Macular Thickness and Its relation with Age and Gender in Healthy Eyes Using Cirrus-HD Optical Coherence Tomography

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Abstract

Purpose of the Study: To provide a normative data for macular thickness in healthy Iraqi eyes using Zeiss cirrus HD-OCT and to determine the effects of age and gender on their measurements.

Materials and Methods: Two hundred healthy adult volunteers (≥20 years), four hundred eyes underwent macular cube scanning using Zeiss cirrus-HD OCT. Macular thickness from all 9 regions of the Early Treatment Diabetic Retinopathy Study map was documented for each subject. Variations in macular thickness by age and gender were determined.

Results: The mean age of volunteers was 37±10.4 (range 21-67)years. The mean of central foveal thickness was 254.6±17.3Mm, the mean macular thickness was 279.0 ± 10.7 Mm, and the macular volume was 10.0 ± 0.4 mm3.Females were found to have a significantly thinner macula (P< 0.001) than males in all 9 ETDRS regions except outer inferior quadrant. Central foveal thickness was found to have very weak correlation with age which was not statistically significant. All other macular regions, mean macular thickness and volume showed statistically significant nonlinear reduction with age(p value<0.001).

Keywords: *Macular Thickness, Healthy Eyes, OCT*

Introduction

Macular edema is a common cause of impaired vision, and the degree of deterioration in visual acuity is significantly correlated with the degree of increment in macular thickness [1]. This increase in retinal thickness due to fluid accumulation is happened in many ocular diseases or interventions like diabetic retinopathy, age-related macular degeneration, post intraocular surgery, central serous chorio-retinopathy (CSCR), retinal vein occlusion and intraocular inflammatory conditions. Traditional investigations that used for evaluating macular thickening or oedema, such as slit lamp bio-microscopy, fundus photography and fluorescein angiography (FA), can provide only qualitative information, which is relatively insensitive to subtle changes in macular thickness [2]. Many studies showed significant differences in macular thickness amongst subjects of different race, gender and age [3]. Macular changes with increasing age involve alterations in its function, structure and blood supply [4]. Many genetic and environmental factors may enhance the aging process or induce an irreversible and progressive loss of central vision [5]. Some of these factors seem to be affected by sex hormones [6]. Gender related differences exist in both healthy and diseased eyes. It has been suggested that the macula is thinner in females than males [7].

Background on OCT: Optical coherence tomography (OCT) has revolutionized ophthalmic clinical practice. OCT uses low coherence interferometry of light to examine the retina in vivo (10). With progression of this technology, a true, non-contact, non-invasive "optical biopsy" of the posterior segment of the eye is achievable.

Macular map on OCT: According to early treatment diabetic retinopathy study map(11), macula is divided into 9 regions with 3 concentric rings measuring

1 mm (innermost ring), 3 mm (inner ring) and 6 mm in diameter (outer ring) centered on the fovea. The innermost 1 mm ring is the fovea while the inner 3 mm inner ring and outermost 6 mm ring are further divided into four equal regions.

