Academic Journal of Medical Sciences
ISSN: 2708-2725
ORIGINAL ARTICLE

Central Macular Thickness Measurement in Healthy Eyes by Optical Coherence Tomography among Ophthalmic Clinic Outpatient Attendants

***Mudhher Ghani Abdulla*[1*], *Ali Abbas Hassan Fazaa* [2], *Naseera Naser Frak*[3]**

Author's Information
1.M.B.CH.B, H.D-Ophthalmology. Al-Karkh Health Directorate / Abo- Graib General Hospital, Baghdad-Iraq
2.C.A.B(OPTH.),DO, FICO, VR Consultant, Faculty of Medicine, Ibn Sina University for Medical and Pharmaceutical Sciences, Baghdad-Iraq
3.M.B.CH.B, C.A.B(OPTH.), Al-Karkh Health Directorate/ Al Karakh General Hospital, Baghdad-Iraq.

Corresponding author:
Mudhher Ghani Abdulla
mudher1978@yahoo.com

Funding information
Self-funded

Conflict of interest
None declared by author

ABSTRACT

Background: *Knowing the macular thickness in normal subjects' eyes is important for evaluating, treating and following up of the eyes with the various pathological disorders. The Optical Coherent Tomography (OCT) is a significant beneficial non-invasive and rapid ophthalmic diagnostic tool in several pathological conditions*

Objective: *To determine the average central macular thickness measurement in healthy eyes of Iraqi participants and its variation by gender and age using SD optical coherence tomography.*

Participants and Methods: *Two hundred eighty eyes of one hundred forty heathy subjects were enrolled in this cross-sectional study to estimate the macular thickness using SD-OCT device at Department of ophthalmology at AL–SADR medical city from the 1st December,2020 to the 1st April,2021. All participants were evaluated clinically and scanned by SD-OCT using cubic macular thickness analysis in six radial scans centered at fovea; and dividing the macula into nine quadrants according to ETDRS (Early Treatment Diabetic Retinopathy Study). OCT parameters of macular thickness were analyzed with baseline variable including age, gender and laterality. In statistical analysis, Data were analyzed using SPSS programmed version 26. Level of significance of ≤ 0.05 considered significant difference.*

Results: *The mean age of the 140 participants was 44.3 ± 12.9 (range 21 to 60) years. The mean measurement values of central foveal thickness and macular thickness were 237.3 ± 22.8 µm and 273.9 ± 16.2 µm, respectively. No significant differences were found in the central foveal thickness across the age or gender, (P. value >0.05). The males were found to have a significantly higher macular thickness than females in all 8 quadrants of ETDRS regions (P < 0.05); but the central foveal thickness was found to be statistically insignificant. The mean macular thickness showed a statistically significant variation across the age and gender pf the patients.*

Conclusion: *This study provided average normative data for macular thickness in healthy Iraqi eyes using SD-OCT. This will provide a baseline for diagnosing and treating macular changes and disorders in Iraqi eyes in future.*

Keywords:
Optical Coherence Tomography, Central Macular Thickness, Measurement, Healthy Eyes

1. INTRODUCTION

The macula provides the central visual ability of the eye with sharp, high-resolution image and fine detail vision. However, any disturbance or defect in macula, such as macular edema, increases the thickness of the central macula due to abnormal accumulation of fluid in the macula, thereby reducing the ability of this central vision. Thereafter the success of treatment is determined by comparing the current thickness with the actual thickness of the central macula after treatment (1). Among the common causes of vision impairment is edema of macula, so the acuity of vision is mainly related to the degree of retinal thickening in this area(2). Therefore, assessment and knowledge of normal macular thickness in the normal population will be essential for the evaluation, treatment and monitoring of various ocular diseases (3). There are many systemic and eye diseases that cause changes or increases in central macular thickness, such as diabetes, retinal vein obstruction, uveitis, and central serous chorioretinopathy. On the other hand, many diseases like Age related macular degeneration (AMD) in the elderly can cause macular atrophy (4). Fundus photography, slit lamp bio-microscopy and fluorescein angiography are traditional ophthalmic devices and investigations provide qualitative assessment to the thickness of the macula, and are relatively not sensitive to subtle changes of the macular thickness (5). The advent of OCT has revolutionized the clinical practice of ophthalmology, helping clinicians to measure accurately, detect minor changes in macular thickness, and monitor the effects of various treatments (6,7). Optical coherence tomography (OCT) is medical device with non-excisional optical biopsy technique that obtain high or ultra-high resolution and axial cross-sectional image in non-invasive, non-contact and rapid manner. It allows a qualitative and quantitative assessment of the morphology and physiology of the eye in vivo. In addition to basic mapping of tissue morphology / structure using OCT tools, OCT-derived data can also be used for a variety of applications, including mapping retinal functions, retinal blood flow estimation as well as eye optical properties determination (8–13). Optical coherence tomography (OCT) measurements are an important tool in clinical trials because provide good information about the anatomical and physiological features of the eye and help diagnose and control a number of ocular diseases (1). Optical coherence

