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RESEARCH ARTICLE

OBSERVATION OF CENTRAL MACULAR THICKNESS AND MICROVASCULATURE BY OPTICAL COHERENCE TOMOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN AN AMBLYOPIC PATIENT

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Abstract

Purpose: Documented the macular area changes regarding thickness and vascularity on an amblyopic patient by optical coherence tomography and optical coherence tomography angiograph.

Patients and methods: A case control observational study. AllPatients were attended to Ain shams university clinic and the clinic of Ophthalmology Department of Re- search Institute of Ophthalmology in period between October 2020 to May 2021.the study included 40 patients, age between 7-18y, with unilateral amblyopic eye and divided into 4 groups each group 10 patients, unilateral amblyopic with strabismus, anisometropia, sensory deprivation compared to control study. The patients excluded with history prematurity, trauma, neurologic or systemic disease, uncooperative patients, eccentric fixation, and patients with refractive errors more than 6 Diopters. The thickness and vascularity of macular area were investigated and documented byoptical coherence tomography (OCT) and optical coherence tomography angiograph (OCTA).

Results: The central thickness (1mm) of macula in all groups were non-significant compared with the control group except in sensory amblyopic groupthere was a significant increase in the thickness compared to control group with p -value 0.033.The vascularity of FAZ area, superficial capillary plexus (SCP) and deep capillary plexus (DCP), are not statistically significant (p-value was 0.0412 & 0.154) respectively.

Conclusion: Thestudy helps in understanding the changes in central macular thickness and FAZ microvasculature by OCT and OCTA that may play a role in pathophysiology and the management of different types of an amblyopic pediatric patient.

Introduction:-

Amblyopia is a disorder that targets the development of sight. It is due to the failure of cortical visual development in one or both eyes from ocular pathology early in life and It is the most common cause of decreased vision in a single eye among children and younger adults [Kyle Blair,2022].The age at which children are most sensitive to

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amblyopia is during the first 2 to 3 years of life, and this sensitivity gradually decreases until the 7 years of age; when visual maturation is complete and the retinocortical pathways and visual centers become resistant to abnormal visual input [Sandra BS,2021]. The main ocular alterations that predispose to amblyopia are deprivation of visual stimuli (pupil occlusion by ptosis, opacities of optical media, nystagmus, and many others), alteration of sharpness of visual stimuli by refractive changes (high ametropia and/or anisometropia), and non-corresponding images received by each eye (strabismus). Individuals with amblyopia often have restricted career options and reduced quality of life, including less social contact, cosmetic distress (if associated with strabismus), low self-esteem, visual disorientation, and fear of losing vision in the other eye [Webber AL,2018]. Although it has been reported that amblyopia primarily causes cerebral anatomical alterations in lateral geniculate bodies and the visual cortex, it can also affect retinal layers and vascular structures[Karabulut M ,2019] so in this study by using the OCT and OCTA it helped to document and reportany changes in thickness and vascularity in macular area that participate to know the peripheral point of pathophysiology of amblyopia .

Patient And Methods:-

A case control observational study. AllPatients were attended to Ain shams university clinic and the clinic of Ophthalmology Department of Research Institute of Ophthalmology in period between October 2020 to May 2021.the study included 40 patients, age between 7-18y, with unilateral an amblyopic eye and divided into 4 groups each group 10 patients, unilateral amblyopic with strabismus, anisometropia, sensory deprivation in comparisonwith the control study. The patients excluded with history prematurity, trauma, neurologic or systemic disease (including diabetes mellitus, hypertension, cardiovascular disease, and renal disease), uncooperative patients, eccentric fixation and patients with refractive errors more than 6 Diopters. An amblyopic eye defined when the best corrected visual acuity (BCVA) using Snellen's chart in one eye was at least two Snellen visual acuity lines worse than the fellow eye, and the anisometropia was defined as an inter-ocular difference in refraction of at least 1.5 diopters (D). All participants encountered , full ophthalmological examination including manifest and cycloplegic refraction by using (Topcon Auto-refractometer RM 8900) , anterior segment examination , posterior segment examination ,cover - uncover, alternating cover test and extraocular muscle motility test. OCT and OCTA (Heidel- berg engineering, OCT spectralis, Germany) for measurement the macula area and documented the changes in patient groups that divided into four groups: Group (I): Control group (10 patients). Group (II): Strabismic amblyopia (10 patients). Group (III): Ani- sometropic hypermetropic amblyopia (10 patients). Group (IV): Sensory deprivation (10 patients).

