AIM OF THE WORK

The aim of the work is to evaluate normal macular thickness in the Egyptian children using optical coherence tomography (OCT).

SUBJECTS
AND
METHODS

SUBJECTS AND METHODS

I. Subjects

The study was conducted on 100 eyes of 50 healthy children aged from 6-16 years, attending or referred to the ophthalmology outpatient clinic of Alexandria Main University Hospital.

Inclusion criteria

To be enrolled, subject had to have no ocular problems other than refractive error (not more than spherical equivalent of ± 4 diopters) and no history of systemic disease.

Exclusion criteria

- Children who had congenital ocular abnormality.
- Children with strabismus.
- Children with amblyobia.
- Family history of glaucoma.
- High intraocular pressure.
- Abnormal optic disc.
- History of intraocular surgery.
- Children with neurological, metabolic, vascular or other disorder were excluded.

II. Ethical considerations

Written informed consent to participate in this study was obtained from children's parent.

III. Methods

All children received a full ophthalmic examination including:
- Detailed assessment of visual acuity using "tumbling E" chart.
- Slit lamp evaluation including dilated fundus examination.
- Assessment of intraocular pressure (IOP) by Perkin's Tonometer.
- Pupils were dilated with cyclopentolate 1% four times separated by 5 minutes, refraction was done 30 minutes after last cycloplegic drops.
- Macular thickness measurement by spectral-domain OCT (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany).

OCT scanning

An internal fixation light was used to center the scans on the fovea of the subject. The images in this study were generated by the fast volume scan; 20°×20° (6×6 mm) raster scans consisting of 25 horizontal lines (B-scan sections) that were spaced 240 microns apart with 512 A-scans per B-scan. For each horizontal line, 9 B-scans were averaged with the automatic real-time (ART) mode to reduce speckle noise. The fast scan was chosen as it is less time consuming and more comfortable for the patient as compared to the dense scan.

Image artifacts and scan exclusion

OCT scans were checked. Only the scans with a numerical quality score of more than 16/40 decibels (db), and that were in the blue range of the quality bar, were defined as

having good signal strength and were collected. For each scan, the color thickness map and individual horizontal line scans were reviewed for any retinal abnormalities or image artifacts. Any scans in which a retinal pathology was detected were excluded

Macular thickness measurement

Macular thickness values were calculated automatically by the software 5.3.2.0) included in the machine. The retinal thickness in each frame was calculated as the distance between the first signal from the vitreoretinal interface and the signal from the outer border of the RPE.
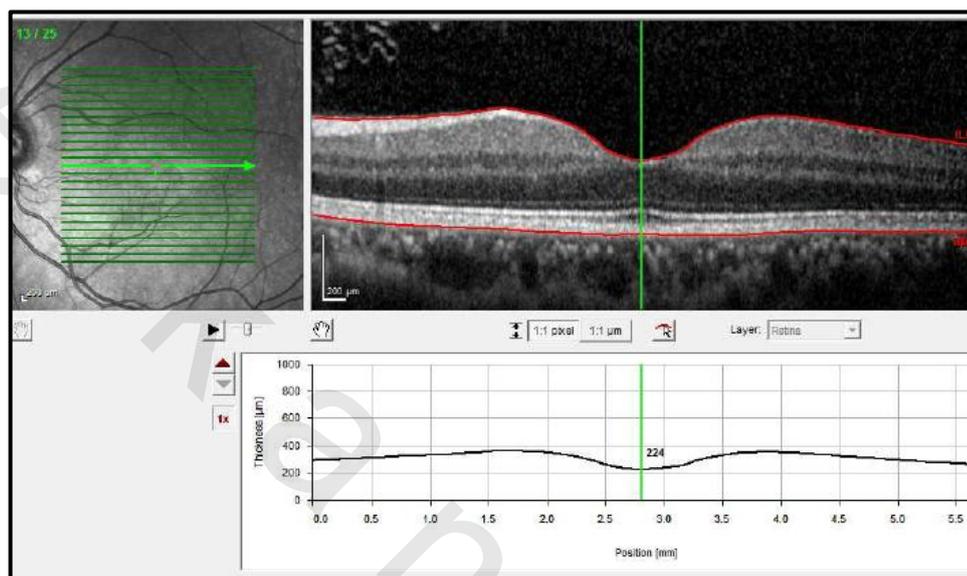

Figure (16): Thickness profile by the Spectralis SD-OCT. Segmenation lines shown in red.

To analyze retinal thickness, the software algorithm of the spectralis OCT interpolating thickness of the area between the scans was used. It provides a circular map analysis in which the average thickness is displayed as a colour code or numeric values in the nine Early treatment diabetes Retinopathy Study (ETDRS) areas.[88] (Figure 17)
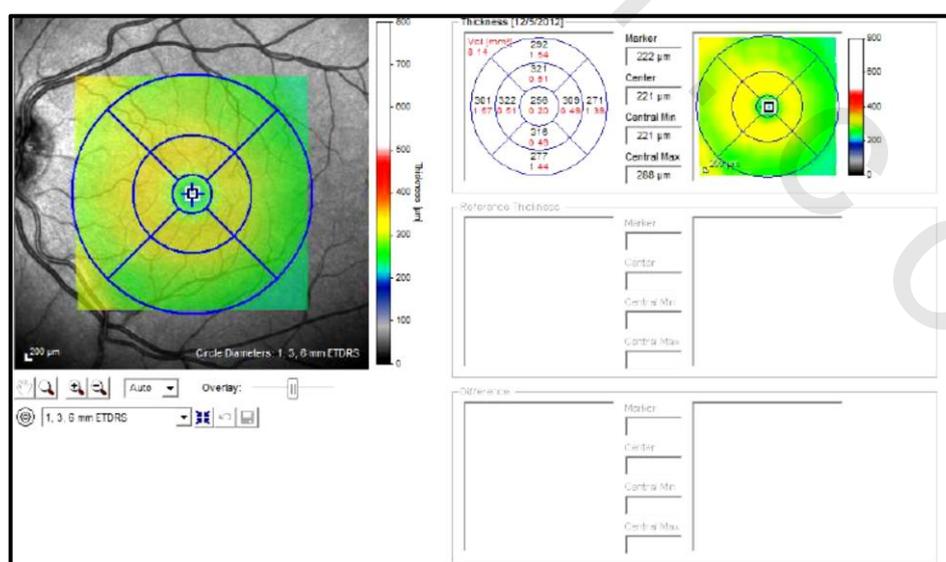

Figure (17): Thickness map by the Spectralis SD-OCT.