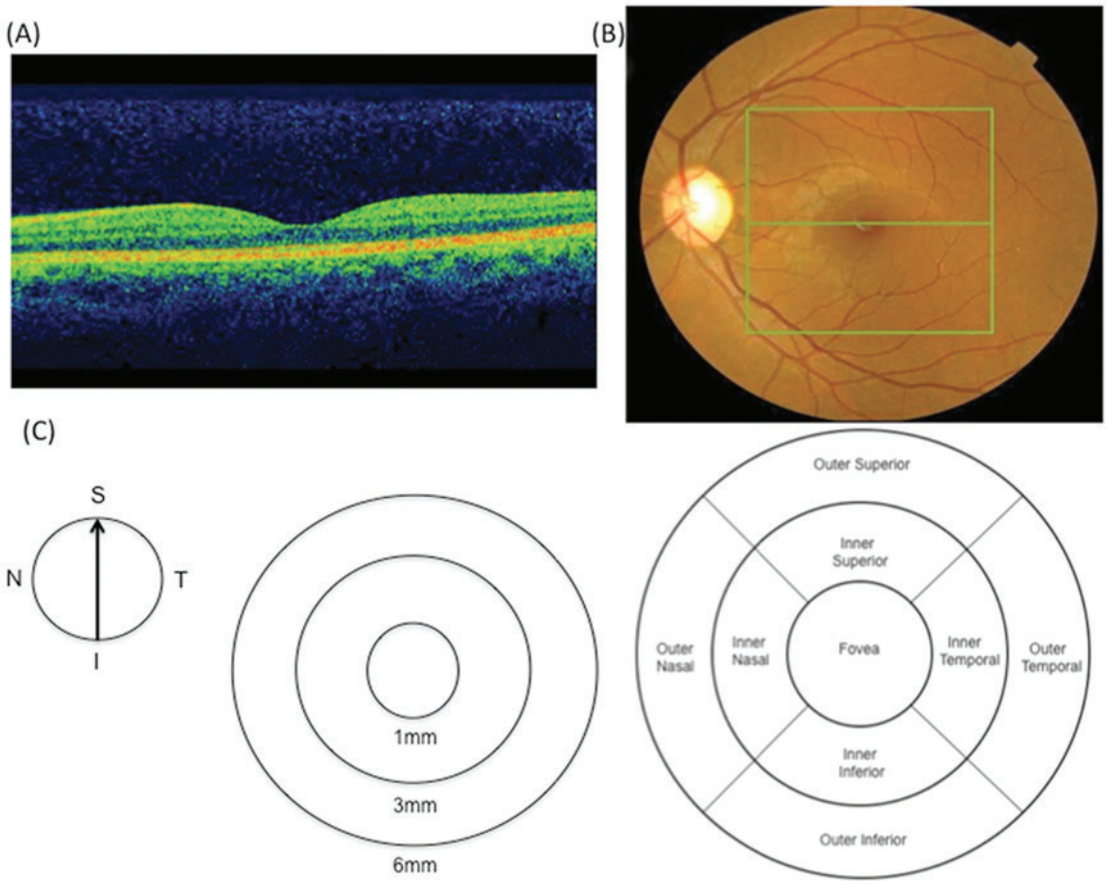

Figure 1.Example of macular thickness measurements obtained with Cirrus HD OCT system.(12)

Subjects and Methods

Subjects: In this cross sectional study, four-hundred eyes of two-hundred healthy Iraqi volunteers, underwent macular thickness measurements by OCT at Ibn-Alhaithem Teaching Eye Hospital between April 2017 and February 2018 and the measures were matched for age and gender. Each volunteer was informed of the purpose of the study, and a verbal informed consent was obtained from all participants before examination. Each one underwent a complete medical history, ophthalmic history and examination, including (best corrected visual acuity by Snellen's chart, applanation tonometry by Goldman tonometer, slit lamp biomicroscopic examination, dilated fundus examination by non-contact 90 D slit lamp indirect lens) then referred to be examined by OCT.

Inclusion Criteria:

1-Age range between 20 and 70 years.

2-Best corrected visual acuity (BCVA) ≥6/6 using snellen's chart.

3-Refractive error between -1 and +1 diopter.

4. Intra ocular pressure less than 21 mmHg.

5. Signal strength of OCT ≥ 6.

exclusion criteria:

1-Age less than 20 and more than 70.

2-Best corrected visual acuity (BCVA) worse than 6\6 using snellen's chart.

3- Intraocular pressure more than 21 mmHg or any

evidence of glaucoma.

4- Eyes with a media opacity that obscures OCT view or signal of OCT less than 6.

5- Eyes with retinopathy due to any diseases like hypertension, diabetes or neuro-ophthalmological disorders or previous uveitic attacks.

6- Patients with history of interventional ocular surgeries or laser.

Optical coherence tomography scanning: All the volunteers were examined by the same OCT device (cirrus HD OCT Carl Zeiss Meditec, Dublin, CA, model 5000 and software version 7.0). this OCT has a Speed of 27,000 A-scans/second, axial resolution of 5 Mm, single compact unit and contour maps of ILM-RPE. Pupillary dilatation was done by using topical tropicamide 1% eye drops, imaging was performed 2 times for each subject, on the same day, by same experienced operator trained in using the Cirrus HD OCT system.

Macular thickness measurements: The macular thickness map protocol was used for macular thickness measurements. It consists of a series of 6 to 24 equally spaced line scans covering an area of 6×6 mm in the macular region displayed with numeric averages of thickness measurements for each of the 9 map regions within a 6×6 mm area centered on the fovea, as defined by the ETDRS(11).

Statistical analysis: Data were analyzed using the statistical package for social sciences (SPSS) version 24. Descriptive statistics presented as simple frequencies, percentages, mean and standard deviation. Independent sample or student's t test for two groups was used to compare means between males and females while ANOVA test (analysis of variance) was used to compare the means across the age groups. The mean difference was calculated to assess the variation in the values in both gender and across the age groups.The predicted relationship between age and retinal thickness, in fovea, pericentral and peripheral ring of macula assessed using fractional polynomial multiple linear regression . Level of significance of ≤ 0.05 considered significant difference or correlation.