OCT Macular Scan

Equipment:

OCT2 Module ofHeidel- berg engineering, OCT spectralis, Germany

Scanning parameters:

FAST volume scan: 20°x20° (6x6mm)- 25-line volume scan, ART [automated real-time trackingvalue of 9]with fast speed of 85000 HZ.

Image and data:

All eyes are scanned by same trained doctor with dilated pupil at least 5mm. The macular scan was composed of six linear scans centered at the fovea by 55° widefield OCT.The macular thickness map analysis,bySpectralis OCT2 provides a circular map analysis in which the average thickness is displayed as a color code or numeric values in the nine Early Treatment Diabetes Retinopathy Study (ETDRS) areas. The ETDRS map consists of three concentric rings with diameters of 1mm (central), 3mm (inner), and 6mm (outer), the inner and outer rings are divided into four areas. The thickness of the foveola was defined as the distance between the innermost and outermost foveolar surfacesand all measurements were calculated automatically by the software in different planes.

OCTA Macular Scan

Equipment:

Heidel- berg engineering, spectralis OCT Angiography, Germany.

Scanning parameters:

A rectangular 10mm X 5mm area macular scan protocol witha lateral resolution of 11 μm/pixel

Image and data:
All eyes are scanned by same trained doctor with dilated pupil at least 5mm. OCTA of the superficial and deep networks in macular area were captured and automatically segmented to visualize the retinal superficial capillary plexus (SCP) and deep capillary plexus (DCP). SCP OCTA scan images were segmented with the inner boundary at the internal limiting membrane (ILM) and the outer boundary at 10μm above the inner plexiform layer (IPL). DCP scan images were segmented with an inner boundary 10ɯm above the IPL and the outer boundary

10μm below the outer plexiform layer (OPL). FAZ area was measured at both the superficial and deep capillary plexus, using software "Draw region" tool to outline FAZ area manually, and software automatically calculate the outlined area.

Statistical analysis:
Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The measurement of inter observer reliability of FAZ area calculations were tested by using Intraclass correlation coefficients (ICCs). The comparison between two independent groups with quantitative data and parametric distribution were done by using Independentt-test.

Results:-
The mean age in control group is 10.51±1.71and 11.62±3.11 in amblyopic groups, while the mean BCVA was 0.0±0.0 for control group and in strabismic, anisometropic and sensory deprivative groups were 0.37±0.140, 42±0.23 and 0.52±0.13 respectively which is statistically significan in compared to control group (p-value <0.001) [table 1].

On OCT, the total macular thickness including the FAZ in comparing between the control group and amblyopic groups revealed that no statistically significant difference (p- values were >0.05) except the FAZ area in sensory deprivative group was significant increase in the thickness compared to control group with (p-value 0.033) [fig:1][table 2].

On OCTA, The FAZ area on SCP, show that no statistically significant difference (p-value 0.0412) between the control group and amblyopic patients' group while also FAZ area on DCP shows no statistically significant difference (p- value 0.153)[fig:2] [Table 3].

Discussion:-
Amblyopia had been thought to be a disease associated with an abnormality of the retina. However, amblyopia-induced cerebral changes were later shown to mainly occur in the visual cortex and the lateral geniculate body [Kavitha, V,2019].TheAbsence of normal vision stimulation may also lead to less or no apoptosis of retinal ganglion cells in amblyopic eyes, eventually leading to thicker RNFL of the amblyopic eye than nonamblyopic eye [Wu SQ ,2013].OCT is a rapid, noninvasive, office-based imaging technique allowing objective quantification of retinal structures with high resolution, including determination of peripapillary RNFL thickness and macular thickness, in our study OCT is used to determine the central macular thickness as Few studies have suggested that there is no difference in macular thicknesses in children with unilateral amblyopia [Rajavi Z ,2014,Kee SY ,2006] .On the contrary, few studies have shown that the increase thickening of the macula occurs in anisometropic and strabismic amblyopia [Wu SQ ,2013,Yen MY,2004]. In our study no significant difference in central macular area including FAZ in a unilateral amblyopic patient in comparison to a normal person except in sensory deprivation amblyopic where the thickness is increased than normal person. Zherenetal [Zheren Xia ,2020] reported that no difference in macular thickness in anisometropic amblyopia and this results were consistent with the study of Chen et al. [Chen.W ,2017] which matches with our study. In contrast the Kasemetal [KASEM M ,2017] reported that There was a significant increase in the macular thickness and macular volume in all amblyopic eyes comparing to the other fellow eyes but in sensory deprivation amblyopia reported no significant increase in contrast to Kim etal [Kim YW ,2013]reported there was a significant increase in the foveal thickness as in our study although we excluded the eccentric fixation of amblyopic patient.