The ETDRS map (Figure 18) consists of three concentric rings with diameters 1 (central), 3 (inner), and 6 (outer) mm. The inner and outer rings were divided into four areas. The retinal thickness within the inner circle 1 mm in diameter was defined as the central subfield (CSF) thickness. The mean retinal thickness of the four areas in the inner ring was defined as the mean inner macula (MIM) thickness. The mean retinal thickness of the four areas in the outer ring was defined as the mean outer macula (MOM) thickness. The centering of the measurements at the fovea was checked. If deemed necessary, the ETDRS grid was shifted to compensate for minor fixation errors.
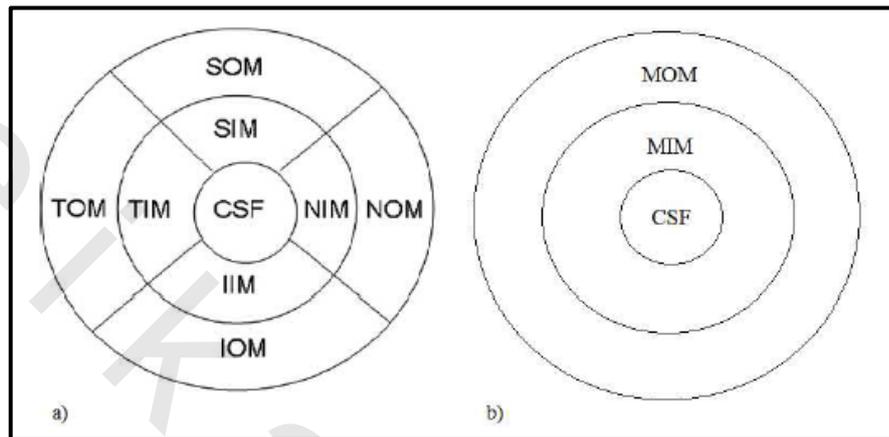

Figure (18): a) Depiction of the standard 9 ETDRS subfields. CSF _ central subfield; IIM _ inferior inner macula; IOM _ inferior outer macula; NIM _ nasal inner macula; NOM _ nasal outer macula; SIM _ superior inner macula; SOM _ superior outer macula; TIM _ temporal inner macula; TOM _ temporal outer macula, b) MIM_ mean inner macula; MOM_ mean outer macula.[89]

RESULTS

RESULTS

The study included one hundred eyes of fifty Egyptian children 52% (26 children) were females and 48% (24 children) were males. The mean age was 10.2±2.7 years; ranging from 6 -16 years.

Children were divided into three subgroups based on age: 6- less than 10 years of age (n=24), 10- less than 14 years (n=17) 14-16 years (n=9). (Table 1)

Table (1): Personal characteristics among the studied healthy Egyptian children.

Personal characteristics	Studied children (n=50)	
	No.	%
Age (years)		
6-<10	24	48.0
10-<14	17	34.0
14-16	9	18.0
Min-Max	6-16	
Mean±SD	10.2±2.7	
Gender		
Male	24	48.0
Female	26	52.0

The mean central subfield thickness was 259.9±22.8 μm. The average inner macular subfields thicknesses of the superior, inferior, temporal and nasal quadrant were 343.7±18.1, 340.0±17.6, 330.4±16.8 and 341.2±16.9 μm, respectively, and the average outer macular subfields thicknesses were 302.4±24.9, 294.1±17.9, 290.3±20.1, 315.5±19.5 μm, respectively. (Table 2)

Table (2): Macular measurements using optical coherence tomography among the studied healthy Egyptian children.

Macular subfields	Macular measurements in microns	
	Min-Max	**Mean±SD**
CSF	209-361	259.9±22.8
MIM	279.3-373.3	338.8±16.4
SIM	269-377	343.7±18.1
NIM	290-375	341.2±16.9
IIM	290-382	340.0±17.6
TIM	268-364	330.4±16.8
MOM	256.5-361.0	300.6±17.4
SOM	250-477	302.4±24.9
NOM	257-409	315.5±19.5
IOM	246-357	294.1±17.9
TOM	236-394	290.3±20.1
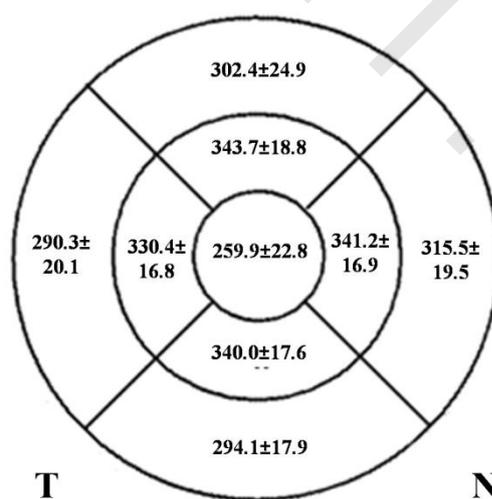
T= Temporal
N = Nasal.

Fig. (19): Mean and standard deviations of macular thickness (in micrometers) of each ETDRS sector in 50 healthy Egyptian children.

The macular thickness generally showed normal distribution as evidenced by the percentage of subjects within ± 2SD from the mean (Table 3). (Fig. 20-22) show the distribution curve of CSF, MIM, MOM.

Table (3): Percentage of cases within±2SD from the mean macular thickness.