Results

Age and gender distribution of the study: Two hundred participants were enrolled in this study with a mean age of 37.9 ± 10.4 (range: 21 – 67) years. Males represented 64% of the studied group, (Table 3.1.). A total of 400 eyes were examined.

Table 1. Age and gender distribution of the studied group (N = 200)

Variable	No.	%
Age (year)		
21 – 30	49	24.5
31 – 40	84	42.0
41 – 50	36	18.0
> 50	31	15.5
Mean ± SD*	35.9 ± 12.4	-
Range	21 – 67	-
Gender		
Male	128	64.0
Female	72	36.0

Distribution of the macular thickness : Table 2. summarizes the mean values of retinal thickness at central foveal and other 8 quadrants, the mean reported retinal thickness varied according to the quadrant where it measured, It ranges from thicker value of (325µm) at inner nasal , to the thinner value of (254.6µm) at the central foveal. The table also involves mean macular thickness and macular volume in the last 2 lines.

Table 2. Distribution of macular thickness of total eyes according in different quadrants from thicker quadrant toward thinner one (N = 400)

Parameter	Mean µm	SD	Minimum µm	Maximum µm
Inner nasal	325.0	15.2	241	367
Inner superior	323.9	15.1	290	378
Inner inferior	321.2	14.9	289	382
Inner temporal	310.5	14.5	278	367
Outer nasal	295.7	15.3	236	346
Outer superior	277.6	14.8	171	330
Outer inferior	269.1	14.2	206	374
Outer temporal	261.7	13.4	206	309
Central foveal	254.6	17.3	218	295
Mean macular thickness	279.0	10.7	257	316
volume cube (mm3)	10.0	0.4	9.3	11.4

Comparison of macular thickness on basis of gender: The comparison of retinal thickness in both genders revealed significant difference in all measurements that males are likely to have thicker macular measurements than females (p value <0.001) in all parameters (mean macular thickness, central foveal thickness and macular volume). Also males have thicker measurements in other eight quadrants than females (p value <0.001)except Outer inferior quadrant at which males had relatively higher thickness but the difference did not reach the statistical significance, (P>0.05), (Table 3).

Table 3. Comparison of mean macular thickness in different quadrants between both genders in the studied group (N = 200)

Parameter	Male		Female		mean difference	Statistic	
	Mean µm	SD	Mean µm	SD		t test	P. value
Central foveal	262.1	18.4	241.4	9.2	20.7	9.29	< 0.001
Inner nasal	328.5	15.6	318.8	12.4	9.7	6.40	< 0.001
Inner inferior	324.2	14.8	315.9	13.6	8.3	5.57	< 0.001
Inner temporal	314.2	14.8	303.9	11.3	10.3	7.24	< 0.001

Cont... **Table 3. Comparison of mean macular thickness in different quadrants between both genders in the studied group (N = 200)**

Inner superior	327.6	16.0	317.3	10.5	10.3	6.96	< 0.001
Outer nasal	298.5	15.5	290.6	13.6	8.0	5.14	< 0.001
Outer inferior	269.9	15.2	267.6	12.1	2.3	1.54	0.125
Outer temporal	264.4	14.0	257.0	10.8	7.5	5.55	< 0.001
Outer superior	279.3	16.2	274.5	11.5	4.7	3.09	< 0.001
Mean macular thickness	281.5	11.2	274.5	8.1	6.7	6.5	< 0.001
Volume cube (mm3)	10.1	0.4	9.9	0.3	0.22	5.9	< 0.001

Comparison of macular thickness on basis of age: Further assessment of the retinal thickness across different age groups which categorized in decades, revealed a significant correlation between retinal thickness and age; in all quadrants, retinal thickness was thicker in younger age groups of 40 years and younger, and became thinner with advancing age above 40 years of life, (P<0.001), in all comparisons across the age groups and the 8 quadrants. The central foveal was insignificantly different across the age, (P>0.05). (Table 4).

Table 3.4. Comparison of mean macular thickness in different quadrants by age of the studied group (N = 200)