OCT angiography (OCTA) is becoming part of everyday clinical practice because it is a dye-free technique ;requires a short time for acquisition, suitable for examination of children's eyes. And allows for a stratified evaluation of the retinal microvasculature. FAZ finding regarding SCP and DCP in our study there was no statistically significant

difference between unilateral amblyopic and control cases asnumerous previous studies agree with this finding as they did not find any difference in FAZ measurements between amblyopic and fellow normal eyes [Pujari A ,2019,Yilmaz Cinar,2021]. Still, a recent study form Araki et al .[Araki S,2019] reported a reduced SCP FAZ area in eyes with unilateral amblyopia in addition, enlargement of DCP FAZ in amblyopic eyes was also detected by Sobral et al. [Sobral I,2018].Thus, there does not seem to be clear for us to draw some definitive conclusions on the role of the FAZ area in amblyopic eyes.thus there a question rises ;are the usage of anti-amblyopic drugs can increase FAZ compensatory microvascular SCP , DCP for improve the visual impulse ?! Further studies on large scale needs to understand about the actual FAZ microvasculature and the role in management of amblyopia. Our limitation in the study are small scale of amblyopic patient number and assessment of choroidal vascular assessment.

Tables

Table 1:- The difference between 4 groups regarding visual acuity.

p-value >0.05: Non significant (NS). p-value <0.05: Significant. •: One Way ANOVA test.

VA	Control group	Strabismic amblyopia	Anisometropic amblyopia	Sensory deprivative amblyopia	p -value
Mean ± SD Range	0.00±0.00 0-0	0.37±0.14 0.3-0.6	0.42±0.23 0.3-1	0.52±0.13 0.4-1	<0.001

Table 2:- Comparison between control group and patients' group regarding total macular thickness.

Full macular thickness	Control group	Strabismic amblyopia	Anisometropic amblyopia	Sensory deprivative amblyopia	p -value
FAZ Range	251.60 ± 17.95 229-278	253.50 ±21.55 220-285	249.70 ± 19.37 227-273	276.10 ± 15.91 248-291	0.040
3mm: Superior: mean Range	356.20 ± 12.45 326-364	334.00 ± 13.01 317-361	342.10 ± 18.54 316-365	343.50±30.32 283-395	0.503
Inferior: Mean Range	336.40 ± 10.04 317-345	332.10 ± 14.71 306-352	334.50 ± 17.43 311-362	334.0 ±23.25 276-353	0.866
Nasal: Mean Range	336.60 ± 13.43 311-354	331.50 ± 14.96 307-361	336.70 ± 19.17 310-366	340.80 ±24.12 283-361	0.724
Temporal: mean Range	326.60 ± 10.43 312-3443	317.60 ± 15.05 300-339	322.00 ± 16.11 301-342	324.80 ±24.12 266-351	0.540
6mm Superior mean Range:	305.60 ± 12.40 273-316	301.90 ±20.07 279-341	301.00 ± 11.25 285-3232	300.30 ±21.70 253-317	0.881
Inferior: mean Range	298.60 ± 17.74 254-313	290.20 ± 18.58 263-315	292.00 ± 12.51 271-306	281.20 ± 19.33 246-302	0.179 0.894
Nasal mean Range	318790 ± 14.67 286-333	312.60 ± 17.15 294-341	316.00 ± 13.62 301-343	312.90 ±24.52 257-333	0.541
Temporal: mean Range	291.40 ± 13.49 257-304	281.70 ± 13.89 256-303	285.20 ± 14.47 265-311	281.30 ±21.71 244-3087	

p -value >0.05: Non significant (NS). p -value <0.05: Significant (S) - One Way ANOVA test.

Table 3:- Comparison between control group and patients' group regarding mean FAZ (mm ^{2}) area in SCP and DCP.