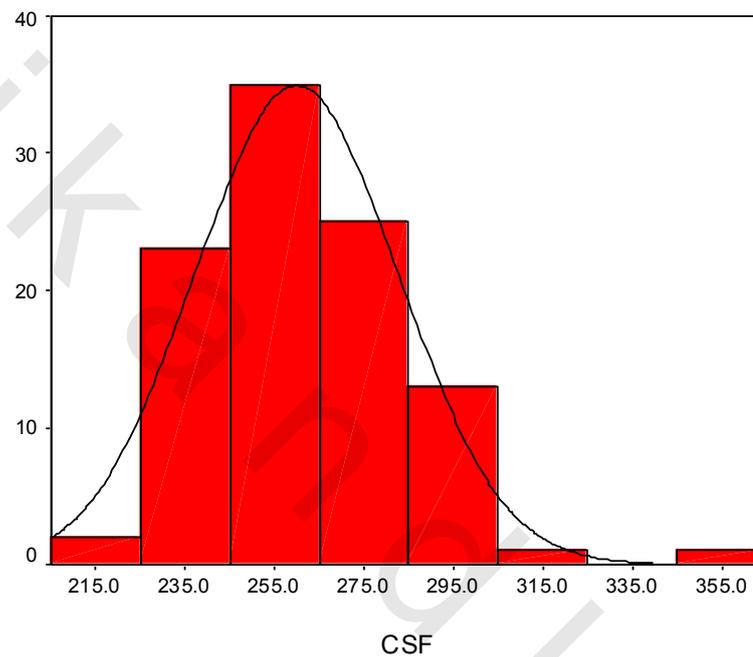| Sector	%
CSF	96.0
MIM	97.0
MOM	95.0

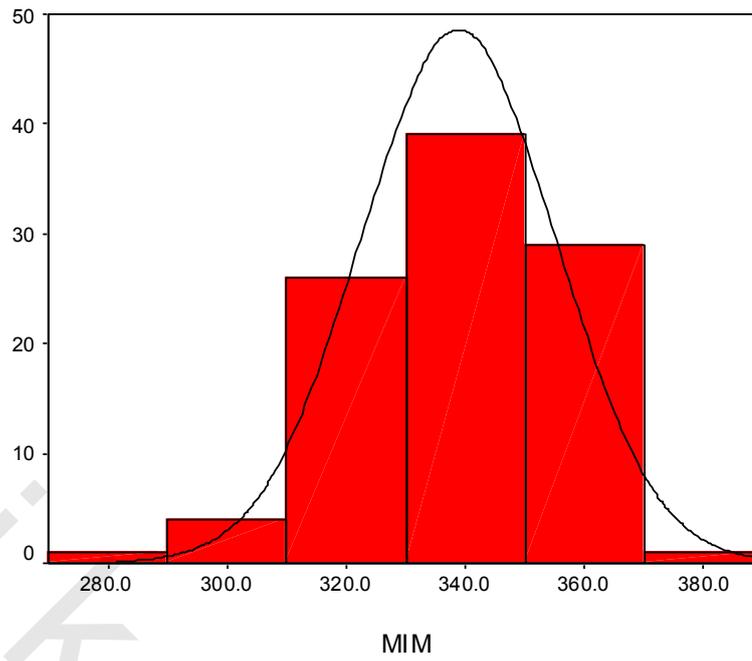**Fig. (20):** Distribution curve and histogram of CSF.

23

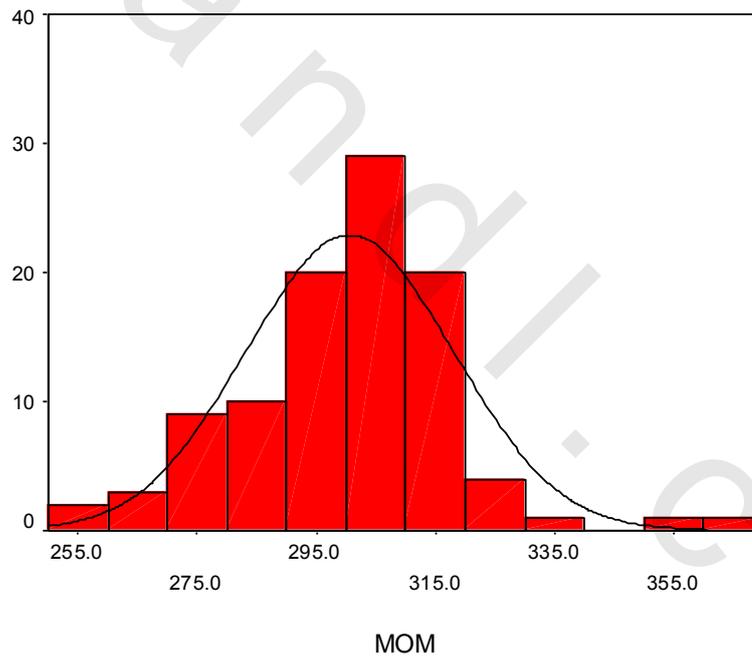**Fig. (21):** Distribution curve and histogram of MIM.

Fig. (22): Distribution curve and histogram of MOM.

24

The macular thickness was least at the central subfield followed by outer macular ring. The inner ring was the thickest macular region (Table 4).

A global comparison of the thicknesses of inner macular subfields found that they were significantly different from each other (P<0.0001). Pair-wise comparison of inner macular subfields, with Bonferroni correction for multiple comparisons, showed no significant difference in mean thickness between the inner nasal region with the inner inferior and inner superior regions (p> 0.05). The inner temporal region was significantly thinner than all other inner macular regions (Table 5).

