INTRODUCTION

More than 371 million people are suffering from diabetes, worldwide. However, half of diabetics remain undiagnosed and the toll is on constant rise.1 In Pakistan, the prevalence of diabetic retinopathy and type II diabetes has been reported to be 27% and 10%, respectively.2,3 Amongst its various ocular complications, diabetic retinopathy (DR) is the most important cause of visual loss and blindness.4,5 Diabetic retinopathy can deteriorate a patient's life standards rendering him a dependant entity in the society, which is the reason why early detection of DR is advocated.6 A common cause of vision loss in patients with diabetic retinopathy is macular edema.7

Optical coherence tomography (OCT) has emerged as an objective method of high-resolution cross-sectional imaging of the retina.8 It allows retinal thickness quantification in diabetic retinopathy with excellent reproducibility.9 Diabetic macular edema has been associated with reduction of visual acuity for years.10 However, the presence of macular edema does not necessarily preclude good vision.11,12 Nussenblatt et al. were able to demonstrate that the degree of macular thickening, rather than the presence of macular edema, was significantly correlated with visual acuity.13 As new therapies for retinal diseases are introduced, OCT's value in the quantification of retinal thickening and subretinal exudation is becoming pivotal, but it is expensive and not readily available.

A surrogate outcome is the one that predicts or predate a measure of clinical interest. Here, visual acuity was evaluated as a surrogate measurement of retinal thickness. However, a surrogate outcome can be considered significant only if a strong correlation exists between it and the measure of primary interest. It should also be less expensive, easy to perform and should be able to predict long-term changes.14

The aim of this study was to evaluate the correlation between the central macular thickness (CMT) using OCT and best-corrected visual acuity in diabetic macular edema.

METHODOLOGY

This descriptive study was performed at Al-Shifa Trust Eye Hospital, Rawalpindi, from August 2011 to August 2012. Eighty eyes of 68 patients, fulfilling the inclusion criteria were enrolled from the Retina Department. Potential eligibility was assessed as part of a routine-care examination, which included history, general physical examination and ophthalmic examination. Best-
Corrected visual acuity was recorded on Snellen visual acuity chart, which was then converted to logMar scale. Inclusion criteria were diagnosis of diabetes mellitus by a registered medical practitioner, definite retinal thickening due to diabetic macular edema (macular edema or clinically significant macular edema) based on clinical examination and ETDRS criteria, and pupil dilated to 5 mm or larger. Exclusion criteria were history of chronic renal failure requiring dialysis or kidney transplant, congestive heart failure currently under treatment, blood pressure > 180/110 (systolic above 180 or diastolic above 110) and non-diabetic macular edema. Others were corneal, lenticular or media opacities, intraocular inflammation, history of glaucoma, other vitreoretinal pathology, previous intraocular surgery of less than one year duration, clinical suspicion of macular ischemia and previous panretinal photocoagulation or macular photocoagulation.

For subjects who were eligible for the study, the study protocol was discussed with the patient. They were fully explained about the whole procedure, their questions were answered and informed consent was taken. Demographic profile was recorded. The pupils were dilated about 30 minutes prior to the OCT, which was performed by using Carl Zeiss Stratus OCT and by same operator every time. The retinal thickness was recorded at fovea. Each optical coherence tomograph was evaluated to be of adequate quality for submission.

Data was analyzed on SPSS version 15.0 and Matlab version R2010b. Mean ± S.D was calculated for age, visual acuity and retinal thickness at fovea. Frequency as percentage was presented for gender. Median foveal thickness was calculated for varying visual acuity. The data on visual acuity measured in logMar, age, duration of diabetes and foveal thickness was assessed for assumptions of normal distribution. Normality of data was assessed using the Shapiro-Wilk test and visual inspection of histogram, normal P-P plot and normal Q-Q plot. To assess the relation between foveal thickness and best corrected visual acuity, Spearman correlation coefficient was used as the data was not normally distributed. A p-value ≤ 0.05 was considered significant.

RESULTS

Among the 68 cases, there were 36 males (52.9%) and 32 females (47.1%). Their mean age was 56.52 ± 6.89 years (ranging from 38 to 74 years). The mean duration of diabetes was 12.79 ± 5.884 years (ranging from 3 to 25 years). Majority of the patients were above 45 years. Only 8.8% (n=7) eyes were from patients between 35 - 45 years, 42.5% (n=34) were between 46 - 55 years, 40% (n=32) between 56 - 65 years, and 8.8% (n=7) were 66-75 years. The median visual acuity measured on logMar scale was 0.80 (ranging from 0.20 to 1.80) with an interquartile range of 0.40. The median foveal thickness was 373.50 micron, ranging from 183 to 825µ, and interquartile range of 164µ. The best-corrected visual acuity (on logMar scale) with corresponding foveal thickness and their inverse relation is given in Table I.

The Shapiro-Wilk test for foveal thickness revealed that the data was not normally distributed D (80) = 0.926, p < 0.001. The visual acuity data was also not normally distributed as depicted by the Shapiro-Wilk test, D (80) = 0.926, p < 0.001. Age of respondents was following the assumptions of normality, D (80) = 0.933, p < 0.001. The visual acuity data was also not normally distributed among respondents as depicted by Shapiro-Wilk test, D (80) = 0.993, p=0.001.

There was moderate positive correlation between foveal thickness and visual acuity in logMar, which was statistically significant (rs = 0.574, p < 0.001). There was a positive linear pattern of relation between visual acuity and foveal thickness; however, this was not followed in eyes with poor visual acuity (worse than logMar VA 1). For eyes with visual acuity upto 1 on logMar scale, the Spearman correlation coefficient was 0.645, p < 0.001. The data on 11 eyes with visual acuity more than 1 on logMar scale showed no significant correlation between foveal thickness and visual acuity; rs = -0.522, p > 0.05. Foveal thickness was found to be positively correlated with the duration of diabetes. However, this was a weak correlation (rs = 0.249, p=0.026). Table II.

