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Original Article

CORRELATION BETWEEN MACULAR AND IRIS AND MACULAR THICKNESS IN CONTROLLED VERSUS UNCONTROLLED DIABETIC PATIENTS

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Abstract

Background: *Diabetes mellitus (DM) can lead to ocular complications, including diabetic retinopathy (DR) and macular edema. The current research compared iris thickness (IT) and central macular thickness (CMT) between controlled and uncontrolled diabetic patients.* ***Methods:*** *Sixty patients participated in the cross-sectional study, aged ≥18 years with controlled (n=20) and uncontrolled (n=20) DM, and non-diabetic controls (n=20). CMT and IT at1,2, and 3 millimeters from the margin of the pupil were measured using optical coherence tomography (OCT) and anterior segment imaging, respectively.* ***Results:*** *Compared to the control group, both diabetic groups had considerably decreased CMT ($p < 0.001$), but comparable between controlled and uncontrolled diabetics. There were no discernible variations in IT between the groups regardless of the distance. The results showed that CMT and IT had a significantly negative correlation with diabetics under control at 2 mm ($r = -0.569$, $p = 0.008$), but not at other distances.* ***Conclusions:*** *Diabetic patients exhibited macular thinning regardless of glycemic control, while IT was unaffected. Interestingly, lower CMT correlated with reduced IT at specific locations (IT2 and IT3) in controlled diabetics, suggesting a potential relationship between these ocular parameters in this population.*

Keywords: *Diabetes mellitus, Diabetic retinopathy, Macular thickness, Iris thickness, Optical coherence tomography*

1. Introduction

Diabetes mellitus (DM), characterized by persistent hyperglycemia due to impaired insulin production or action, inflicts significant morbidity and mortality across multiple bodily systems [1]. The American Diabetes Association stratifies type 2 DM patients based on glycosylated hemoglobin (HbA1c) levels, with uncontrolled diabetes defined as HbA1c > 7% and controlled diabetes as HbA1c ≤ 7% [2]. Diabetic retinopathy (DR), a preventable microvascular complication, represents the leading cause of blindness among the adult population worldwide [3]. Its prevalence is anticipated to escalate by 2030 due to increasing diabetes rates and sedentary lifestyles [4]. One-third of DM patients develop DR, with disease duration constituting a major risk factor. Secondary macular edema contributes significantly to

vision loss in DR patients [5]. Diabetic macular edema can manifest at any DR stage and becomes treatment-refractory in advanced phases, underscoring the importance of early detection and intervention strategies [6]. Multiple factors influence DR progression, including hyperglycemia, hypertension, diabetes duration, and HbA1c levels [7], which may also impact macular thickness (MT) changes and confer diabetic macular edema risk [8]. Visual acuity in DR frequently correlates with foveal involvement, perifoveal capillary perfusion, and central foveal retinal thickness. Approximately 10% of DR cases develop diabetic macular edema [9]. Optical coherence tomography (OCT) enables cross-sectional retinal imaging and MT quantification, potentially facilitating early DR detection and treatment [10]. Retinal lesions result from microvascular damage caused by chronic hyperglycemia, which impacts both the anterior and posterior portions of the eye when diabetes is present [11]. Some examples of these conditions include neovascularization, microaneurysms, exudates, venous abnormalities, intraretinal microvascular anomalies, and hemorrhages. Also, in diabetic patients, a thicker iris near the pupil coincides with a thicker macula, suggesting that retinal changes from diabetic retinopathy might be reflected in the iris structure closest to the pupil [4,11]. Though the onset timing, iris structural changes remain understudied. Therefore, the current research compared iris and macular thickness between controlled and uncontrolled diabetic patients.

