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Comparing characteristics of the optic nerve head among subjects with suspected glaucoma in different ages of onset

Топографска процена папиле видног живца код деце и одраслих са сумњом на глауком

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SUMMARY

Introduction/Objective Evaluation of the optic nerve head (ONH) is an inevitable procedure in the diagnosis of glaucoma. One of the most common imaging techniques for a quantitative assessment of the topography of the ONH is the Heidelberg retinal tomography II (HRT II).

The aim of this study was to determine quantitative stereometric parameters of the ONH by using the HRT II and to investigate any damage of neuroretinal rim in children with suspected glaucoma and compared these data with the group of adults with suspected glaucoma.

Methods This comparative study included 167 (167 eyes) children aged 11 ± 3 years with suspected juvenile glaucoma and 175 adult participants (175 eyes), aged 60 ± 3 years, also with suspected glaucoma, examined between January 2013 and April 2014. Optic nerve head topography and retinal nerve fiber layer thickness measurements were assessed using a HRT II.

Results Data analysis in this study showed that the average mean values for children/adults were: disc area (mm^2) $2.828 \pm 0.489 / 2.663 \pm 0.412$ ($p < 0.001$); rim area (mm^2) $1.873 \pm 0.391 / 1.667 \pm 0.275$ ($p < 0.001$); cup/disc area ratio $0.369 \pm 0.125 / 0.369 \pm 0.101$ ($p = 0.530$); mean retinal nerve fiber layer thickness (mm) $0.223 \pm 0.078 / 0.219 \pm 0.055$ ($p = 0.494$). Statistically significant difference in damage of neuroretinal rim, between children and adults, was found in temporal (T) and temporal-inferior (Ti) segments.

Conclusions There were differences in some of the investigated quantitative parameters of the ONH between children and adults, as optic disc size, cup and rim area and rim volume. By using MRA, difference in the damage of the neuroretinal rim, when comparing children and adult optic discs appeared only in T and Ti segments, which means that optic disc cupping has spread more in children than in adults.

Keywords: Heidelberg retina tomography; optic disc; stereometric parameters; primary open angle glaucoma; juvenile glaucoma

САЖЕТАК

Увод/Циљ Преглед папиле видног живца (ПВЖ) представља основу приликом постављања дијагнозе глаукома. Једна од најчешћих дијагностичких метода за квантитативну процену топографије ПВЖ је Хајделбергова томографија ретине II (ХТР II).

Циљ рада је био одредити помоћу ХТР II квантитативне стереометријске параметре папиле код деце са сумњом на јувенилни глауком и упоредити те параметре са групом одраслих особа такође са сумњом на глауком.

Метод У студију је укључено 167 деце узраста 11 ± 3 година са сумњом на јувенилни глауком и 175 одраслих старости 60 ± 3 година са сумњом на глауком у периоду од јануара 2013. до априла 2014. Преглед ПВЖ и перипапиларне регије обављен је употребом ласер скенинг томографа ХРТ II.

Резултати Просечне вредности стереометријских параметара код деце/одраслих биле су: површина ПВЖ (mm^2) $2,828 \pm 0,489 / 2,663 \pm 0,412$ ($p < 0,001$); површина неуроретиналног обода (mm^2) $1,873 \pm 0,391 / 1,667 \pm 0,275$ ($p < 0,001$); однос пречника екскавације и пречника папиле $0,369 \pm 0,125 / 0,369 \pm 0,101$ ($p = 0,530$); просечна дебљина слоја нервних влакана $0,223 \pm 0,078 / 0,219 \pm 0,055$ мм ($p = 0,494$). Оштећење неуроретиналног обода показало је статистичку значајност у темпоралном (Т) и темпорално доњем (Тд) сегменту код деце у односу на одрасле испитанике.

Закључак У овој студији постојала је разлика у вредностима неких стереометријских квантитативних параметара ПВЖ између деце и одраслих и то: површина ПВЖ, површина и запремина неуроретиналног обода. Неуроретинални обод је био ужи у Т и Тд сегменту код деце, тј. више ширила глаукоматозна екскавација.

