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Analysis of the Quantitative Dermatoglyphic Traits of the Digito-Palmar Complex in Patients with Primary Open Angle Glaucoma

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A B S T R A C T

Patient with primary open angle glaucoma (PAOG), which is known to have a genetic predisposition, and their immediate relatives unaffected with PAOG, may have some changes in dermatoglyphic traits of the digito-palmar complex, since the trabecular meshwork develops at the same time and with the same hereditary base like dermatoglyphs, which have high genetic transmission. The objective of this study is to determine whether differences in quantitative dermatoglyphic traits of the digito-palmar complex exist between patients with glaucoma and the phenotipically healthy population and whether their family members have the same dermatoglyphic changes. The quantitative dermatoglyphic traits in patients suffering from glaucoma, first-degree members of their family and the phenotypically healthy population have been screened in this study. Descriptive statistics, univariate analysis of variance (ANOVA) and post hoc (Tukey HSD) method have been used. The results have shown that there is a link between the quantitative dermatoglyphic traits of the digito-palmar complex in patients affected by glaucoma and a first-degree healthy member of their family, as well as the difference between patients with glaucoma and their first-degree relatives, which may discriminate them from the phenotypically healthy population. The results of the study mostly affirm the existence of genetic predisposition for the development of primary open-angle glaucoma, thus emphasizing the relevance of hereditary factors in the etiopathogenesis of this disease.

Key words: *dermatoglyphs, primary open angle glaucoma, family history*

Introduction

Primary open-angle glaucomas (POAG) are chronic, progressive optic neuropathies that have in common characteristic morphological changes at the optic nerve head and retinal nerve fibre layer, with the absence of other ocular diseases or congenital anomalies. Progressive retinal ganglion cells death and visual field loss are associated with these changes[1]. Substantial advances in the understanding of the genetic transmission of glaucoma have been made in recent years[2,3]. Several chromosomal loci associated with POAG have been mapped by use of linkage analysis. Mutations in the genes responsible for trabecular meshwork development induced glucocorticoid response (myocilin/TIGR) gene and were determined to cause most cases of autosomal-dominant juvenile glaucoma and to play a role in adult-onset POAG[4]. In 2002, Rezaie and collaborators[5] identified another causative gene optin and described its protein optineurin, gene which was previously identified as *FIP-2* in other organs[6], and noticed alterations in this gene in patients with POAG. The increased risk of glaucoma in family members of patients with POAG has long been recognized, and several studies have screened relatives of patients with POAG for manifestations of the disease[7,8]. Epidemiologic data from the Baltimore Eye Survey, the largest population-based study of patients with POAG and unaffected controls, confirm that a family history of POAG is an important risk factor in the development of the disease[9]. The Barbados Eye Study also suggested that persons most likely to have glaucoma are older with a family history of glaucoma[10]. Rotterdam Eye Study[11] and Glaucoma Inheritance Study-Tasmania[12] came to the same conclusions.

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The formation of tiny channels in the trabecular meshwork of an angle is completed by the 21st week of the intrauterine development. These channels are responsible for the resistance to aqueous humor outflow and for the elevated intraocular pressure (IOP) in patients with POAG.

Dermatoglyphs are epidermal patterns on fingers, palms, and soles. They are completely formed by the 21st week of the intrauterine development and furthermore, are totally resistant to any external factor, remaining unchanged until the end of a person's life. Dermatoglyphs have highly hereditary characteristics[13]. The trabecular meshwork develops simultaneously with the development of dermatoglyphs of digito-palmar complex and from the same germ layers (skin from ectoderm and mesoderm, and angle structures from mesoderm). Therefore, genetic changes that result in predisposition for POAG might also influence the formation of dermatoglyphs during the early intrauterine period. Factors, which have a negative impact on the formation of a chamber angle, may also induce changes in the formation of dermatoglyphic digito-palmar complex of patients with POAG. Immediate relatives of the patient with a glaucoma, which is proven to have genetic predisposition, may also have certain changes in dermatoglyphic traits of the digito-palmar complex

The purpose of this study is to determine: 1) Whether there are statistically significant differences in quantitative dermatoglyphic traits of the digito-palmar complex between patients affected by POAG and the phenotypically healthy population. 2) Whether the immediate relatives of POAG patients, who are not affected by the disease, have the same changes in dermatoglyphic traits.

Materials and Methods

For the purpose of this study, 45 patients with POAG were examined (22 male and 23 female patients). The clinical examination included collection of a detailed family history of glaucoma, refraction, and application tonometry, as well as biomicroscopy with gonioscopy, ophthalmoscopy, and visual field testing by using standard full-threshold automated static perimetry. In their families, two or more patients with POAG were registered with the same disease. One immediate relative of a POAG patient from such a family, unaffected by the disease was examined in the study as a control group – totally 42 relatives (19 males and 23 females). Another control group consisted of 108 phenotypically healthy people, 52 males and 56 females, who didn't have POAG in their families.

The digito-palmar prints were taken and analyzed according to the Cummins and Midlo[14] methods, and some advices techniques were taken from the book Miličić and colaborators[15].

