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RESEARCH ARTICLE

Evaluation of retinal nerve fiber layer and choroidal structure in obese children and adolescents

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ABSTRACT

Aim: Obesity-related vascular damage and endothelial dysfunction have deleterious effects on the ocular vasculature. It was aimed to examine optical coherence tomography (OCT) parameters in obese and overweight children and to define their relationship with metabolic markers in this study.

Methods: The patient group consisted of 26 obese, 24 overweight patients aged between 8 and 18 years. The control group consisted of 25 healthy children with normal body mass index (BMI). This was a cross-sectional observational study. Serum glucose, lipid parameters, and homeostasis model assessment of insulin resistance (HOMA-IR) were investigated. Measurement of choroidal thickness was performed with Cirrus HD-OCT (Carl Zeiss Meditec Inc., Dublin, CA, USA). Retinal nerve fiber layer (RNFL) thickness was determined by an automatic computer algorithm without the need for user measurement.

Results: There were no differences in subfoveal, nasal, temporal choroidal thickness, and RNFL between obese, overweight, and control groups (p>0.05). A positive (linear) moderate relationship was found between RNFL and the HOMA-IR of 26 patients in the obese group (r=0.389) (p=0.049). A positively weak correlation was found between height and RNFL in obese patient group (r=0.264, p=0.028).

Conclusion: In the study, RNFL thickness increased as HOMA-IR level increased in obese children and adolescents. RNFL decreased as the height increased in obese children and adolescents. We believe that more comprehensive data about the effect of obesity on RNFL and choroidal thickness will be obtained with prospective studies in which the obese patient group with insulin resistance is taken separately and disease durations are defined, and long-term patient follow-up is performed.

Keywords: Choroidal thickness, insulin resistance, obese children, retinal nerve fiber layer

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INTRODUCTION

Childhood obesity is an increasingly common health problem in developed and developing countries, regardless of age, gender, and ethnicity (1). In the occurrence of hypertension, diabetes mellitus, dyslipidemia, and progressive cardiovascular diseases, obesity is crucial (2). Obesity-related vascular damage and endothelial dysfunction have deleterious effects on the ocular vasculature and ocular blood flow (3). The choroid provides metabolites to the retinal pigment epithelium. Choroid has an essential impact on evaluating the ocular vascular structure (4).

Optical coherence tomography (OCT) was first used by Huang et al. (5). It is a basic non-invasive test for macular and optic nerve diseases. OCT takes images of the retina using a laser beam. It is also suitable for children as it is a non-contact, transpupillary, and painless imaging method (6). SD-OCT has allowed choroidal thickness measurement and detection of choroidal changes nowadays (7).

The number of studies investigating OCT parameters in obese and overweight children is limited in the literature and the results contradicts with each other. We aimed to investigate OCT parameters in obese and overweight children and to determine the relationships with metabolic markers.

MATERIAL AND METHODS

In our cross-sectional observational study, 26 obese and 24 overweight patients aged between 8 and 18 years who were brought to the pediatrics clinic of the hospital between July 2022 and December 2022 were included. 25 healthy children with normal weight were included in the healthy group. Informed consent was obtained from the parents of the children before the eye examination. The patients and the control groups were selected by randomization. The study was carried out with the permission of the Ethical Committee of University Hospital. (Date: 26.05.2022, Decision Number: 2022-61, report number:2022-71). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The weight of the patients was measured with electronic scales. Their height was measured standing with the Harpenden Stadiometer. The BMI formula was obtained by dividing the weight measurement by the height's square. A BMI between 18.5-24.99 was defined as normal weight, between 25-29.99 overweight, 30 and above were defined as obese. Triceps thickness and waist circumference were measured using a non-stretchable paper tape. After fasting for 10 hours, blood samples were taken from patients. Serum glucose and lipid parameters have been investigated. The homeostasis model assessment of insulin resistance (HOMA-IR) was detected as fasting insulin × fasting glucose / 405 to learn about insulin resistance (8). The patients were referred to ophthalmology for choroidal and optic nerve evaluations.

Inclusion criteria included having full visual acuity (according to the Snellen chart) and no eye pathology other than refractive error. The right eyes of the children were included in the study. Of the volunteers, participants with hypertension, diabetes mellitus, cardiac anomaly, those who were pregnant or breastfeeding, those who had undergone ocular surgery, those who had myopia greater than 3D, hypermetropia, and astigmatism greater than 1D weren't included in either of the groups in the study. A complete ophthalmoscopic evaluation of visual acuity, intraocular pressure measurement, light reflexes, eye movements, and anterior and posterior segment examination has been made.

Measurement of choroidal thickness with optical coherence tomography and RNFL analysis

Upon the instillation of 5% tropicamide, Cirrus HD-OCT was used for the measurement. Measurements with signal quality below 6 in both choroidal thickness and RNFL analysis were excluded.