tomography (OCT) is a fundamental diagnostic tool that measures and images both anterior and posterior ocular structures, including the cornea, retina, macula, and optic nerve head (14). Previous studies have shown significant differences in central macular thickness (central foveal thickness) between race, sex, and age (15,16). Macular aging has been associated with changes in the function and structure and blood supply (17,18). Progressive and irreversible loss of central vision due to aging process can be triggered or accelerated by many environmental and genetic insults (19), as in the case of age-related macular degeneration. Some of these factors appear to be regulated by sex hormones (20–23). There are sex differences in healthy and diseased eyes and different sight threatening disorders to the retina, such as age-related macular degeneration and idiopathic macular hole is associated with women in reproductive age. It has been suggested that the macula in females being thinner than males. However, there is inconsistency as to whether mean macular thickness (MMT) varies with age and gender in published papers (24–28). It is known that a woman's gender, changes in sex hormones, and age-related hormonal changes influence macular activity. Although there is some evidence that estrogens affect maintenance of retinal function its effect on mean macular thickness (MMT) is minimal as measured by OCT. These variations can be important parameters when comparing retinal thickness measurements with a diagnosis of eye disease (28–31).

2. METHODOLOGY

This was a cross-sectional study conducted at the department of ophthalmology at Al–Sadr medical city during the period from 1st December,2020 to 1st April,2021 and involved 140 Iraqi subjects with 280 healthy eyes. During the

Subjects:

Two hundred eighty eyes of one hundred forty healthy subjects (age 21 – 60 years) were involved conveniently in this cross-sectional study to estimate the macular thickness using SD OCT device. Sample size was calculated according to standard equation of sample size for cross-sectional studies. All participants were examined clinically by taking detailed medical history and previous ocular history and assessment (including: visual acuity (best corrected) using Snellen's chart. Intra-ocular pressure was measured by an air Puff-tonometer.

Additionally, after a slit-lamp examination and fundal examination, all participant subjects were examined with CT with Cubic-Macular thickness analysis in 6 radial scans centered at fovea. The macula subdivided into 9 quadrants in accordance with ETDRS. Furthermore, mean macular thickness was evaluated.

Inclusion Criteria

1. Participant was included if he/she met the following criteria: 1- Age older than 18 years.
2. Had visual acuity (best corrected) of 6/6 or better.
3. Refractive error between (–0.5) and (+0.5) diopter sphere or astigmatism.
4. Had an IOP of Less than 21 mmHg, and no history of glaucoma.
5. Had 6 or more OCT signal strength

Exclusion Criteria

Participant was excluded if he/she had one or more of the following:

1. Media Opacities that cause unclear viewing with OCT.
2. Retinopathies due to hypertension, diabetes, age related macular degeneration, macular dystrophies, macular holes, retinal vascular disease etc. or neuro-ophthalmological disease or previous intra ocular inflammatory diseases
3. Previous ocular surgeries including cataract, refractive, glaucoma, posterior segment surgeries or any laser therapy or cryotherapy.
4. Traumatic injuries of the eyes involving the retina.

Data Collection

The collected data included demographic, clinical examination findings; visual acuity and IOP and OCT findings and macular thickness.

Optical Coherence Tomography Scanning

All study participants were examined with the same OCT device. Pupillary dilatation was done by using topical tropicamide 1% eye drops, for each participant, 3 times imaging were performed at the same day. All imaging done by the same expert operator with good experiences and training in using of SD-OCT systems. Quality factor of 6/10 or greater was considered for all scan's images. The closer image to fovea was taken when it is possible, therefore, the thinner point of macula was imaged. The only accepted images are those with

completely distinguishable full extent and depth of retina with no artifact due to blinking or incidental eye movement at imaging.

The macula was divided into 9 regions: Fovea, 4 inner and 4 outer regions. To measure the macular thickness, the distance between inner-borders of retinal-pigment epithelium and Internal limiting membrane (ILM) was measured in all 9 regions. To measure macular thickness, the protocol of macular thickness map was applied. All measurement obtained by OCT were reported for each participant for each of the 9 macular map regions. Macular thickness calculated as the mean thickness of the 9 ETDRS map regions.