2. Patients and Methods

A cross-sectional study was undertaken on a sample of 60 participants, all of whom were 18 years of age or older and of both genders, with controlled and uncontrolled DM, in the Ophthalmology dept. at Sohag Univ., Egypt from January 2024 to May 2024. This trial was conducted following ethical approval and with informed consent from all participants. The exclusion criteria encompassed patients with axial length below 21 mm or above 25 mm, a medical history of ocular conditions like glaucoma or uveitis, prior refractive or ocular surgery, corneal opacity, neurodegenerative or cardiovascular diseases, anemia, or the usage of medications unrelated to diabetes treatment. The individuals were categorized into three distinct groups: Group I (n=20) contained individuals with uncontrolled diabetes, Group II (n=20) consisted of individuals with controlled diabetes, and Group III (n=20) included individuals without diabetes. The methodology involved evaluating all patients through demographic data age and sex, HbA1c levels, medical and ophthalmic history, and a full ophthalmic examination. Visual acuity, best-corrected visual acuity, intraocular pressure, refractive error, axial length, fundus examination, and inspection of the anterior and posterior segments were all part of the examination. The 3D OCT-1 imaging system was used to quantify MT after the pupils were dilated. Images with a quality strength of 25 or higher were included for examination if they were well-focused, centered, and free of eye movement. Retinal thickness was measured within a 6-mm radius around the macula using the "Macula map" scanning mode. The fovea served as the center point for linear scans that covered the upper, lower, nasal, and temporal quadrants of the macula region at diameters of 1 mm, 3 mm, and 6 mm, respectively. A center zone with a diameter of 1 mm, an inner ring with a diameter of 1-3 mm, and an outside ring with a diameter of 3-6 mm were created by segmenting the macula. There are nine separate regions

since two radial lines split each ring into four equal parts (top, bottom, left, and right). The research used the mean MT from every ring. On one eye, IT measures were taken by hand, starting at 1 mm intervals and continuing to the iris root at 2 mm and 3 mm intervals. In addition, a number of metrics were documented for every eye. These included macula, fovea, and segment image thicknesses; the quantity of crypts and furrows; the intensity of iris color; and the ratio of collarette to diameter. Severe 20°×20° (6×6 mm) scans with 25 horizontal lines were used to get macular OCT images. The CMT, which stands for the average thickness inside a 1 mm diameter region in the middle of the fovea, was computed automatically by the Spectralis program. Prior to pupil dilation, these photos were taken. Using a slit-lamp with a 16x magnification and no flash, iris photography and grading were carried out in a dark room illuminated by 20 Lux. Using a preexisting grading system [12], the examination comprised iris furrows, crypts, color, and the ratio of collarette to iris diameter. crypts of iris were ranked from 1 to 5: the absence of crypts was indicated by grade 1, followed by grade 2 with 1 to 2 crypts, grade 3 with at least 4 crypts less than 1 mm, grade 4 with at least 4 crypts 1 mm or larger, and grade 5 with numerous crypts 1 mm or larger, covering the whole surface of the iris. grade 1 indicated the absence of furrows, grade 2 indicated five or less furrows or furrows smaller than 180°, and grade 3 indicated furrows bigger than 180°, according to the length and number of furrows. The reference scale was used to classify iris colors into five groups, starting from lightest to darkest. Using a conventional linear measuring method, the ratio of collarette to iris diameter was determined. In order to conduct a thorough assessment, the patient underwent anterior segment OCT imaging on a horizontal plane. The patient was positioned with their pupils dilated so that the SD-OCT's anterior segment lens could obtain a clear image of the iris. At 1, 2 and 3 mm intervals from the pupil line to the iris root, and at three distinct distances from the front to the back of the iris, thickness measurements were collected. The primary outcome was IT measurements at distance 1 mm from the margin of pupil. Measurements of IT at 2 and 3 millimeters from the edge of the pupil and MT were the secondary outcomes.

2.1. *Sample size calculation*

The sample size calculation for the study was performed using G*Power 3.1.9.2 (Universität Kiel, Germany). A pilot study involving 5 cases in each group was conducted, and the results revealed that the mean (± standard deviation) IT measurements at 1 mm distances from the pupil margin were 467.20 ± 83.52 μm in group I, 427.60 ± 38.75 μm in group II, and 415.20 ± 31.45 μm in group III. The sample size determination was based on the following considerations: an effect size of 0.433, a 95% confidence limit, a power of 80% for the study, a group ratio of 1:1, and an additional case added to each group to account for potential dropouts. Consequently, the study aimed to recruit 20 patients in each group.