In the reading of the choroid, the enhanced depth imaging system (EDI) mode of the device was used. The first measurement site was made subfoveal. Then, measurements were made from 6 points in the temporal and nasal directions from the subfoveal region, 3 temporal and 3 nasals, at 500 micron intervals and up to 1500 microns. Temporal and nasal choroidal thicknesses were calculated by taking the average of 3 choroidal thicknesses. Since the measurements were done manually, they were repeated by two different individuals. The mean choroidal thickness was found by taking an average of 7 measurements. Automatic computer mechanism defined retinal nerve fiber layer thickness (RNFL).

Categorical variables were presented as numbers. Continuous variables were presented as mean ± SD (min-max, median, Q1-Q3 when available). For the comparison of categorical expressions, the Chi-square test was applied. Continuous variables were tested for normal distribution using the Shapiro-Wilk test. Post hoc p analysis was performed after the study (Table 1). In the matched groups, Mann Whitney U test was performed. Kruskal Wallis analysis was performed that did not show normal distribution. Post hoc Bonferroni analysis was used to determine the source of the difference between the groups. To define the relation between continuous variables, the correlation test of Spearman's rho was made. A p-value less than 0.05 ($p<0.05$) was considered statistically significant. Analysis was performed using statistical package SPSS version 23.0 (IBM Corp., Armonk, NY, USA) for Windows.

RESULTS

26 obese patients, 24 overweight patients, and 25 healthy control patients were included in the research. 34 of them were boys and 41 of them were girls. Children's average age was 168 months in the obese patient group, and it was higher than the overweight and healthy children ($p=0.016$). When the differences between the groups were examined; the weight, BMI, and triceps thickness values were found higher in obese patients than others ($p<0.01$). The levels of HOMA-IR were 5.25 (4.22-6.18) in the obese patient group, 3.75 (2.59-5.15) in the overweight group and 3.3 (2.15-4.9) in the healthy control group. It was higher in obese children than in overweight and healthy children ($p=0.003$). Cholesterol and triglyceride levels were compared between the groups but there was no statistically significant correlation between groups in terms of cholesterol and triglyceride ($p>0.05$). Data for clinical, anthropometric measurements and other biochemical analyses are shown in Table 1.

There were no differences in subfoveal, nasal, temporal, or mean choroidal thickness between obese, overweight, and healthy subjects (respectively p=0.451, 0.677, 0.175, 0.472). No statistical significance was found on RNFL thickness. Intraocular pressure was measured in the obese patient group, overweight and healthy children. Intraocular pressure was lower in obese children 10 (10-12) mmHg than overweight children 12 (10-12.75) mmHg but the difference was not statistically significant ($p>0.05$). Median values of choroidal thickness, RNFL, and intraocular pressure are shown in Table 2.

The correlation between variables and RNFL in the obese patient group is made by Spearman correlation analysis and is shown in Table 3. A moderate positively (linear) relationship has been detected between the right eye RNFL thickness and the HOMA-IR value of 26 patients in the obese group ($r=0.389$) ($p=0.049$). A negatively weak correlation was detected between the height measurement and the right eye RNFL thicknesses in the obese patient group ($r=-0.26$, $p=0.028$). It was not detected any relation between weight, triceps thickness, waist circumference, BMI which were other anthropometric measurements and RNFL thicknesses ($p>0.05$). There was no significant correlation between both glucose and cholesterol levels and RNFL levels ($p>0.05$).

The patients were diagnosed with obesity when they came to the outpatient clinic for examination and were then sent for an eye examination. Therefore, it is not known how long these patients have been obese. These patients are not followed for a certain period of time due to obesity.