Кључне речи: Хајделбергова ретинална томографија; глава оптичког нерва; стереометријски параметри; примарни глауком отвореног угла; јувенилни глауком

INTRODUCTION

Evaluation of the optic nerve head (ONH) is an inevitable procedure in the diagnosis of juvenile glaucoma. However, it is not easy to detect the first glaucomatous changes on a disc because of the great variability in the appearance of the optic nerve that often makes an accurate distinction between glaucomatous and healthy optic nerve rather difficult [1, 2]. On the other hand, the problems in the diagnosis of juvenile glaucoma are usually difficulty in getting useful visual field information in

children (especially young children). In the absence of a reliable visual field result, ophthalmologists must rely on an evaluation of structural changes on the optic disc, which according to the reported results, may precede the development of the reproducible perimetry defects by several years [3-5]. A confocal scanning laser tomography, the Heidelberg Retina Tomography (HRT; Heidelberg Engineering, Heidelberg, Germany), is one of the promising tools for the evaluation of the optic nerve head in glaucoma patients due to high reproducibility and ability to measure three-dimensional parameters [6, 7]. HRT has been used in recent years to perform quantitative measurements of the optic nerve head and provides measures of optic nerve head topography [8]. It has been proved to be highly reproducible and also shows good agreement with clinical estimates between optic nerve head structure and visual function [9-11].

Glaucoma has been categorized by the age of onset and the angle characteristics. Juvenile-onset primary open-angle glaucoma (JOAG) is accepted to a certain extent that it is a subset of adult Primary open angle glaucoma (POAG) with an earlier age of onset. However, JOAG and POAG differ from each other with regard to their inheritance, prevalence, and severity of presentation [12]. There is a lack of papers on comparative morphometric analysis of optic nerve head using confocal scanning laser ophthalmoscopy among Primary open-angle glaucoma and Juvenile-onset primary open-angle glaucoma, or their suspects.

The aim of this study was to determine quantitative stereometric parameters of the optic nerve head by using the Heidelberg Retina Tomography II and to investigate any damage of neuroretinal rim in children with suspected glaucoma and compare these data with the group of adults also with suspected glaucoma.

METHODS

This prospective comparative study included 167 (167 eyes) children aged between 5-16 years (mean age of 11 ± 3 years) with suspected juvenile glaucoma and 175 adult participants (175 eyes), aged between 55-66 years (mean age of 60 ± 3 years) also with suspected glaucoma. All of them were examined between January 2013 and April 2014 at the Clinic for Eye Diseases, Clinical Center of Serbia in Belgrade. All subjects underwent a complete ophthalmic examination by a glaucoma specialist including visual acuity (Snellen chart), slit-lamp biomicroscopy, gonioscopy, IOP measurement with Goldmann applanation tonometry and fundus examination using indirect ophthalmoscopy with Volk Superfield lens 90D. Diagnostic observation also included a visual field test using the Threshold C 24-2 Swedish Interactive Testing Algorithm (SITA) standard program with Humphrey visual field analyzer II (Carl Zeiss, Germany) and scanning laser ophthalmoscopy-Heidelberg retinal tomography (HRT II, Heidelberg Engineering, GmbH, Dossenheim, Germany, version 2.02). Central corneal thickness values were measured by ultrasonic pachymeter (Alcon laboratories, OcuScan®RxP Ophthalmic Ultrasound system, Fort Worth TX) by trained ophthalmic technicians. The pachymetry measurement recorded for each eye was the average of 3 measurements

taken per eye. Refractive error was measured with autokeratorefractometer (Topcon KR-7000) and was calculated as spherical equivalent in diopters (D), as the sum of the sphere and half the refractive astigmatism.

Subjects included in the study were glaucoma suspects with either glaucomatous-appearing optic disc and IOP under the 22 mm Hg or with healthy appearing optic disc and IOP of 22 mm Hg or above. The criteria for determining the glaucomatous-appearing optic disc were assessed by the clinical impression of a glaucoma specialist. "Glaucomatous-appearing optic disc" must include one or more of the following: 1) excavation-undermining of the neuroretinal rim; 2) notching—it was considered if it involved 2 clock hours; 3) focal or diffuse atrophy of neuroretinal rim area-neuroretinal rim thinning involving 2 or more clock hours; 4) vertical cup-disc ratio more than 0.6 or 5) vertical cup-disc asymmetry between the eyes of 0.2 or more [1]. Participants included in the study did not receive anti-glaucoma medications nor did they undergo surgery.

Inclusion criteria were: 1) best-corrected visual acuity better than 0.8; 2) spherical refraction within ± 5.0 D; 3) cylindrical correction within ± 1.5 D; 4) open angle on gonioscopy and 5) normal visual field.