Global and pair-wise comparison of outer macular regions showed that they were all significantly different from each other (all P< 0.0001). The outer temporal region was the thinnest, followed by the inferior outer and superior outer regions. The nasal outer region was the thickest (Table 6)

Table (4): **Comparison of macular thickness measurements in the main regions of the ETDRS.**

	CSF	MIM	MOM	ANOVA test F (P)
Mean±SD	259.9±22.8	338.8±16.4	300.6±17.4	427.9 (P<0.0001*)
P1		↑78.9 P<0.0001*	↑40.7 P<0.0001*	
P2			↓38.2 P<0.0001*	

P: P value for ANOVA test with repeated measures for comparing between different periods

P1: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between CSF with MIM and MOM

P2: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between MIM and MOM

*significant at P≤0.05

Table (5): **Comparison between macular thickness measurements in different sectors of the inner macula ring.**

Inner macula ring	SIM	NIM	IIM	TIM	ANOVA test F (P)
Mean±SD	343.7±18.1	341.2±16.9	340.0±17.6	330.4±16.8	7883.81 (P<0.0001*)
P1		↓2.5 P=0.314	↓3.7 P=0.144	↓13.3 P<0.0001*	
P2			↓1.2 P=0.623	↓10.8 P<0.0001*	
P3				↓9.6 P=0.0001*	

P: P value for ANOVA test with repeated measures for comparing between different periods
P1: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between SIM and other parameters
P2: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between NIM with IIM and TIM
P3: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between IIM and TIM
*significant at P≤0.05

Table (6): **Comparison between macular thickness measurements in different sectors of the outer macula ring.**

Outer macula ring	SOM	NOM	IOM	TOM	ANOVA test F (P)
Mean±SD	302.4±24.9	315.5±19.5	294.1±17.9	290.3±20.1	**F=28.882 (<0.0001*)**
P1		↑13.1 P<0.0001*	↓8.3 P=0.007*	↓12.1 P<0.0002*	
P2			↓21.4 P<0.0001*	↓25.2 P<0.0001*	
P3				↓3.8 P=0.159	

P: P value for ANOVA test with repeated measures for comparing between different periods
P1: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between SOM and other parameters
P2: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between NOM with IOM and TOM
P3: adjusted Bonferroni p-value for ANOVA with repeated measures for comparison between IOM and TOM
*significant at P≤0.05

The macular measurements stratified by sex are presented in table 8. Male gender was associated with a statistically significant greater inner macular thickness compared to female. The average inner macular thickness of the superior, inferior, temporal, nasal and the average of MIM subfields in males were 347.8±19.3, 344.6±18.3, 335.3±17.8, 345.9±163 and 343.4 ± 17.3 μm respectively. While in females were 339.9±16.1, 335.8±16.1, 325.9 ±14.6, 336.8±16.4 and 334.6 ± 14.4 μm respectively. There was no significant difference in the central subfield and outer ring thickness between both sexes. Examples of thickness maps of partiaipants in the current study with different gender are shown in (fig. 23).

Table (7):   Macular measurements using optical coherence tomography among the studied healthy Egyptian children in relation to their gender.
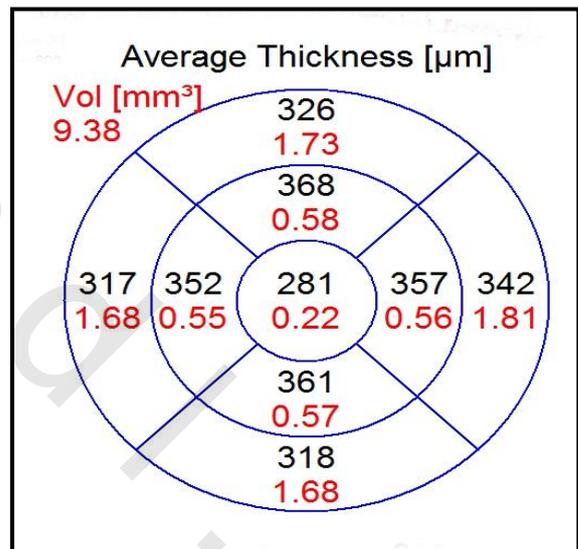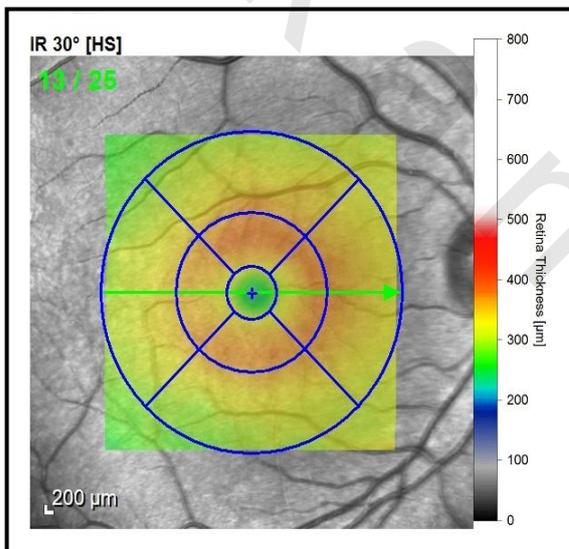
Macular measurements	Gender		Significance
	Male (n=48)	Female (n=52)	
CSF			
Min-Max	226-303	209-361	t=1.879
Mean±SD	264.3±18.8	255.8±25.4	P=0.063
MIM			
Min-Max	279.3-373.3	308.3-353.5	t=2.776
Mean±SD	343.4±17.3	334.6±14.4	P=0.007*
SIM			
Min-Max	269-377	307-370	t=2.238
Mean±SD	3347.8±19.3	339.9±16.1	P=0.027*
NIM			
Min-Max	290-375	292-359	t=2.774
Mean±SD	345.9±16.3	336.8±16.4	P=0.007*
IIM			
Min-Max	290-382	290-364	t=2.578
Mean±SD	344.6±18.3	335.8±16.1	P=0.011*
TIM			
Min-Max	268-364	301-351	t=2.896
Mean±SD	335.3±17.8	325.9±14.6	P=0.005*
MOM			
Min-Max	264.5-361.0	256.5-353.3	t=0.043
Mean±SD	300.6±17.2	300.5±17.7	P=0.966
SOM			
Min-Max	250-477	261-340	t=0.352
Mean±SD	303.3±31.7	301.5±16.8	P=0.725
NOM			
Min-Max	284-349	257-109	t=0.62
Mean±SD	314.2±15.0	316.6±22.9	P=0.536
IOM			
Min-Max	258-357	246-349	t=0.276
Mean±SD	293.6±16.7	294.6±18.9	P=0.783
TOM			
Min-Max	236-348	257-394	t=0.557
Mean±SD	291.5±18.5	289.2±21.5	P=0.579