Table 1. Comparison of body mass measurements and biochemical analysis

	Obese (a)	Overwheight (b)	Contro l(c)		
	Med (Q1-Q3)	Med (Q1-Q3)	Med (Q1-Q3)	p‡	Post Hoc p
Age (month)	168 (131.5-180)	125.5 (111.25-175)	121 (114.5-156)	**0.016***	a-b; p=0.027
Height (cm)	163 (156.88-165.78)	149.05 (140.5-162)	151 (143-155.9)	**0.001****	a-b; p=0.034 a-c; p=0.003
Weight (kg)	86.25 (72.75-94.43)	60.95 (55.05-68.15)	51 (45.45-57.2)	**0.000****	a-b; p=0.000 a-c; p=0.000 b-c; p=0.006
BMI (kg/m^2)	32.75 (30.37-33.8)	27 (26.07-27.9)	23 (21.45-23.9)	**0.000****	a-b; p=0.000 a-c; p=0.000 b-c; p=0.006
Systolic tension (mmHg)	120 (110-126.25)	105 (100-120)	110 (95-120)	**0.011***	a-c; p=0.009
Diastolic tension (mmHg)	80 (70-80)	70 (60-80)	70 (60-70)	**0.026***	a-c; p=0.024
Triceps thickness (mm)	33 (31.88-34.25)	31 (28.25-32)	27 (25-27.25)	**0.000****	a-b; p=0.008 a-c; p=0.000 b-c; p=0.000
Waist circumference (cm)	104 (99.75-108.38)	91.5 (89-96.75)	80 (72-85)	**0.000****	a-b; p=0.000 a-c; p=0.000 b-c; p=0.000
Glucose (g/dl)	92 (88-98)	82 (84-96)	82 (80-91)	**0.046**	
Total cholesterol (mg/dl)	143 (134-170.5)	157 (138.5-183.75)	157 (140.5-176.5)	0.494	
HDL cholesterol (mg/dl)	47 (35.75-53.25)	50 (42.25-59.75)	50 (45-56.5)	0.352	
LDL cholesterol (mg/dl)	81 (72.75-94.25)	83.5 (74.25-105.5)	89 (77-103.5)	0.300	
Triglyceride (mg/dl)	114 (89.25-156.75)	100.5 (84.5-159)	102 (79.5-126.5)	0.283	
HOMA-IR	5.25 (4.22-6.18)	3.75 (2.59-5.15)	3.3 (2.15-4.9)	**0.003****	a-b; p=0.019 a-c; p=0.008

* $p<0.05$, ** $p<0.001$; †: Chi-square, ‡: Kruskal Wallis, Post Hoc Bonferroni, BMI: body mass index, HOMA-IR: The homeostasis model assessment of insulin resistance.

Table 2. The measurements of choroidal thickness, RNFL, intraoculary pressure in obese and overwheight and control groups

Variable	Obese (n=26)	Overwheight (n=24)	Control (n=25)	p‡
	Med (Q1-Q3)	Med (Q1-Q3)	Med (Q1-Q3)	
Subfoveal choroidal thickness (µm)	302.5 (266-348.5)	329 (257.5-355)	313 (280-371.5)	0.451
Nasal choroidal thickness (µm)	273 (216-301)	281 (229-330)	260 (235.5-314)	0.677
Temporal choroidal thickness (µm)	272 (257.5-310)	298.5 (245.8-328.8)	300 (274-354)	0.175
Average choroidal thickness (µm)	285 (245.75-314.5)	306 (254.8-335.5)	300 (262.3-342)	0.472
RNFL (µm)	92.5 (85.75-95.25)	91 (83.25-96.25)	95 (84-97)	0.733
Intraoculary pressure (mmHg)	10 (10-12)	12 (10-12.75)	10 (10-14)	0.313

* p<0.05, ‡: Kruskal Wallis, RNFL: retinal nerve fiber layer.

Table 3. Correlation between RNFL and variables in obese patient group

	RNFL	
	r	p
Age	-0.319	0.112
Height	-0,26*	**0.028**
Weight	0.001	0.998
BMI	0.278	0.169
Sistolic tension	-0.136	0.507
Diastolic tension	-0.165	0.420
Triceps thickness	0.076	0.711
Waist circumference	0.250	0.219
Glucose	0.031	0.880
HOMA-IR	0.389*	**0.049**
HDL cholesterol	-0.249	0.219
LDL cholesterol	-0.070	0.734
Triglyserid	-0.046	0.822

* p<0.05, Spearman's rho RNFL:retinal nerve fiber layer, BMI: body mass index, HOMA-IR: The homeostasis model assessment of insulin resistance.

DISCUSSION AND CONCLUSION

When comparing obese patients, overweight and healthy control groups, triceps thickness, height, weight, waist circumference, and BMI measurements were significantly higher in obese patients. HOMA-IR and RNFL thickness are significantly positively correlated in obese children. Height measurement and RNFL thicknesses are significantly negatively correlated. Subfoveal, nasal, temporal and mean choroidal thicknesses, and RNFL levels did not differ significantly between obese, overweight, and healthy children.

For the retina to be functional, an anatomically standard choroidal structure is crucial. Various systemic pathologies may affect the choroid (9). It is probable to observe alterations in the choroid with the developments in optical coherence tomography technologies (7).