2.2. *Statistical analysis*

The statistical analysis was conducted using SPSS version 27 (IBM©, Chicago, IL, USA). The normality of the data distribution was assessed through the Shapiro-Wilk test and the examination of histograms. Quantitative data exhibiting a parametric distribution were reported as mean and standard deviation values and the analysis

was performed using one-way analysis of variance (ANOVA) with post hoc Tukey's test for multiple comparisons. Qualitative variables were presented as frequencies and percentages, and the Chi-square test was employed for their analysis. A two-tailed P-value less than 0.05 was considered statistically significant.

3. Results

The demographic characteristics of the study participants were comparable across the three groups, tab. (1). The CMT measurements revealed significant differences among the study groups. While the CMT values were comparable between Group I (172.4 ± 7.56 µm) and Group II (175.2 ± 9.44 µm) (P= 0.927), both diabetic groups exhibited significantly lower CMT compared to Group III (331 ± 39.61 µm) (P < 0.001). These results suggest that diabetic individuals, regardless of their glycemic control status, tend to have thinner central macular regions compared to non-diabetic individuals, tab. (2) The study assessed IT at three different locations: IT1, IT2, and IT3. The analysis revealed no statistically significant differences in IT measurements among the three groups. The mean IT1 values were 457.9 ± 51.46 µm in Group I, 483.6 ± 29.41 µm in Group II, and 481 ± 51.31 µm in Group III (P= 0.150). The mean IT2 values were 300.5 ± 61.08 µm, 282.2 ± 35.78 µm, and 304.1 ± 37.67 µm in Groups I, II, and III, respectively (P= 0.286). Finally, the mean IT3 values were 476.7 ± 69.87 µm in Group I, 493.7 ± 40.68 µm in Group II, and 472.1 ± 48.77 µm in Group III (P= 0.425). These findings suggest that IT is not significantly affected by the presence or control status of DM in the studied population, tab. (3). In Group I, no significant correlation was observed between CMT and either IT2 (r= 0.080, P= 0.735) or IT3 (r= -0.013, P= 0.955). Similarly, in Group III, there was no significant correlation between CMT and IT2 (r= -0.274, P= 0.242) or IT3 (r= 0.015, P= 0.947). However, in Group II, a significant negative correlation was found between CMT and IT2 (r= -0.569, P= 0.008), while no correlation was observed between CMT and IT3 (r= -0.089, P= 0.708). These findings suggest that in controlled diabetic patients, lower CMT may be associated with reduced IT at specific locations, potentially indicating a relationship between these ocular parameters in this population, tab. (4**)**

Table 1: Demographic data of the studied groups

		Group I (n=20)	Group II (n=20)	Group III (n=20)	P value
Age (years)		60.1 ± 6.45	61.8 ± 8.26	60.3 ± 8.49	0.759
Sex	▪ ***Male***	11 (55%)	10 (50%)	9 (45%)	0.819
	▪ ***Female***	9 (45%)	10 (50%)	11 (55%)	

Data are presented as mean ± SD or frequency (%).

Table 2: Central macular thickness of the studied groups

	Group I (n=20)	Group II (n=20)	Group III (n=20)	P value	
CMT (um)	172.4 ± 7.56	175.2 ± 9.44	331 ± 39.61	**<0.001***	P1=0.927 P2<0.001* P3<0.001*

:** *significant as P value<0.05. Data are presented as mean ± SD.* ***P1: *P value between group I and group II,* ***P2:*** *P value between group I and group III,* ***P3:*** *P value between group II and group III,* ***CMT:*** *Central macular thickness.*

Table 3: Iris thickness of the studied groups

	Group I (n=20)	Group II (n=20)	Group III (n=20)	P value
IT1 (um)	457.9 ± 51.46	483.6 ± 29.41	481 ± 51.31	0.150
IT2 (um)	300.5 ± 61.08	282.2 ± 35.78	304.1 ± 37.67	0.286
IT3 (um)	476.7 ± 69.87	493.7 ± 40.68	472.1 ± 48.77	0.425

