-microscope and +90-diopter lens (Volk, USA). The status of diabetic retinopathy and diabetic macular edema of each eye was determined by using international clinical diabetic retinopathy and diabetic macular edema disease severity scales (Wilkinson et al., 2003).

The data was entered and analyzed using Statistical Package for Social Sciences (SPSS) 23.0 (IBM, NY, USA). For quantitative variables, distribution curve was plotted and if it was normal, we calculated the mean and the standard deviation of the variable. If it was not normally distributed, we calculated the median and 25% quartile values. For qualitative variables, we calculated frequencies and percentage proportions. For associating the outcome variables to the independent variables, we calculated Odds Ratio.
(OR), its 95% confidence interval (CI) and two-sided P value. We also added variables that could influence the association of myopia to DR into the regression model using step out method. The results were reported in adjusted odds ratio. A p-value of <0.05 was considered as statistically significant.

Results

A total of 654 eyes of 327 subjects with DM participated in the study, 61.4% were males and 38.6% were females. The mean age (± SD) was 54.95 ± 11.65 years. Table 1 summarizes the demographic characteristics of the subjects.

The overall prevalence of any stage of diabetic retinopathy, in at least one eye, among the study group, was 35.8% (n=117). Figure 1 shows the prevalence of grades of DR. The proportion of DR patients with Clinically Significant Macular Edema (CSME), was 37.6%, which accounts for a prevalence of 13.5% of the total sample.

After excluding pseudophakic eyes (n=74) and eyes where autorefraction could not be done due to media problems (n=29), data from 553 eyes of 261 subjects were analyzed. The average SE was 0.05 (±3.18). There were 112 (20.3%) eyes with myopia out of them 63 (56.3%) were mild, 27 (24.1%) were moderate and 22 (19.6%) were high. Eyes with hyperopia were 194 (35.1%) and emmetropic eyes were 247 (44.7%). Figure 2 summarizes the refractive errors prevalence in our study group.

Logistic regression analysis after adjustment for age, gender and duration of diabetes are presented in Table 2 which shows that myopia is negatively associated with DR and this association was statistically significant (OR = 0.543, CI (0.299 – 0.986), p=0.037). Not only that, increased severity of myopia was associated with decreased OR of DR (OR = 0.413, CI (0.177 – 0.963), p=0.041). Refractive status of the eye and severity of myopia has no effect on the development of CSME.

Discussion

This study provides population based data on the magnitude of DR and myopia among adult Saudi diabetics and association of myopia and its various grades to presence and stages of DR.

The 35.8% prevalence of DR in our study matched with the 31.3% presented by Al Ghamdi et al. (2012), 30% by Khan et al. (2016), 36.8% by Al Ghamdi et al., (2012), 36.1% by Parving et al. (2016), and 27.8% by Jain et al. (1965) all done in Saudi Arabia. It should be noted that these reported rates of DR were from different parts of Saudi Arabia; many of them were part of the Rapid Assessment for Avoidable Blindness

Table 1: Demographic characteristics of the subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases with DM² n (%)</th>
<th>Cases with DR² n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>327 (100)</td>
<td>117 (35.8)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>201 (61.4)</td>
<td>81 (69.2)</td>
</tr>
<tr>
<td>Female</td>
<td>126 (38.6)</td>
<td>36 (30.8)</td>
</tr>
<tr>
<td>Age (Mean ± S.D) (y)</td>
<td>54.95 ± 11.65</td>
<td>57.47 ± 9.70</td>
</tr>
<tr>
<td>Duration of DM (Mean ± S.D) (y)</td>
<td>11.14 ± 7.83</td>
<td>15.7 ± 7.45</td>
</tr>
</tbody>
</table>

*Diabetes Mellitus, $ Diabetic Retinopathy
Table – 2. Binary logistic regression analysis using backward conditional approach for factors associated with Diabetic Retinopathy and CSMD

<table>
<thead>
<tr>
<th>Refractive errors</th>
<th>DR* OR (95% of CI)</th>
<th>P</th>
<th>CSME* OR (95% of CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperopia (reference category)</td>
<td>--</td>
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</tr>
<tr>
<td>Emmetropia</td>
<td>0.829 (0.528-1.302)</td>
<td>0.355</td>
<td>0.79(0.442-1.370)</td>
<td>0.386</td>
</tr>
<tr>
<td>Myopia</td>
<td>0.543 (0.299-0.986)</td>
<td>0.037*</td>
<td>0.759(0.367-1.570)</td>
<td>0.457</td>
</tr>
<tr>
<td><strong>Myopia Severity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (reference category)</td>
<td>--</td>
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<tr>
<td>Moderate + High</td>
<td>0.578 (0.322-0.878)</td>
<td>0.024*</td>
<td>0.799(0.236-2.866)</td>
<td>0.597</td>
</tr>
</tbody>
</table>