Exclusion criteria were coexistence of any other ophthalmic pathology other than glaucoma and IOP above 26 mm Hg.

All subjects received a detailed explanation about the study and signed an informed consent form in accordance with the principles embodied in the Declaration of Helsinki. An informed consent to participate in the study was taken from all adult participants or from the guardians (if participants were below 18 years of age). The Ethics Committee of the Clinical Center of Serbia within which the study was undertaken approved this study.

Study participants underwent ocular imaging with the commercially available HRT II (HRT II, Heidelberg Engineering, GmbH, Dossenheim, Germany, version 2.02). The HRT is a confocal scanning laser ophthalmoscope that provides software-generated measurements describing the topography of the surface of the optic disc and adjacent peripapillary retina. The right eye of each participant selected for the study was examined for the first time by means of HRT II. The same observer analyzed all HRT images after proper adjustment for refractive error and astigmatism.

Twelve stereometric parameters [disc area (mm^2), cup area (mm^2), rim area (mm^2), cup-to-disc area ratio (C/D ratio), cup volume (mm^3), rim volume (mm^3), mean retinal nerve fiber layer (RNFL) thickness, RNFL cross sectional, height variation contour (mm), mean cup depth (mm) and maximum cup depth (mm) and cup shape measure (mm)] of children and adults have been taken into consideration in this study. We also investigated data for the mean RNFL thickness, rim area, rim volume and C/D ratio in each of the 6 segments [temporal (T), temporal-inferior (Ti), temporal-superior (Ts), nasal (N), nasal-superior (Ns), nasal-inferior (Ni)].

Moorfields regression analysis (MRA) is a part of HRT program, representing the method for analyzing regression logarithmic of the global and 6 segment rim areas (T, Ti, Ts, N, Ni, Ns) to the

matching disc areas and compares the results to a normative database. It defines these areas as damaged or outside normal limit, borderline and normal based in the 95% and 99.9% confidence intervals: “normal” if all of the measurements fall within the 95% confidence intervals (CI); “borderline” if at least one falls between the lower 95% and 99.9% CI; and “outside normal limits” if at least one rim area measurement is less than the lower 99.9% CI.

By using MRA, the percentage of the participants who had normal, borderline and/or outside normal limit neuroretinal rim (T, Ts, Ti, N, Ns and Ni) was determined, so these data were compared between children and adult groups.

Statistical Analysis

Standard descriptive statistics were used. Student’s *t*-test and Mann-Whitney test was used for comparison of the variables between studied groups. Chi-square test was used to evaluate the significance of the differences between categorized data. Individual differences were considered to be statistically significant for $p < 0.05$. SPSS version 21.0 (SPSS Inc, Chicago, Ill) was used for all statistical calculations.

RESULTS

During observation period, 167 children and 175 adults were enrolled in this study. Baseline demographic characteristics of enrolled participants, intraocular pressure, best corrected visual acuity and refractive error in diopter are shown in the Table 1.

Table 1. Characteristics of the participants in both studied groups.

Variables	children	adults	<i>p</i>
Number of participants, n	167	175	
Male/female, n (%)	90(54) / 77(46)	59(34) / 116(66)	0.001
Age (y), mean±SD (range)	11.2±3.1 (5–16)	60.1±3.2 (55–65)	<0.001
IOP (mmHg) (range)	16.5±3.1 (10–25)	19.7±2.8 (12–26)	0.584
CCT, μ m, mean±SD (range)	578 ± 35 (503–620)	547 ± 35 (453–601)	0.032
Best corrected VA (range)	0.98±0.048 (0.8–1.0)	0.98±0.027 (0.8–1.0)	0.755
Refractive error, SE (D), (range)	-2.50 (-5.00 - +1.00)	-1.50 (-4.50 - +2.00)	0.313

IOP - intraocular pressure; VA – visual acuity; SE – spherical equivalent; D – Diopter

The mean children age was 11.2±3.1 years (range 5–16 years) and they were predominantly male (54 %) and in the adults group the mean age was 60.1±3.2 years (range 55–65 years) and they were predominantly female (66 %). IOP mean in children was 16.5±3.1 mmHg (range 10–25 mmHg) and in adults it was 19.7±2.8 mmHg (range 12–26 mmHg) ($p=0.584$). There was statistically significant difference in mean CCT in 2 studied groups, children/adults: 578 ± 35 μ m (range 503–620 μ m) / 547 ± 35 μ m (range 453–60 μ m) ($p=0.032$). Visual acuity in children and adults were 0.8 or better. They were predominantly myopic and in children spherical equivalent ranged between –5.00 and +1.00 D and in adults between –4.50 and +2.00 D.