Data are presented as mean ± SD, ***IT:*** *Iris thickness.*

Table 4: Correlation between CMT and IT of the studied groups

		CMT		
		Group I	***Group II***	***Group III***
IT2 (um)	***r***	0.080	-0.569	-0.274
	P value	0.735	**0.008***	0.242
IT3 (um)	***r***	-0.013	-0.089	0.015
	P value	0.955	0.708	0.947

****:*** *significant as P value<0.05,* ***CMT:*** *Central macular thickness,* ***r:*** *correlation,* ***IT:*** *iris thickness.*

4. Discussion

DM is a chronic metabolic disorder that affects various organs, including the eyes. Ocular complications, such as DR, are well-documented consequences of uncontrolled hyperglycemia [13-16]. The study included three groups with similar average ages and gender distributions. Previous studies by Adhi et al. [17]; Çubuk et al. [18] have highlighted the potential impact of age and gender in healthy persons on ocular parameters, such as MT, and noticed that males were higher in MT than females with no association with age. The analysis of CMT revealed significant differences among the study groups. While the CMT values were comparable between Group I (172.4 ± 7.56 μm) and Group II (175.2 ± 9.44 μm) (P= 0.927), both diabetic groups exhibited significantly lower CMT compared to Group III (331 ± 39.61 μm) (P < 0.001). These findings are consistent with previous research that has documented thinning of the macula in diabetic patients, regardless of their glycemic control status [19,20]. The decreased CMT observed in both diabetic groups could be attributed to the chronic effects of hyperglycemia on the retinal vasculature, leading due to microvascular damage, retinal thinning, and subsequent macular thinning [4,16, 21]. Previous studies have suggested that the degree of macular thinning may be influenced by the severity and progression of DR [6,9,13]. Our study examined IT at three different locations (IT1, IT2, IT3) and found no statistically significant differences among the groups. The mean IT values across the three locations did not show significant variation with P-values of 0.150, 0.286, and 0.425 respectively for IT1, IT2, and IT3. These findings suggest that IT is not significantly affected by the presence or control status of DM in the studied population. These results aligin with a previous study by Demirtas et al. [4], which found that diabetes duration was not associated with IT. While the relationship between diabetes and iris structure has been relatively unexplored, our study contributes to the limited existing literature on this topic. Also, Kansara et al. [22], found that no significant association between stage of DR and IT even in dilator or sphincter muscle region. While Su et al. [23] utilized OCT to measure iris volume in glaucoma and type 2 diabetes; observed that compared to non-diabetic controls, iris volume was raised in primary open-angle glaucoma with diabetes, but decreased in primary angle-closure glaucoma with diabetes. The study investigated the correlation between CMT and IT measurements (IT2 and IT3) within each group. Neither IT2 nor IT3 showed a significant correlation with CMT in Groups I nor III. In contrast, CMT and IT2 in Group II showed a strong a negative correlation

(r= -0.569, P= 0.008), but CMT and IT3 in Group II showed no correlation (r= -0.089, P= 0.708), suggesting that lower CMT may be associated with reduced IT at specific locations in this population. Regarding the correlation between CMT and IT, the study presents a novel finding. The negative correlation between these parameters in controlled diabetics indicates a possible relationship not previously explored in the literature. Controlled diabetic patients may exhibit alterations in ocular hemodynamics and vascular permeability, which could affect both macular and IT through glycemic control. However, Demirtas et al. [4], found a significant positive correlation between IT within 1 millimeter of the pupil's edge and MT (r= 0.32, p= 0.016). A few limitations involving relatively small sample size may limit the generalizability of the findings. Moreover, the study's cross-sectional design makes it difficult to draw any firm conclusions on the relationship between ocular characteristics and diabetes control.

5. Conclusions

Diabetic individuals had thinner central macular regions compared to non-diabetics, regardless of glycemic control. However, IT was not significantly affected by diabetes. To our surprise, we found that CMT and IT were negatively correlated at some sites in patients with managed diabetes, suggesting a potential relationship between these ocular parameters in these people.

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