Data Management and Analysis

The statistical package for social sciences (SPSS) version 26 software for windows was utilized. Variables presented as frequencies, percentage, mean, and standard deviation according to the variable type. Appropriate statistical tests were applied according to the type of variables compared. Statistical significance was set at P. value of 0.05 or less to be significant

3. RESULTS

Two hundred eighty normal eyes of one hundred forty healthy subjects (21- 60 years old) were enrolled in this study with mean age of 44.3 ± 12.9 years. There were 70 males (50%) and 70 females (50%). The distribution of the study sample according to the age group and gender is shown in (**Table 1**). The mean retinal thickness of each macular region and the mean macular thickness are shown in (**Table 2**), where the macular thickness was thinnest at fovea (237.3 µm), thickest within inner 3 mm ring (306.3 µm inner nasal macula), and the thickness reduced at the outer 6 mm ring (259.02 µm at outer temporal macula). The thickest region was the nasal macula followed by the superior and the inferior areas while the thinnest region was the temporal macula. The mean retinal thickness of each macular region and the mean macular thickness did not significantly different between right and the left eyes, (P value > 0.05); except the inner and outer nasal areas (P <0.05), (**Table 3**). On the basis of age factor, there was a significant correlation between the retinal thickness and the age; in all quadrants, the macular thickness was higher in younger age (21-29) and (30-39) years and became lower with increasing age (40-49) and (50-60) years, with P. value =0.0001, in all comparisons across the age group and the 8 quadrants. The central foveal

thickness was not significantly different across the age factor with P >0.05. The mean macular thickness was clinically significant across the age factor, and showed thicker values in younger (<40 years) age group and thinner values in advancing (>40 years) age group with P =0.0001, (**Table 4**). To assess strength of correlation between dependent variables and age as scale independent variable, bivariate Pearson's correlation analysis was performed. However, all resulted correlation coefficients were negative and less than 0.4 indicated weak inverse significant correlation, (**Table 5**). In males, correlations of each, Foveal, pericentral and peripheral thickness against age was weak inverse and statistically significant, (P<0.05), while not statistically significant in females, (**Table 6**). Males have relatively higher macular thickness than females in all parameters (central foveal thickness, mean macular thickness and the 8 quadrants); and approached the significant difference at the inner 3 mm ring (all quadrants) and mean macular thickness with p <0.05; but the difference did not reach the statistical significance (P value > 0.05) at the central foveal region and the outer 6 mm ring (except outer nasal area with p=0.02), (**Table 7**).

Table 1. Age and gender distribution of the studied group

Variable		No.	%
Age(years)	21-29	22	15.7
	30-39	32	22.9
	40-49	24	17.1
	50-60	62	44.3
Gender	Female	70	50.0
	Male	70	50.0

Table 2. Descriptive statistics for the retinal thickness of each macular region of 140 Iraqi subjects in the study

CVT	Minimum	Maximum	Mean	SD
	197	383	237.3	22.8
Inner Superior	209	383	305.4	22.9
Inner Inferior	230	352	304.9	19.2
Inner Temporal	209	341	293.9	20.3
Inner Nasal	208	361	306.3	21.97
Outer Superior	195	380	267	20.2
Outer Inferior	192	338	260.8	18.95
Outer Temporal	196	381	259.02	21.4
Outer Nasal	206	381	278.2	22.9
Mean Thickness	212.5	361.3	273.9	16.2

Table 3. Comparison of macular thickness measurement between right and left eyes

CT		OD	OS	P. Value
		235.5 ± 22.04	239.1 ± 23.4	0.20
3 mm ring	Superior	306.2 ± 21	306.7 ± 24.7	0.90
	Inferior	304.8 ± 20.4	304.9 ± 18.02	0.90
	Temporal	295.8 ± 19.3	292.04 ± 21.1	0.10
	Nasal	302.4 ± 22.6	308.1 ± 21.1	0.03*
6 mm ring	Superior	267.9 ± 21.2	266.6 ± 19.1	0.60
	Inferior	260.2 ± 18.9	261.4 ± 19.02	0.60
	Temporal	259.4 ± 22.4	258.6 ± 20.3	0.80
	Nasal	275.9 ± 24.6	281.7 ± 20.7	0.03*
	Mean thickness	272.9 ± 15.5	274.9 ± 16.8	0.30