Summary statistics for the optic disc morphometric characteristics of interest are presented in Table 2, 3, 4, 5 and 6.

Table 2. Values of global optic nerve head parameters in both studied groups.

Stereometric parameters	Children		Adults		P
	Range	Mean ± SD	Range	Mean ± SD	
Disc area (mm ²)	1.685-4.571	2.828±0.489	1.780-3.745	2.663±0.412	0.001
Cup area (mm ²)	0.042-2.758	1.157±0.527	0.187-1.957	1.011±0.381	0.0024
Rim area (mm ²)	1.873-3.593	1.873±0.391	0.908-2.630	1.667±0.275	<0.001
Cup/disc area ratio	0.021-0.639	0.369±0.125	0.081-0.599	0.369±0.101	0.530
Cup volume (mm ³)	0.001-1.122	0.387±0.262	0.028-1.078	0.327±0.203	0.065
Rim volume (mm ³)	0.123-1.343	0.437±0.196	0.127-0.850	0.382±0.132	0.039
m RNFL	0.052-0.467	0.223±0.078	0.091-0.398	0.219±0.055	0.494
RNFL cross sectional	0.034-2.873	1.357±0.473	0.522-2.190	1.262±0.327	0.048
Mean cup depth	0.074-0.677	0.307±0.096	0.111-0.631	0.309±0.098	0.889
Maximum cup depth	0.200-1.316	0.744±0.181	0.379-1.278	0.758±0.180	0.552
Height variation contour	0.171-1.553	0.370±0.149	0.183-0.655	0.356±0.081	0.706
Cup shape measure	-0.412-0.058	-0.144±0.078	-0.309-0.048	-0.152±0.081	0.264

These summary statistics include the range, the mean and SD for each characteristic in each group. Table 2 shows a comparison of global optic nerve head parameters by HRT II between two studied groups. There were statistically significant differences between children and adults in these stereometric parameters: disc area (mm²): 2.828±0.489 vs. 2.663±0.412, (p<0.001), cup area (mm²): 1.157±0.527 vs. 1.011±0.381 (p=0.0024), rim area (mm²): 1.873±0.391 vs. 1.667±0.275 (p<0.001), rim volume (mm³): 0.437±0.196 vs. 0.382±0.132 (p=0.039) and RNFL cross sectional 1.357±0.473 vs. 1.262±0.327 (p =0.048). However, no significant differences were found in the mean cup to disc ratio, cup volume, mean RNFL, mean and maximum cup depth (p>0.05).

We further analyzed cup to disc ratio, rim area, rim volume and mRNFL in each segments (T, Ts, Ti, N, Ns, Ni). Values of C/D area ratio in each of the six segments in the both studied groups are summarized in table 3. In T, Ti, N, Ns C/D ratio were larger in children than in the adults group with

Table 3. Values of C/D area ratio in each of the 6 segments in the both studied groups.

C/D area ratio segments	Children		Adults		P
	Range	Mean ± SD	Range	Mean ± SD	
Temporal	0.081-0.864	0.592±0.106	0.230-0.822	0.543±0.146	0.044
Temporal-superior	0.000-0.724	0.408±0.133	0.069-0.704	0.430±0.123	0.133
Temporal-inferior	0.010-0.813	0.388±0.122	0.007-0.737	0.349±0.144	0.045
Nasal	0.000-0.738	0.239±0.162	0.000-0.680	0.218±0.149	0.084
Nasal-superior	0.000-0.636	0.317±0.154	0.000-0.588	0.303±0.135	0.588
Nasal-inferior	0.000-0.524	0.207±0.124	0.000-0.662	0.219±0.128	0.686

it there were statistically significant differences in temporal: 0.592±0.106 vs. 0.543±0.146 (p=0.044) and temporal inferior: 0.388±0.122 vs. 0.349±0.144 (p=0.045) segment. Rim area was larger in each six segments in children than in adults (Table 4) and statistically significant in all segments. Also, rim

Table 4. Values of the rim area in each of the 6 segments in the both studied groups.