§Adjusted for age, gender and duration of diabetes, *Significant at 5% level of significance, †Diabetic retinopathy, ‡clinically significant macular edema

Fig.-1. Detailed Prevalence of grades of Diabetic Retinopathy

DR: Diabetic Retinopathy; PDR: Proliferative; Diabetic Retinopathy; NPDR: Non Proliferative Diabetic Retinopathy

(RAAB), targeting 50 years and older population; and all of them were conducted in big cities. In contrast, our study had relatively younger participants and was done in a medium sized city, which is the case of most Saudi cities. Our DR prevalence is also almost similar to the global estimate of 34.6% in the study of Yau et al. (2012) which analyzed 35 studies from all over the world (Joanne, 2012).

Myopia was present among one in five diabetics in our study. Perhaps for the first time, refractive error profile of Saudi diabetics was estimated, which is similar to Lim et al. (2010) (23.4%) in the Singapore Malay Eye Study and to Ganesan et al. (2012) (19.9%).
We noted that myopia in diabetic patients had a negative association to the DR and this association was having a dose response relationship. Lim et al. (2010) also had similar result and they suggested that the axial length of the eyeball had confounding effect on this association of myopia and DR. Pan et al. (2013) studied the role of myopia on DR, AMD and glaucoma and they also suggested that the axial length of eye ball had significant influence on DR progression. These two previous studies had an East Asian population while Tayyeb et al. (2014) studied Pakistani population and suggested that it is the axial length in myopia, which has the protective action on DR among diabetics. Unfortunately, in our community-based study, we had not measured the axial length of diabetic eyes. So we could not conclude about the role of axial length in myopia among Saudi diabetics.

However, some other studies did not find an association between myopia and the presence of DR. (Ganesan et al., 2012) This keeps the field open for further studies on different populations to support or to reject that effect.

In our study, although we did not find a negative association to CSME, it was significantly and negatively associated to DR. This is in contrast to the findings of Pan et al. (2013) Pathophysiological influence of myopia on DR and CSME could be different. The disease severity grading also focuses on CSME independent of NPDR and PDR, both for screening and management (Shimada, 2004) Further studies are needed to study this differential influence of myopia on DR and DME.

The mechanism by which myopia lowers the risk of DR is not fully understood. Several plausible mechanisms have been proposed and they are revolving around decreased ocular blood flow, decrease oxygen demand and decrease in inflammatory cytokine. In axial myopia elongation of the globe causes stretching of the retina, making it thin, which may result in decrease blood flow that lowers pressure exerted on vessel walls, and thus may result in a protective effect against DR progression (Lam et al., 2002; Benavente-Pérez et al., 2010; Berisha et al., 2010). In addition, thinning of the retina may decrease retinal metabolism that decrease oxygen demand and so could protect against PDR. Increased ocular volume in myopic eyes may cause decrease in inflammatory cytokine concentration and hence reduce DR complications (Al Wadaani et al., 2012).

Posterior vitreous detachment (PVD) is a known protective factor for the progression of DR (Ono et al., 2005). The myopic refractive error was also noted as an independent risk factor for PVD (Chuo et al., 2006). Thus, negative association of DR and its stages among myopia noted in our study could be explained by presence of PVD. Further studies and detailed documentation of PVD in cases of both myopia and diabetes is therefore recommended to confirm this pathophysiology of DR in myopic diabetic eyes.

There were few limitations in our study. Although most of the myopias are axil specially the high ones (Ganesan et al., 2012) we did not measure the axial length to differentiate between axial and refractive myopia. The criteria to label refractive status were by using the auto-refractometer. This equipment often gives more myopic results compared to the manual refraction (Payerols et al., 2016). Thus, cases of myopia are likely to be over-represented, therefore, readings of more than -0.75D were considered as emmetropic in the present study.

In conclusion, grades of myopia seem to be negatively associated to the presence and severity of DR among Saudi diabetic eyes. It is too early to suggest that myopia is playing a protective role against DR.
The research to understand real mechanism of this phenomenon is encouraged.

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References