t: t-test   *significant at P≤0.05
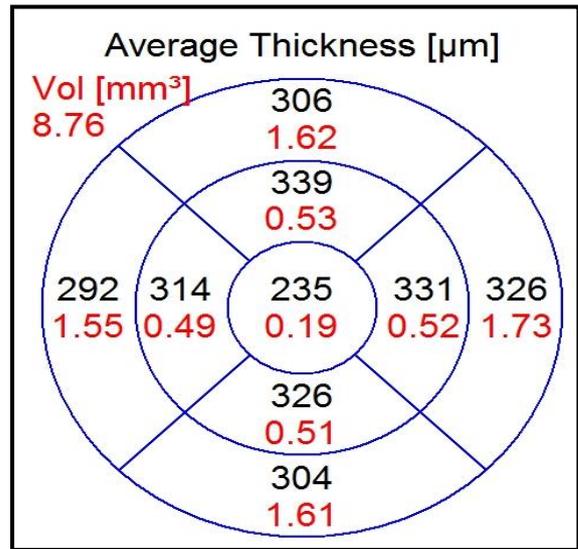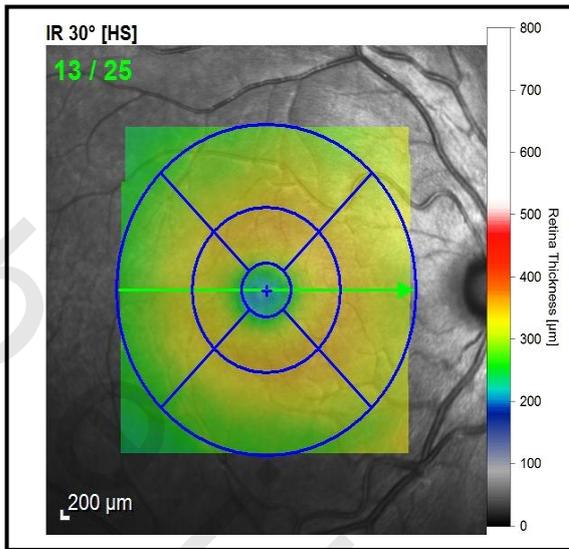
Fig. (23): (a) Thickness map of the right eye of a 9 years old female. (b) Thickness map of the right eye of a 7 years old male.

There was no significant difference between right and left eye in the all nine ETDRS subfields. (Table 8)

Table (8): **Macular measurements using optical coherence tomography among the studied healthy Egyptian children in relation to laterality of eye.**

| Macular measurements	Eye laterality		Significance
	OD (n=50)	OS (n=50)	
CSF			t=0.319
Min-Max	210-361	209-303	P=0.751
Mean±SD	260.6±24.7	259.1±20.9	
MIM			t=0.068
Min-Max	304.3-373.3	279.3-363.5	P=0.946
Mean±SD	338.9±15.5	338.7±17.4	
SIM			t=0.193
Min-Max	307-377	269-373	P=0.847
Mean±SD	343.3±17.4	344.0±18.9	
NIM			t=0.035
Min-Max	292-370	290-375	P=0.972
Mean±SD	341.1±15.9	341.3±17.9	
IIM			t=0.124
Min-Max	290-382	290-370	P=0.902
Mean±SD	339.8±17.9	340.2±17.5	
TIM			t=0.64
Min-Max	301-364	268-354	P=0.524
Mean±SD	331.5±15.9	329.3±17.8	
MOM			t=0.227
Min-Max	256.5-353.3	256.8-361.0	P=0.821
Mean±SD	300.2±17.0	300.9±17.9	
SOM			t=1.223
Min-Max	261-340	250-477	P=0.224
Mean±SD	299.3±16.6	305.4±31.1	
NOM			t=0.179
Min-Max	257-409	258-344	P=0.859
Mean±SD	315.8±21.9	315.1±17.0	
IOM			t=0.145
Min-Max	246-349	249-357	P=0.885
Mean±SD	293.9±17.4	294.4±18.4	
TOM			t=0.68
Min-Max	254-394	236-324	P=0.498
Mean±SD	291.7±22.5	288.9±17.4	