Rim area segments	Children		Adults		p
	Range	Mean ± SD	Range	Mean ± SD	
Temporal	0.081-0.651	0.301±0.096	0.087-0.464	0.265±0.069	<0.001
Temporal-superior	0.103- 0.443	0.257±0.063	0.079-0.326	0.233±0.043	<0.001
Temporal-inferior	0.076-0.650	0.257±0.071	0.058-0.345	0.214±0.043	<0.001
Nasal	0.199-1.086	0.545±0.133	0.206-1.021	0.510±0.106	0.022
Nasal-superior	0.069-0.555	0.257±0.154	0.141-0.334	0.233±0.430	<0.001
Nasal-inferior	0.168-0.554	0.292±0.065	0.123-0.446	0.255±0.053	<0.001

volume was greater in all segments in children than adults but statistically significant in temporal ($p=0.006$), temporal inferior ($p<0.001$) and nasal-inferior ($p=0.0026$) segment (Table 5). Analyzing

Table 5. Values of the rim volume in each of the 6 segments in the both studied groups.

Rim volume segments	Children		Adults		p
	Range	Mean ± SD	Range	Mean ± SD	
Temporal	0.010–0.100	0.029±0.016	0.000–0.080	0.024±0.012	0.006
Temporal-superior	0.008–0.131	0.049±0.023	0.008–0.126	0.045±0.019	0.211
Temporal-inferior	0.006–0.259	0.061±0.033	0.010–0.134	0.048±0.021	<0.001
Nasal	0.000–0.272	0.063±0.059	0.000–0.237	0.044±0.046	0.144
Nasal-superior	0.004–0.253	0.066±0.036	0.015–0.167	0.064±0.026	0.927
Nasal-inferior	0.024–0.268	0.091±0.039	0.018–0.175	0.078±0.030	0.0026

the mean RNFL we did not find statistically significant differences in each of the 6 segments between two studied groups (Table 6).

Table 6. Values of the mean retinal nerve fiber layer (mRNFL) in each of the 6 segments in the both studied groups.

m RNFL segments	Children		Adults		p
	Range	Mean ± SD	Range	Mean ± SD	
Temporal	0.096–0.168	0.079±0.030	0.038–0.142	0.075±0.020	0.114
Temporal-superior	0.021–0.493	0.252±0.088	0.104–0.501	0.262±0.077	0.526
Temporal-inferior	0.024–0.628	0.265±0.107	0.055–0.453	0.242±0.082	0.706
Nasal	0.050–0.700	0.246±0.113	0.030–0.460	0.233±0.079	0.059
Nasal-superior	0.198–0.615	0.284±0.122	0.089–0.569	0.303±0.088	0.258
Nasal-inferior	0.109–0.648	0.330±0.110	0.137–0.512	0.323±0.083	0.474

Reading of the MRA findings of both groups, statistically significant difference in damage of neuroretinal rim was found in T ($p<0.001$) and Ti segment ($p=0.0046$), between children and adults (Table 7).

Table 7. Moorfields regression analysis (MRA) results.

Segments (%)	Children			Adults			P
	IN	BL	OUT	IN	BL	OUT	
Temporal	98 (77.2)	27 (21.3)	2 (1.6)	122 (96.1)	5 (3.9)	0 (0)	<0.001
Temporal-superior	119 (93.7)	6 (4.7)	2 (1.6)	114 (89.8)	12 (9.4)	1 (0.8)	0.2695
Temporal-inferior	101 (79.5)	21 (16.5)	5 (3.9)	117 (92.1)	9 (7.1)	1 (0.8)	0.0046
Nasal	93 (73.2)	21 (16.5)	13 (10.2)	106 (83.5)	13 (10.2)	8 (6.3)	0.1498
Nasal-superior	95 (74.8)	23 (18.1)	9 (7.1)	95 (74.8)	29 (22.8)	3 (2.4)	0.8285
Nasal-inferior	105 (82.7)	14 (11)	8 (6.3)	105 (82.7)	13 (10.2)	9 (7.1)	0.9772

IN-normal; BL-borderline; OUT-outside normal limit.

Data for T segment for children/adults were (in percent): normal (77.2/96.1%), borderline(21.3/3.9%), outside normal limit (1.6/0%) and for Ti segment were normal (79.5/92.1%), borderline (16.5/7.1%), outside normal limit (3.9/0.8%). There was no statistically significant difference in other segments.