Erşan et al. (10) detected that subfoveal choroidal thickness was thinner in obese children. In the study of Topcu-Yilmaz et al. (4), they found that subfoveal choroidal thicknesses of obese patients who had insulin resistance were significantly thinner than in healthy children in those with foveal 1000 µm and 1500 µm temporal locations. However, Bulus et al. (3) reported that subfoveal choroidal thickness was detected to become higher in obese children and adolescents. Celik et al. (11) reported that choroidal thickness in the subfoveal region was increased in obese patients. There were also differences in terms of choroidal thickness in obese children between the studies. We did not detect significant differences in obese children compared to healthy children with normal BMI relating to temporal, subfoveal, and mean choroidal thicknesses. However, the mean BMI of the patients in our study was lower than that of other studies. Since obese patients with hypercholesterolemia were not included as a different subgroup, it may affect the outcome as an additional risk factor. The mechanism of metabolic changes in obesity is quite complex. While a vasoconstriction state may occur due to the hyperdynamic cardiac state and sympathetic discharge occurring in obesity, an increase in vascular permeability and thickening of the choroid can be expected due to increased inflammatory markers in obesity (12). As a common result of these mixed mechanisms, no effect on the choroid may have occurred.

Evaluation of RNFL has a significant importance in optic nerve damage's identification in hypertension, inflammatory diseases owing to avoid definite visual field disorders (13). In the study by Özen et al. (14) of 38 obese and 40 healthy children, there was a reduction in RNFL thickness in obese patients. On the other hand, they realized that this reduction did not make a statistically significant difference compared to healthy children. Baran et al. (15) observed that there were significant thinning of RNFL thicknesses in obese children. It was thought that it may cause an increased risk of developing glaucoma at a younger age, especially in children with central obesity. Pacheco-Cervera et al. (16) reported a significant decrease in RNFL thickness in the morbidly obese patient group (BMI-SDS >4). In the study of Hazar et al. (17), groups of children with obesity and obesity-related hypertension were included and in obesity related hypertension group RNFL was significantly thinner, but inferior RNFL thickness wasn't significantly thinner in the obesity group. There were conflicting results among studies in the literature regarding the effect of obesity on RNFL thickness in children. Optic atrophy and thinning of the RNFL have been reported over time (18). We found that the RNFL thicknesses in obese children were thinner than in healthy children, but the thinning was not statistically significant. The differences between the studies in the literature and our research is that the follow-up period of the patients with obesity were not long, and the body mass indexes were obtained much higher in other studies. Furthermore, this difference in our study may be due to the lack of clear information about how long the patients in the studies have had obesity and the studies were not planned according to the duration of the disease.

In a study examining RNFL thickness in healthy children; no correlation was found between height, weight, gender and RNFL (19). Khawaja et al. (20) reported that a negative correlation between BMI and RNFL in male-female adults without gender predominance. Negatively moderate correlation was detected among height measurement and RNFL in our study. It was observed that RNFL thickness decreased as the height increased in obese pediatric patients. However, no significant correlation was found between BMI and RNFL. Among the anthropometric measurements, only the relationship between height measurement and RNFL differed from the studies in the literature. Tall children were probably older. The age and axial length distribution could have caused this result in this group.

HOMA-IR value and the RNFL thickness positively significantly correlated with each other. We observed that metabolic disorders due to obesity affected the RNFL. The reason for RNFL changes in obesity was not clear. Studies examining the relationship between HOMA-IR and RNFL are very limited in the literature. In studies of Özen et al. (14) and Karti et al. (21), they detected a negative correlation between HOMA-IR and RNFL. There was a positive correlation between HOMA-IR and RNFL in our study. It can be thought that high HOMA-IR values may cause inflammation in the RNFL in the acute period and therefore an increase in RNFL and thinning secondary to atrophy may be observed in cases that become chronic.

Inflammation caused by insulin resistance may cause an increase in thickness in the RNFL with the effect of vascular permeability and edema in the acute period, and thinning by causing atrophy in the chronic period. For this reason, the duration of obesity of patients and how long they suffer from insulin resistance gain importance. It is clear that there is a need to compare the data of obese groups determined according to disease duration.

Study Limitations: The low number of patients included in the study is one of the limitations of this study. The other limitation is that it is not known how long the patients with insulin resistance among obese and overweight patients have insulin resistance.

In our study, we found that RNFL thickness increased as the HOMA-IR level increased, and RNFL decreased as the height increased in obese children and adolescents. It was not detected any difference in RNFL thickness and choroidal thickness among obese children with the healthy control group. We believe that more comprehensive data on the influence of obesity on RNFL and choroid thickness will be obtained with prospective studies that separate obese patient group with insulin resistance, define disease duration and follow patients over time.

Ethical approval

This study has been approved by the Ethical Committee of Ömer Halisdemir University Hospital (approval date 26/05/2022, number 2022-61). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: GYB; Concept: ZYÖ; Design: KRZ, GYB; Data Collection or Processing: ZYÖ, GYB; Analysis or Interpretation: KRZ, ZYÖ; Literature Search: ZYÖ; Writing: ZYÖ. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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