t: t-test
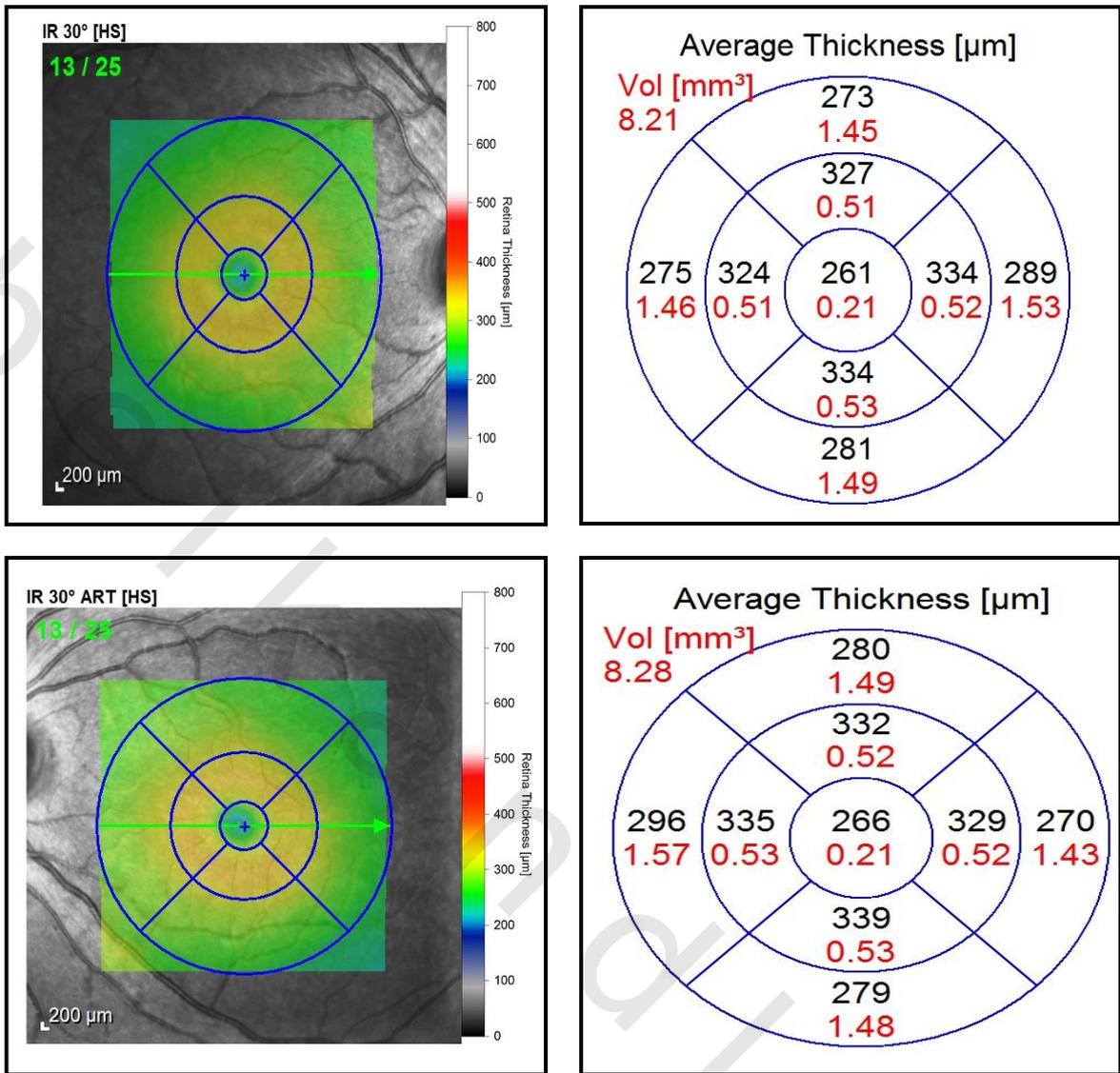
Fig. (24): Thickness map of the right and left eye of a 12 years old female.

In the inner ring macular thickness, there was a statistically significant difference between groups as determined by one-way ANOVA test. The mean thickness of the inner ring of the three groups was increased with age. There is no significant difference between the three groups in CSF and MOM. (Table 9)

Table (9):   Macular measurements using optical coherence tomography among the studied healthy Egyptian children in relation to their age.

| Macular measurements	Age			Significance
	6-<10 years (1) (n=48)	10-<14 years (2) (n=34)	14-16 years (3) (n=18)	ANOVA test
CSF				
Min-Max	209-361	229-310	225-294	F=2.466
Mean±SD	254.7±25.1	264.9±19.3	264.1±20.4	P=0.09
MIM				
Min-Max	279.3-373.3	310.3-361.5	345.5-362.5	F=4.411
Mean±SD	334.9±18.4	339.5±13.3	347.9±12.5	P=0.015*
SIM				
Min-Max	269-377	311-370	318-370	F=3.647
Mean±SD	339.9±20.4	344.2±14.8	352.9±13.9	P=0.03*
NIM				
Min-Max	290-370	311-361	312-375	F=4.855
Mean±SD	337.0±18.6	341.9±12.6	350.9±15.6	P=0.01*
IIM				
Min-Max	290-382	305-364	319-365	F=3.844
Mean±SD	336.2±20.1	340.5±15.1	349.3±10.9	P=0.025*
TIM				
Min-Max	268-364	308-352	305-354	F=3.375
Mean±SD	326.7±19.5	331.3±12.8	338.4±13.3	P=0.038*
MOM				
Min-Max	264.5-361.0	256.5-324.0	284.5-353.3	F=2.114
Mean±SD	302.9±19.1	295.6±15.0	303.7±15.7	P=0.126
SOM				
Min-Max	250-477	261-340	281-326	F=1.467
Mean±SD	306.4±32.2	296.9±15.6	301.8±14.2	P=0.236
NOM				
Min-Max	284-349	257-340	297-409	F=2.627
Mean±SD	316.8±17.0	309.9±18.3	322.2±25.5	P=0.077
IOM				
Min-Max	258-357	246-320	276-306	F=1.567
Mean±SD	297.2±20.8	290.2±16.6	293.5±8.2	P=0.214
TOM				
Min-Max	236-348	257-309	276-394	F=2.111
Mean±SD	291.0±20.9	285.6±14.2	297.3±25.4	P=0.127