DISSCUSION

In the present study, we evaluated stereometric parameters of ONH in suspected primary open angle glaucoma in different ages of onset. Our first purpose was to evaluate morphometric features of the optic disc in children and the second was to compare these data with the data of the group of

adults. The optic disc characteristics have been extensively studied with regard to adult onset POAG but there are few studies relating to the morphometry of Primary juvenile glaucoma discs [13, 14]. On the other hand, HRT have been used in normal children in a few studies [15-18]. Ruberto et al. [15] reported normal values for HRT in comparison with children with CVI, and Tong et al. [16] presented values of myopic 11–12-year-old Singaporean children. Recently, He et al. [17] used HRT to analyse disc and cup area in a twin study of children. In Larsson et al. [18] they investigated the normal values but also repeatability and interocular difference of the ONH, using HRT, in 5-16-year old full term children. They had smaller disc area than in present study (2.16 versus 2.83 mm²), as also rim area (1.75 versus 1.87 mm²) and cup area (0.41 versus 1.15 mm²). Chinese twins, studied by He et al. [17], had also smaller disc area [2.83 (present study) versus 1.97 mm²] and smaller cup area [1.15 (present study) versus 0.50 mm²]. Differences were obvious especially in the cup area because in our study the most of the children had a glaucomatous appearance disc and Larsson [18] and He and al. [17] studied normal children. Also the reason for large discs and large cupping could be the reason that children in our study had myopic refractive errors like in study Jung et al. [19], which suggested that highly hyperopic eyes have significantly smaller optic discs and highly myopic eyes have significantly larger discs than emmetropic eyes.

There were not many studies on comparative morphometric analyses of optic nerve head using confocal scanning laser ophthalmoscopy among primary glaucoma in different ages of onset. In 1996 Jonas and Grudler [13] compared ONH between JOAG and POAG patients and recently Gupta et al. [12] analyzed differences in optic disc characteristics between Primary Congenital Glaucoma, Juvenile, and Adult Onset Open Angle Glaucoma Patients.

The present study found optic discs to be larger in size among patients with suspected JOAG compared with suspected glaucoma in adults. Our parameters were larger than in recently study Gupta et al. [12], optic disc size in JOAG patients was 2.61 mm² versus 2.83 (present study), also significantly larger than in adult POAG eyes [2.44 mm versus 2.663 mm (present study)]. It is right to observe that in Gupta et al. [12], study patients were presenting with a confirmed diagnosis of glaucoma while in our study participants were presenting with suspected glaucoma. One of explanations that children may have larger optic disc sizes might be that a larger disc size may also be inherited with a genetic susceptibility to develop glaucoma. It is known that genetic susceptibility plays a greater role in the causation of glaucoma in children (congenital and juvenile) compared to adults where causation is, more often, multifactorial. Hence, genetic segregation of children affected by glaucoma could also account for the larger optic discs seen within our observations of these young participants compared with our adult participants [20].

On other hand, Jonas and Grudler [13] studied the optic disc morphometry of 37 JOAG and 382 adult POAG patients using stereo disc photographs but did not find a difference in the disc area between the juvenile and adult onset POAG eyes in their population. They used the planimetric

method for calculation, which is known to give larger measurements because of image magnification compared with the confocal scanning laser ophthalmoscope (CSLO).

Measurement of the optic disc and neuroretinal rim is important for the diagnosis and management of glaucoma [21]. It is increasingly recognized that the disc size is a major determinant of other disc parameters such as neuroretinal rim area or cup area or volume [13, 19, 22]. When comparing our data compiled from the children and the adults groups, in addition to larger disc sizes, the children also had larger rim areas which is consistent with the results in previous published studies [23, 24].

In our study children also had greater average cup area and cup volume than adults. Jonas and Grundler [13] also found that cup volume in children with JOAG were larger than in POAG patients. In the study Gupta et al. [12] the cup characteristics demonstrated significantly greater means among JOAG compared with POAG and PCG eyes, included cup depth ($p=0.001$), cup volume ($p=0.024$), and cup to disc area ratio ($p=0.049$). Cup-to-disc ratio as a measure for determining structural change is the most often used clinically by glaucoma specialists to assess structural damage of the optic disc. In present study there was no significant difference in the mean C/D ratio between children and adults (children 0.369 ± 0.125 , adults 0.369 ± 0.101).