FAZ	Control group	Strabismic amblyopia	Anisometropic amblyopia	Sensory deprivative amblyopia	p -value
SCP Mean ± SD Range	0.28±0.04 0.17-0.35	0.35±0.12 0.19-0.5	0.32±0.11 0.22-0.6	0.32±0.03 0.24-0.38	0.411
DCP Mean ± SD Range	0.22±0.03 0.13-0.27	0.26±0.10 0.17-0.45	0.30±0.08 0.19-0.41	0.26±0.04 0.15-0.30	0.153

p -value >0.05: Non significant (NS).
p -value <0.05: Significant (S).
p -value <0.01: Highly significant (HS)

Figures

Figure 1:-Group regarding total macular thickness

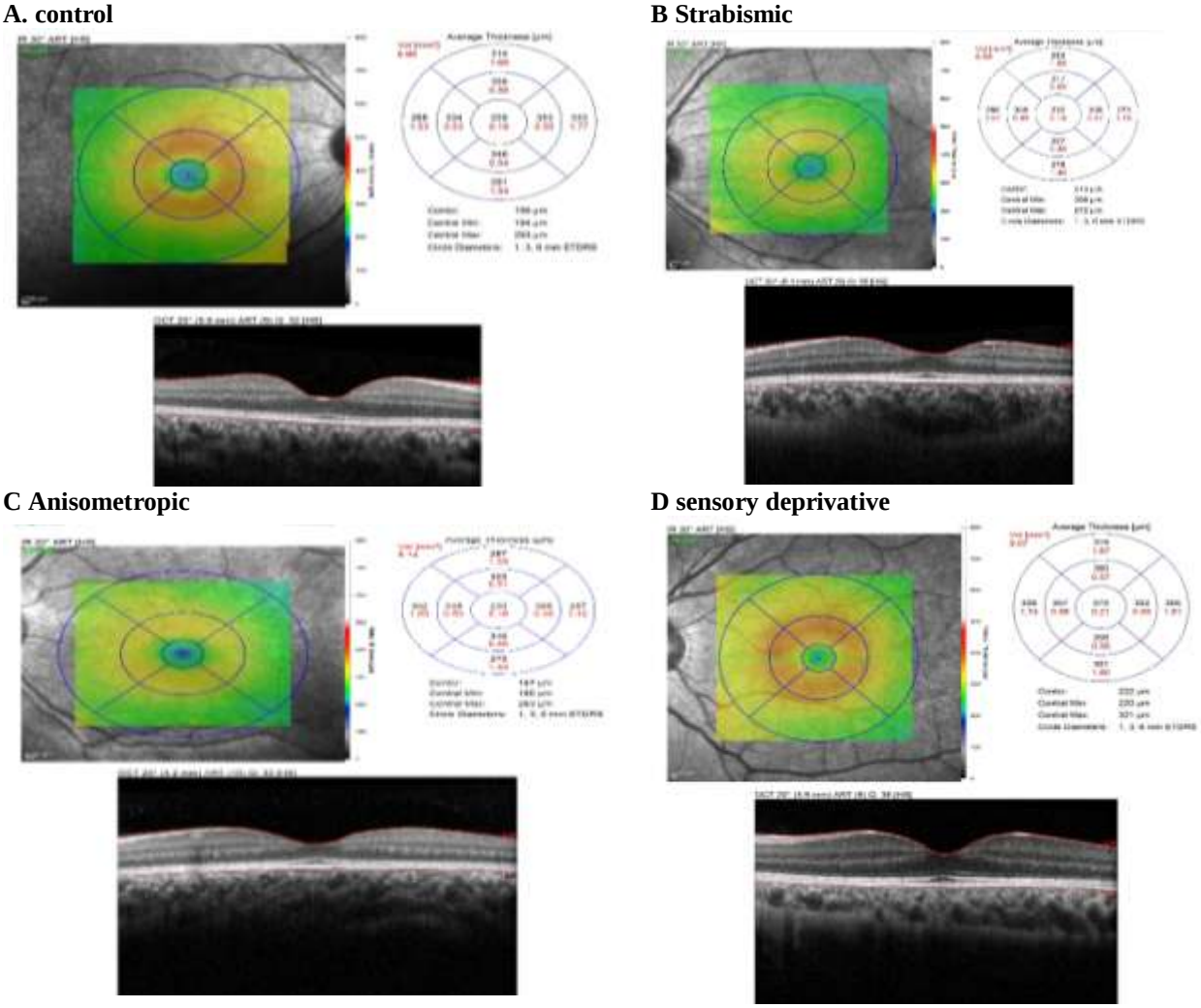
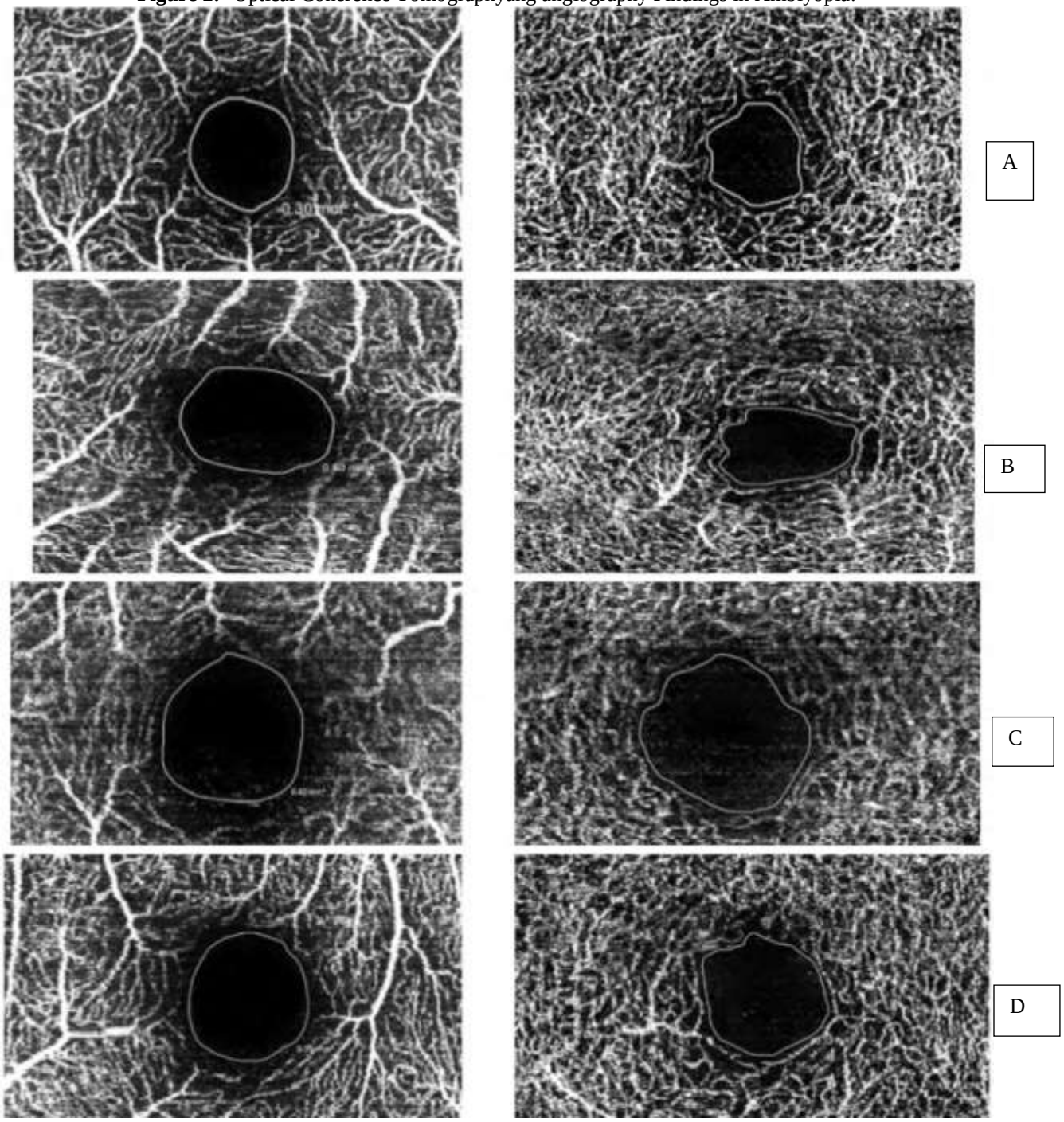


Fig 1:fullmacularthicknessA.control, B.Strabismic,C.anisometropic,D.sensorydeprivativeamblyopia.

Figure 2:- Optical Coherence Tomographyang angiography Findings in Amblyopia.



LEFT. SCP RIGHT. DCP

FIG-2 FAZ in SCP (Left) and DCP (Right) of (A) Control (B) Strabismic amblyopia, (C) Anisometropic amblyopia (D) Sensory deprivative amblyopia.

Conclusion:-

The study helps in understanding the changes in central macular thickness and FAZ microvasculature by OCT and OCTA that may play a role in pathophysiology and the management of different types of an amblyopic pediatric patient.

Instiiutional Review Board Statement
The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of AIN SHAMS UNVERISITY , CAIRO , EGYPT FWA00017585 (protocol code 423].

Conflict Of Interest
The authors declare no conflict of interest.

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