	Age (year)								**ANOVA statistics**	
	21 – 30		**31 – 40**		**41 - 50**		**> 50**			
	Mean µm	**SD**	**Mean µm**	**SD**	**Mean µm**	**SD**	**Mean µm**	**SD**	**F**	**P. value**
Central foveal	250.2	26.8	258.1	33.4	247.6	30.6	254.6	22.7	3.38	0.11
Inner nasal	327.8	13.1	328.5	17.2	318.7	13.2	318.6	9.8	13.0	< 0.001
Inner inferior	322.6	13.2	324.1	16.3	315.6	13.4	318.0	12.8	7.1	< 0.001
Inner temporal	311.2	13.1	313.5	16.7	305.3	12.9	307.1	8.9	7.0	< 0.001
Inner superior	324.3	12.8	328.7	16.8	317.2	13.2	317.9	9.8	15.3	< 0.001
Outer nasal	298.6	15.7	296.5	17.2	294.8	11.0	289.8	11.9	4.5	0.004
Outer inferior	270.1	15.0	270.0	13.2	269.9	17.3	264.1	9.9	3.0	0.029
Outer temporal	259.8	11.5	264.3	15.3	261.5	11.8	258.1	11.3	4.4	0.005
Outer superior	276.9	12.4	281.2	15.3	276.8	13.3	269.6	15.9	10.1	< 0.001
Mean macular thickness	279.5	10.5	281.7	11.4	276.4	9.8	273.9	7.3	10.4	< 0.001
Volume cube (mm3)	10.0	0.4	10.1	0.4	9.9	0.4	9.8	0.3	9.0	< 0.001

Discussion

Normal Macular Tomography: In present study, the central foveal thickness was **254.6 ± 17.3µm**, mean macular thickness was **279.0±10.7 µm** and macular volume was 10.0±0.4mm3. The fovea(innermost 1 mm ring) was the thinnest area of macula. The inner macula(inner 3 mm ring) was thicker in all four quadrants i.e superior, inferior nasal and temporal compared to outer macula(outermost 6 mm ring) , thus the retina thinned towards the periphery. The nasal macula (inner and outer) was found to be significantly thicker than the temporal macula(table 2). The nasal quadrant (**325±15.2µm**) was the thickest in the inner region of the macula, followed by the superior(**323.9±15.1µm**), inferior(321.2±14.9µm) and temporal(**310.5±14.5µm**) quadrants. In the outer region, the nasal quadrant (**295.7±15.3µm**) also was the thickest, followed by the superior(**277.6±14.8µm**), inferior(**269.1±14.2µm**) and temporal (**261.7±13.4µm**) quadrants. These patterns were consistently present in both genders and across all age groups; this attributed to the presence of papillomacular bundle in the nasal macula, so it has the thickest nerve fiber layer than other quadrants, then it comes the superior and inferior arcuate bundling of the nerve fibers and lastly the temporal macula, our results in agreement with other studies (13,14).

Comparison of Macular Thickness on basis of age: In our study, the central foveal thickness did not correlate significantly with age(p value 0.11) as in (table 4). Regarding mean macular thickness and macular volume measurements were significantly thicker in age groups 40 years and less and became thinner in age groups more than 40 years (p value<0.001) as in (table 4) . Regarding macular thickness in other eight quadrants of macula (inner and outer rings) was also thicker in age groups 40 years and less and became thinner with age groups 40 years and more (decreased with age) with p value <0.05 as in (table 4). These results suggest that inner and outer macular regions are thick in young adults, whereas macular thickness tends to have less variable in older adults with a smaller magnitude in thickness changes from the foveola toward the central macula and inner and outer macular regions.

Comparison of macular thickness on basis of gender: Our study showed that central foveal thickness, mean macular thickness and macular volume were greater in males as compared to females (P<0.001). Females were found to have a significantly thinner macula (P< 0.05) than males in all 9 ETDRS regions except outer inferior quadrant which was not statistically significant (P value 0.125) . The central foveal thickness was found to be **262.1 ±18.4 µm** vs **241.4 ±20.7 µm** for males vs females, the average macular thickness was found to be **281.5±11.2µm** vs **274.5±8.1 µm** for males vs females and the macular volume was found to be **10.1±0.4 mm3** vs **9.9±0.3mm3** for males versus females. Tewari et al.(19) and Grover et a.(20) showed no significant difference was seen in the foveal thickness , mean macular thickness and macular volume in men and women which may be due to differences in ethnicity of study subjects or differences in study design . However, other similar studies (18,14) found males to have significantly higher mean macular thickness, foveal thickness and macular volume as compared to females which were in partial agreement with our study as outer inferior quadrant was not statistically siginificant.

Conclusion

The macular thickness was determined in 9 ETDRS regions. The fovea was the thinnest area.Using the criteria of mean ± 2 SDs, which includes 95% of the population, we suggest that 237.7 µm to 272 µm be taken as the normal range for central foveal thickness in the Iraqi population for Zeiss cirrus HD OCT. Females were found to have a significantly thinner macula (P< 0.001) than males in all 9 ETDRS regions except outer inferior quadrant. Central foveal thickness was found to have very weak correlation with age which was not statistically significant.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved and all experiments were carried out in accordance with approved guidelines.

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