We mentioned that previous studies [13, 19, 22] have suggested a correlation of neuroretinal rim area and optic cup area to the optic disc size but the question is the correlation between disc size and RNFL. Budenz et al. [25] have demonstrated thicker RNFL in larger optic discs. In our study RNFL was thinner in adults but we need take into consideration a fact that age is recognized as a significant factor affecting RNFL thickness [26, 27] and normal individuals lose ganglion cells in an age-dependent manner, at an estimated rate as high as 5,000 axons/year, which may translate into considerable axon loss during a 70-year life span [24]. On the other hand our results coincided with results in Savini et al. study [22] showing that RNFL thickness was positively correlated with ONH size. Such a correlation may be the result of either an increased number of nerve fibres in eyes with larger discs or a smaller distance between the circular scan and the true ONH margin [22].

Besides quantitative parameters of the optic nerve head in children and adults, we investigated difference in damage of the neuroretinal rim with MRA comparing children and adult optic discs in which damage was only appearing in T and Ti segments; our conclusion is that optic disc cupping has spread more in children than in adults. MRA indicates normal, borderline and outside normal limits on the basis of a comparison between examined optic disc and a dedicated database of normal eyes and is highly capable of clinically discriminating normal and glaucomatous patients. In our study, there was the statistically significant difference of the percentage distribution in normal, borderline and outside normal limit between children and adults group in T and Ti segments so in that segments neuroretinal rim was more damaged in children compared to adults. Several clinical studies [28] support the idea that damage to the optic nerve and the RNFL can be identified before an alteration in the visual field. This fact is very important in the examination of children, because determination of

visual field and interpretation of the results may cause a problem. Detection and monitoring of glaucoma patients are based on identification of structural and functional changes. We mentioned that in the absence of a reliable visual field results in children, ophthalmologists must rely on evaluation of structural changes on the optic disc. We also know that structural alterations of the optic disc nerve fiber layer complex provide the earliest reliable signs of damage from glaucoma [24, 29]. Accurate and objective quantitative measurements of the optic nerve head and nerve fiber layer are required to improve our ability to regularly recognize early glaucomatous damage. It follows that it is important to evaluate the optic nerve head by using well-established confocal scanning laser ophthalmoscope, the HRT II and to improve detection of early damage [30]. Also HRT is quick and non-invasive technique and therefore is applicable in children.

Our study has some limitations. While HRT has mostly been used in the diagnosis of glaucoma, on the other hand it has been the requirement that the operator manually define a contour line marking the inner border of the ONH margin as defined by the sclera ring. Many of the quantitative measurements are derived from the contour line placement, thereby inducing measurement variability. Second, the problem is that there is a lack of normative database for subjects under the age of 18 and consequently HRT use in children has not been extensively studied. Also, it should be noted that the mean age of these two groups was different, which makes the comparison less accurate. We did not present age-matched control data because the aim of this study was to compare morphologic appearance of optic disc in glaucoma suspects in different ages of onset. In addition, it should be taken into account that all participants have performed visual field with limit that most of the children did not have reliable visual field results. Finally, it is important to highlight that we enrolled in study participants with suspected glaucoma. Even though, by definition, JOAG is characterized with elevated intraocular pressure, but in the clinical practice the most children with suspected JOAG have glaucomatous-appearing optic disc but IOP in normal range and therefore a certain number of these children included in the study.

CONCLUSIONS

The results of the present study showed that there were differences in some of the investigated quantitative parameters of the optic nerve head between children and adults, as optic disc size, cup and rim area and rim volume. By using MRA, difference in the damage of the neuroretinal rim, when comparing children and adult optic discs appeared only in T and Ti segments, which means that optic disc cupping has spread more in children than in adults.

Diagnosis of glaucoma in children remains a challenge for clinicians. The assessment of optic disc and peripapillary RNFL damage in pediatric subjects can be quite challenging especially visual field testing in young children is often unreliable or impossible. Although diagnostic imaging methods lack a normative database for subjects under the age of 18 and their use in children has not been extensively studied, the clinicians would appreciate support by objective methods to differentiate

between normality and abnormality in borderline cases. Hence the aim of this study was to give insight in the characteristics of the optic nerve head of children with suspected glaucoma by using the HRT, what would be the similarities and differences between children and adults with suspected glaucoma and furthermore we hope that it will be helpful in the diagnosis of glaucoma in children.

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