F: ANOVA test

*significant at P≤0.05

31
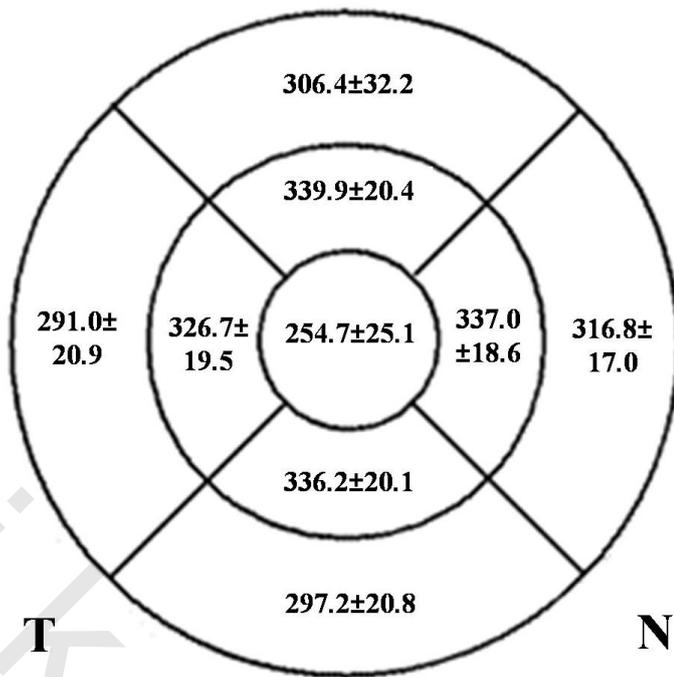
Fig. (25): Mean and standard deviations of macular thickness (in micrometers) of each ETDRS sector in children with age group 6-<10.
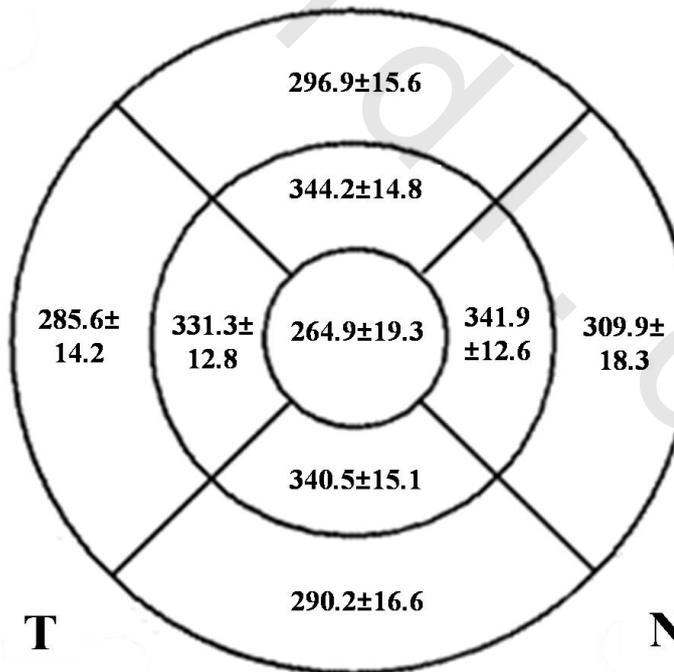

Fig. (26): Mean and standard deviations of macular thickness (in micrometers) of each ETDRS sector in children with age group 10-<14.
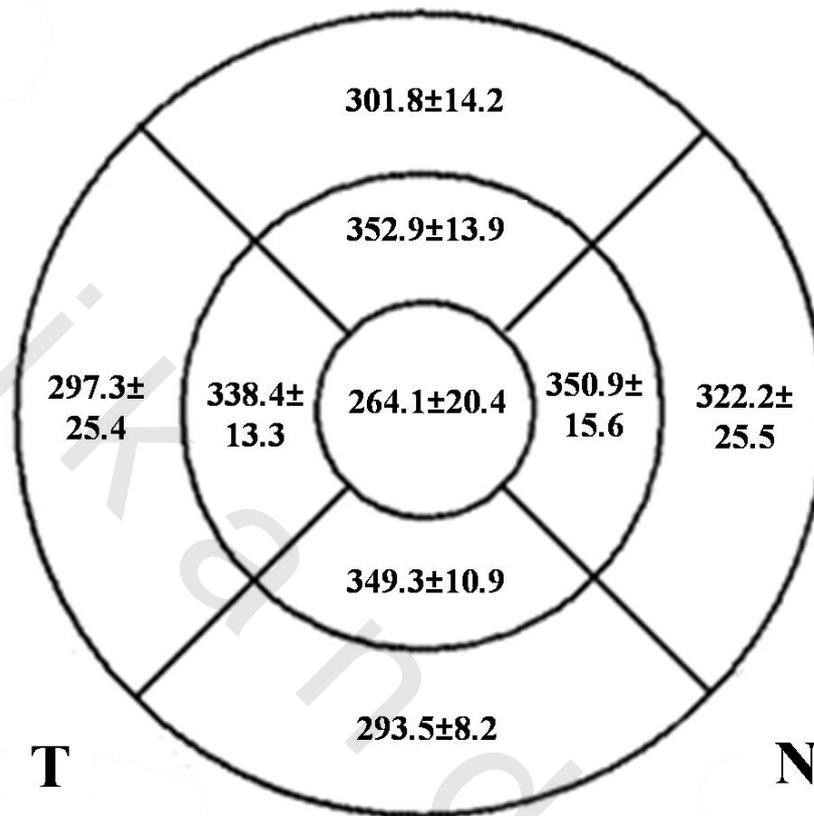
Fig. (27): Mean and standard deviations of macular thickness (in micrometers) of each ETDRS sector in children with age group 14-16.