Values are presented as mean ± SD

Table 4. Comparison of Macular thickness measurement according to age groups

CT		20-29 year (n=44)	30-39 year (n= 64)	40-49 year (n=48)	50-60 year (n= 128)	P. value
		233.4 ± 24.1	238.3 ± 23.4	242.8 ± 16.8	236.1 ± 23.8	0.200
3 mm ring	Superior	313.7 ± 22	314 ± 20.4	311.5 ± 18.4	298.1 ± 23.4	<0.001*
	Inferior	306.4 ± 19.8	313 ± 15.02	311.1 ± 16.9	308.9 ± 19.2	<0.001*
	Temporal	300.2 ± 23.3	297.7 ± 17.5	300 ± 14.6	287.3 ± 20.7	<0.001*
	Nasal	315.2 ± 18.6	314.2 ± 15.3	308.7 ± 18	295.8 ± 23.7	<0.001*
6 mm ring	Superior	273.8 ± 11.8	271.5 ± 19.4	270.3 ± 21	261.5 ± 21.2	<0.001*
	Inferior	271.5 ± 18.6	263.3 ± 14.9	264.4 ± 16.2	254.2 ± 19.7	<0.001*
	Temporal	265.5 ± 22.3	259.7 ± 20.9	261.8 ± 15.9	255.3 ± 22.6	0.030*
	Nasal	290.9 ± 15.4	278.9 ± 38.03	284.4 ± 24.2	270.8 ± 21.9	<0.001*
	Mean thickness	281.5 ± 12	279.1 ± 16.2	277.4 ± 12.4	267.08 ± 16.3	<0.001*

Values are presented as mean ± standard deviations. *Significant

Table 5. Results of bivariate Pearson's correlation analysis

Variable	Correlations against age	
	R	P. Value
Central foveal	-0.302	0.001*
Inner nasal	-0.252	0.001*
Inner inferior	-0.163	0.021*
Inner temporal	-0.147	0.038*
Inner superior	-0.201	0.004*
Outer nasal	-0.181	0.010*
Outer inferior	-0.166	0.019*
Outer temporal	-0.08	0.256
Outer superior	-0.173	0.014*
Mean macular thickness	-0.206	0.003*

R:Pearson's Correlation Coefficient, *Significant

Table 6. Results of bivariate correlation analysis, to clarify the strength and significance of correlations in both genders

Gender		Correlations indices	
Male (n=70)	Retinal thickness at Pericentral ring	-0.337	0.001*
	Retinal thickness at Pericentral ring	-0.200	0.024*
	Foveal thickness	-0.283	0.001*
Female (N = 70)	Retinal thickness at Pericentral ring	-0.071	0.551
	Retinal thickness at Pericentral ring	-0.201	0.090
	Foveal thickness	-0.181	0.131

Table 7. Comparison of macular thickness measurement between males and females

Region		Male (n=70)	Female (n=70)	P. Value
CT		238.3 ± 22.3	236.3 ± 23.3	0.5
3 mm	Superior	312.4 ± 19.6	300.5 ± 24.5	0.0001*
	Inferior	310.1 ± 16.5	299.6 ± 20.4	0.0001*
	Temporal	298.3 ± 18.3	289.5 ± 21.3	0.002*
	Nasal	308.7 ± 22.01	301.9 ± 21.5	0.0009*
6 mm	Superior	268.5 ± 17.5	266 ± 22.5	0.300
	Inferior	262.9 ± 17.1	258.7 ± 20.	0.060
	Temporal	260.6 ± 17.3	257.4 ± 24.8	0.200
	Nasal	281.9 ± 22.6	274.4 ± 30.4	0.020*
	Mean Thickness	277.2 ± 15.7	270.6 ± 16.01	0.001*

Values are presented as mean ± standard deviations. *Significant

4. DISCUSSION

In our study, the central foveal thickness was 237.3 ± 22.8 µm, and the mean macular thickness was 273.9 ± 16.2 µm. The fovea (innermost 1 mm ring) was the thinnest area of macula. All four quadrants i.e. superior, inferior nasal and temporal of the inner macula (inner 3 mm ring) were thicker in compared to outer macula (outermost 6 mm ring); thus, the retina was thinned out towards the periphery. The nasal macula (inner and outer rings) was found to be significantly thicker than the temporal macula. At the inner 3 mm ring, the