<table>
<thead>
<tr>
<th>Visual acuity in logMar</th>
<th>Mean foveal thickness (µm)</th>
<th>Std. Deviation</th>
<th>Mean foveal thickness (µm)</th>
<th>Std. Deviation</th>
<th>Mean foveal thickness (µm)</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>Mean 252.67</td>
<td>65.98</td>
<td>(Snellen equivalent 6/9)</td>
<td>N 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.3</td>
<td>Mean 274.43</td>
<td>83.388</td>
<td>(Snellen equivalent 6/12)</td>
<td>N 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>Mean 324.33</td>
<td>88.51</td>
<td>(Snellen equivalent 6/18)</td>
<td>N 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.6</td>
<td>Mean 403.17</td>
<td>92.525</td>
<td>(Snellen equivalent 6/24)</td>
<td>N 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.8</td>
<td>Mean 339.90</td>
<td>75.177</td>
<td>(Snellen equivalent 6/36)</td>
<td>N 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Mean 497.78</td>
<td>140.287</td>
<td>(Snellen equivalent 6/60)</td>
<td>N 23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>Mean 512.22</td>
<td>156.205</td>
<td>(Snellen equivalent 6/120)</td>
<td>N 9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table II: Correlation of foveal thickness with visual acuity, duration of diabetes and age.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Median</th>
<th>IQR</th>
<th>Correlation with foveal thickness (rs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foveal thickness (µm)</td>
<td>373.50</td>
<td>164</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Visual acuity (LogMar)</td>
<td>0.800</td>
<td>0.40</td>
<td>0.574**</td>
<td>0.000</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>11</td>
<td>10</td>
<td>0.249</td>
<td>0.026</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56</td>
<td>9</td>
<td>0.012</td>
<td>0.919</td>
</tr>
</tbody>
</table>
DISCUSSION
Diabetic macular edema is associated with considerable visual morbidity in diabetic patients. Timely and prompt treatment is dependent on early recognition of diabetic macular edema. OCT has emerged as a major breakthrough amongst the modalities for early detection and then further monitoring of diabetic macular edema. It renders high-resolution cross-sectional images of the retina, and offers a structural and quantitative analysis of clinically significant diabetic macular edema. Since it is an expensive investigation, therefore, it is not readily available in many centers in our country. Therefore, the authors tried to assess the relationship between the foveal thickness and the visual acuity to see their relation. This study has found the correlation between retinal thickness and visual acuity in diabetic macular edema. To the authors’ knowledge, this is the first study that has been done on this topic in our region.

The qualitative relation between macular thickness and visual acuity has long been discussed. However, the evidence for quantitative association became possible only after the advent of OCT. In this study, the authors were able to demonstrate a modest relation between them. However, wide ranges of visual acuities were found with same retinal thickness. Sometimes, the patients had very good visual function even with significant retinal thickness and vice versa. Thus, it can be said that the mechanism of visual function is quite complex, and retinal thickness may be regarded as one of the many contributing factors.

Extensive research has been done internationally, in this regard. In the study by Goebel et al., there was an intermediate correlation between retinal thickness and visual acuity, particularly in patients without macular ischemia. Macular ischemia can thus be considered as a confounding factor in such studies. Therefore, whenever there was a clinical suspicion, such patients were excluded from the present study after confirmation on fluorescein angiogram.

Browning et al. again demonstrated the modest relation between visual acuity and retinal thickness. They found that relationship between the two followed a linear pattern in majority of eyes. However, they had excluded the patients over 70 years of age, foveal thickness over 500 microns, and visual acuity worse than 20/200, from their study. In the present study, the authors did not follow the cut off value of 500 microns, as some of patients fulfilling the rest of inclusion criteria had foveal thickness more than 500 microns. The authors, however, attributed the significant drop of visual acuity as compared to other patients to this massive edema and the unknown duration of disease.

According to the study conducted by Alkuraya et al., visual acuity correlated well with central macular thickness in diabetic macular edema $(r = 0.558, p < 0.001)$. In the study done by Vujosevic, visual acuity and central macular thickness correlated significantly in the NCSME (no clinically significant macular edema) group $(r=-0.6, p=0.008)$, but not in the NE (no edema) $(r=-0.144, p=0.6)$ or in the CSME (clinically significant macular edema) $(r=-0.46, p=0.11)$ groups. In the research done by Alasil et al., the relationship between OCT derived retinal morphology and visual acuities was studied. They found that the quantification and subanalysis of OCT features were of some value in patients with diabetic macular edema (Pearson correlation=0.3248, $p=0.005$). However, they also calculated the photoreceptor outer segment thickness (POS) in their study and found it to be more important predictor of function and visual acuity in DME patients.

According to various other studies, a variable correlation exists between macular thickness and visual acuity ranging from $r^2=0.28$ to 0.73. Thus, many other factors that need to be considered might range from unrecognized macular ischemia and macular microcirculation to duration of macular edema. These factors, especially the latter, is difficult to assess in our setting, where patients do not come to hospitals for routine examination and more often present very late. The results of this study cannot be applied to the patients of renal failure or congestive cardiac failure, as these patients were not included in this research project.

CONCLUSION
There was a modest relationship that existed between retinal thickness and macular edema. However, the two cannot be used interchangeably in clinical practice. Therefore, visual acuity alone is not a reliable surrogate measure for the retinal thickness evaluation; and the two entities can augment yet not replace each other.

REFERENCES