The MIM thickness showed a positive correlation with age shown in (Fig. 29). But the CSF, MOM thickness had no correlation with age. (Fig. 28,30)
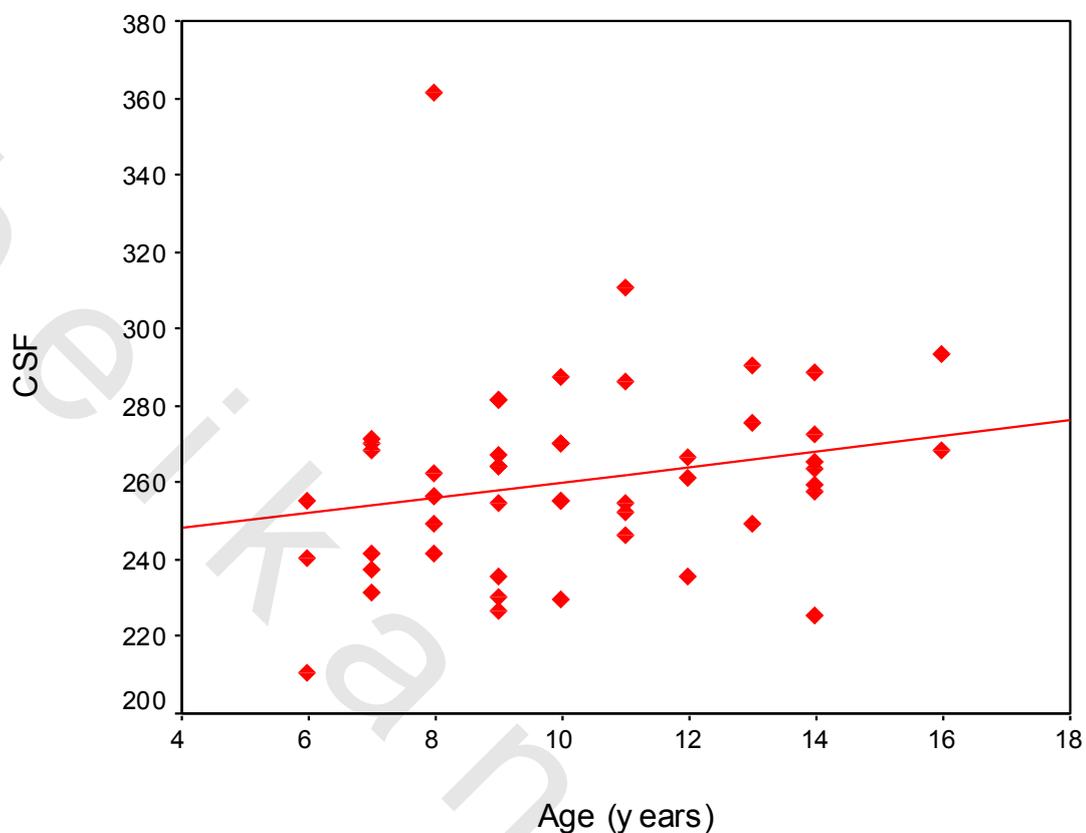

Fig. (28): Scatter graph for correlation between age (years) and CSF among the studied healthy Egyptian children (r=0.22, P=0.125).
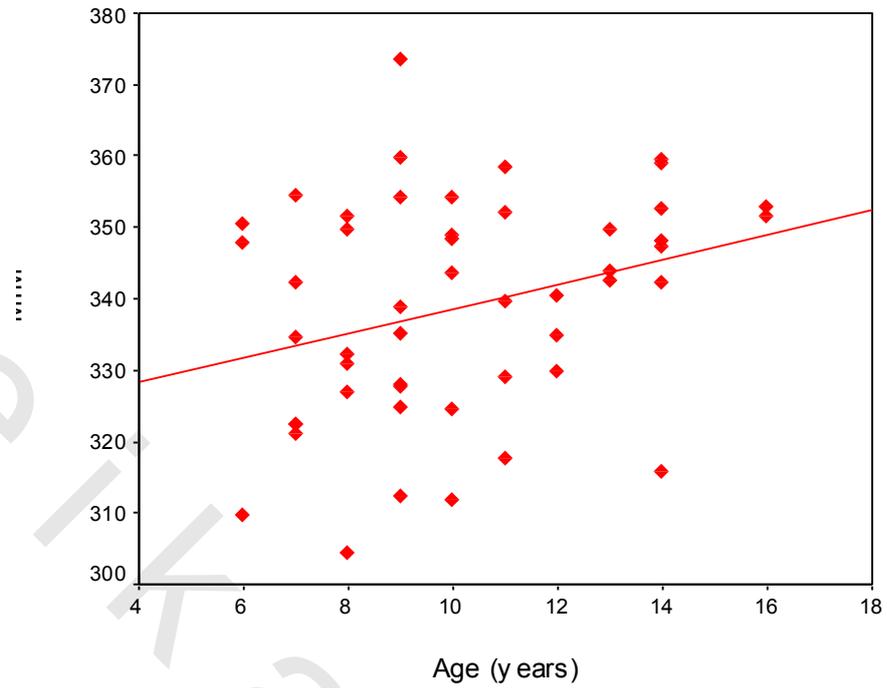
Figure (29): Scatter graph for correlation between age (years) and MIM among the studied healthy Egyptian children (r=0.301, P=0.034*).
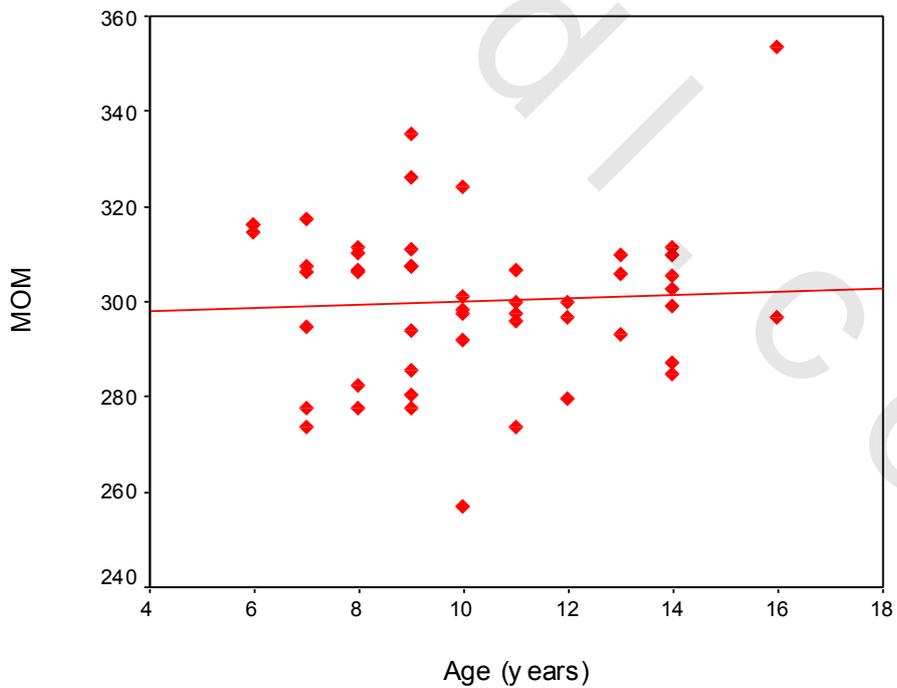

Figure (30): Scatter graph for correlation between age (years) and MOM among the studied healthy Egyptian children (r=0.052, P=0.718).