nasal subfield (306.3 ± 21.97 µm) was the thickest, followed by the superior (305.4 ± 22.9 µm), inferior (304.9 ±19.2 µm) and temporal (293.9 ± 20.3 µm) subfields. In the outer 6mm region, the nasal subfield (278.2 ± 22.9 µm) also was the highest estimation, followed by the superior (267 ± 20.2 µm), inferior (260.8 ± 18.95 µm) and temporal (259.02 ± 21.4 µm) subfields. Other studies like Sull AC et al (32)and Bruce et al. (33) reported foveal thickness of 231 ± 16 µm and 244.83± 17.8 µm respectively; using Topcon OCT system. These values are comparable to our results. The nasal region within the inner 3 mm ring was the thickest area; this is due to nasal macula has thickest nerve fiber layer due to the presence of the papillomacular bundle in it then the superior and inferior arcuate bundling of the nerve fibers and lastly the temporal macula, our results in agreement with other studies (34–36). Ethnic differences in macular thickness and central and inner macular thickness were shown to be significantly thinner in blacks and Asians than in whites, not only in adults but also in children (35). In order to compare our macular thickness measurement with various racial groups, we should have similar OCT device (3D TOPCON OCT), because scanning with different OCT machine may give a different value (32). The central foveal thickness in our study was 237.3 ± 22.8 µm which is near to central foveal thickness in Indian subjects 240.4±18.26 µm and thinner than Iranian subjects 251.4±17.84 µm(77), and thinner than Italians 269±27 µm (35)(74). In this study, the central foveal thickness did not correlate significantly with age (P value = 0.2). Regarding mean macular thickness was significantly thicker in age groups 40 years and less and became thinner in age groups more than 40 years (p value<0.0001). 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 . The decreased thickness variation outside the central macula may result from the loss of ganglion cell and the thinning of the retinal nerve fiber layer associated with aging, which cannot be reflected in the central foveal area because there is no retinal nerve fiber layer (37). This decline in the retinal thickness with age is also supported by histologic decrease in the density of photoreceptors, ganglion cells and retinal pigment epithelial cells with age (38,39). This is in agreement with the findings of Appukuttan et al. (34), Kanai et al. (40), and Manassakorn et al. (41) where significant correlation was found in all ETDRS subfields except the central

subfield. However, Huang et al. (42), Faghihi et al.(36) and Grover et al. (43) did not find a statistically significant association between macular thickness and age which may be due to the small sample size in these studies. Bivariate correlation analysis was done to clarify the strength and significance of correlations in both genders. In males, correlations of each, Foveal, pericentral and peripheral rings thickness against age was weak inverse and statistically significant, ($P<0.05$), while not significant in females. The central foveal thickness for males and females were found to be 238.3 ± 22.3 and 236.3 ± 23.3 µm respectively with P value more than 0.05; this indicates no significant difference and it is comparable or in agreement with the findings of other study like Tewari et al (39) and Grover et al. (43). The mean macular thickness for males and females were found to be 277.2 ± 15.7 and 270.6 ± 16.01 µm respectively with P value less than 0.05; this indicates clinically significant and the males had greater thickness than females. This is in agreement with other studies (44,45). The central foveal thickness for the right and the left eyes of the all subjects was found to be 235.5 ± 22.04 and 239.1 ± 23.4 µm, respectively, with P value more than 0.05; this indicates clinically insignificant. The mean macular thickness for males and females were found to be 272.9 ± 15.5 and 274.9 ± 16.8 µm respectively, with P value more than 0.05; this indicates clinically not significant. This means that there is no correlation between the macular thickness and the laterality variables across the all-macular regions of ETDRS areas.

Limitation of Study

This study doesn't measure the effect of refractive errors and axial length on macular thickness. One OCT device in the hospital of our study, which makes not available all the time. We cannot deny the existence of diseases that are still undetectable for all those included in the study.

5. CONCLUSIONS

The central foveal thickness, mean macular thickness were 237.3 ± 22.8 µm, 273.9 ± 16.2 µm, respectively; and the Iraqi males have thicker macula than females. Central foveal thickness was not associated with age. Age and sex are important factors that should be taken in consideration when interpreting the macular thickness measurement with SD OCT devise. We recommend further studies are needed with larger samples, and long follow up to show the effect of refractive errors, axial length on macular thickness and foveal

thickness, and in women to study the possible association between macular thickness, parity, and hormonal status.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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Citation:

Abdulla M.G, Fazaa A.H, Frak N.N Central Macular Thickness Measurement in Healthy Eyes by Optical Coherence Tomography among Ophthalmic Clinic Outpatient Attendants. AJMS 2024; 10 (3): 143-58