The study examined the following quantitative dermatoglyphic traits of the digito-palmar complex: number of ridges on fingers of both hands (FRR 1–5, and FRL 1–5); on palms: number of ridges between digital triradius a and b (a–b ridge count – rc), b and c (b–c rc) and c and d (c–d rc) right and left, and the atd angle of both hands measured in degrees.

The quantitative dermatoglyphic traits of the digito-palmar complex were analyzed by using descriptive statistics, univariate analysis of variance (ANOVA) and post hoc (Tukey HSD) method.

Results

The results of descriptive statistics comparing quantitative digito-palmar dermatoglyphic traits from POAG patient groups (male and female) and their control groups (immediate relatives and healthy population) are presented in Table 1 for males and Table 2 for females.

By comparing the results of descriptive statistical values in defined groups of examined people, it has been observed that the total number of ridges on fingers was higher for males than for females. The total number of ridges on fingers within the same-sex sample was higher for phenotypically healthy population than for those affected with POAG and their immediate relatives.

For males, significant differences were observed between phenotypically healthy individuals and patients with glaucoma, and their relatives on FRR1, FRR3, FRR5, and FRL3 ($p<0.01$, Table 3). For females, the significant differences in the number of ridges were noticed on FRR1, FRR 4 and FRL4, FRL5 ($p<0.01$) and FRR5 ($p<0.05$) between patients with glaucoma, the relatives and phenotypically healthy female population.

The results of descriptive analysis of palmar ridges have shown (Table 1 and 2) that the total number of ridges was lower for individuals affected by glaucoma in comparison with the members of their families and phenotypically healthy population for both males and females. In males, this difference was strongest on the position a–b rc right and c–d rc left ($p<0.01$). In females, the significant difference was observed on a–b rc right, b–c rc and c–d rc left ($p<0.01$), where the number of ridges was lower for patients than for the control groups. In males, the size of atd angle was approximately the same in all three examined groups, while in females atd angle in patients with glaucoma was higher than in control groups (Table 3).

Further in the investigation, ANOVA with Tukey HSD post hoc test for quantitative dermatoglyphic traits of the digito-palmar complex was performed in order to determine the significance of differences between examined groups.

The statistically significant differences between male and female groups on fingers and palms ware examined (Table 4 and Table 5). It can be clearly seen from Table 4 that in a male group there is statistically significant difference ($p<0.01$) in the ridge counts on FRR1 and FRR5 between male patients with POAG and phenotypically healthy population, as well as between family members of those affected by glaucoma and phenotypically healthy population. There is no statistically significant difference between male patients and their immediate

TABLE 1
DESCRIPTIVE STATISTICS FOR QUANTITATIVE DIGITO-PALMAR DERMATOGLYPHIC TRAITS IN THE GROUP OF MALE GLAUCOMA PATIENTS AND THEIR CONTROL GROUPS (MALE FIRST DEGREE RELATIVES AND MALE HEALTHY POPULATION)

Variable	Patients with glaucoma N=22		First degree relatives N=19		Healthy population N=52	
	X	SD	X	SD	X	SD
Right hand						
FRR 1	15.9	7.4	16.9	6.2	22.1	5.9
FRR 2	12.6	5.3	13.7	7.2	13.3	7.7
FRR 3	10.1	6.1	13.1	7.2	14.9	4.3
FRR 4	16.8	6.3	16.9	6.8	16.8	4.8
FRR 5	12.8	4.7	12.8	4.0	17.9	4.4
a–b rc R	37.1	5.6	40.5	5.4	41.9	6.3
b–c rc R	27.2	7.2	26.1	6.1	26.9	6.3
c–d rc R	33.0	5.2	37.0	5.2	35.7	5.7
atd R	42.6	11.6	41.3	7.6	41.6	7.5
Left hand						
FRL 1	14.2	7.0	18.0	5.1	18.3	6.8
FRL 2	12.1	6.9	13.5	6.3	10.9	6.5
FRL 3	10.1	5.6	15.1	6.4	15.3	6.5
FRL 4	17.3	5.2	16.7	5.7	16.3	5.1
FRL 5	14.1	5.3	15.1	4.9	14.1	4.3
a–b rc L	39.6	5.9	40.8	5.7	39.6	6.4
b–c rc L	25.5	5.9	27.2	5.3	27.2	5.6
c–d rc L	34.1	5.1	40.2	4.8	39.3	5.7
atd L	42.5	8.7	42.7	7.5	42.7	5.7

TABLE 2
DESCRIPTIVE STATISTICS FOR QUANTITATIVE DIGITO-PALMAR DERMATOGLYPHIC TRAITS IN THE GROUP OF FEMALE GLAUCOMA PATIENTS AND THEIR CONTROL GROUPS (FEMALE FIRST DEGREE RELATIVES AND FEMALE HEALTHY POPULATION)

Variable	Patients with glaucoma N=23		First degree relatives N=23		Healthy population N=56	
	X	SD	X	SD	X	SD
Right hand						
FRR 1	13.2	6.3	16.7	6.9	18.4	6.8
FRR 2	10.7	7.4	9.4	6.0	11.7	7.2
FRR 3	11.8	5.1	12.4	6.5	11.3	6.1
FRR 4	11.0	6.0	10.3	6.3	15.4	6.2
FRR 5	9.3	5.4	11.6	4.8	13.5	7.2
a–b rc R	36.4	4.5	38.5	4.7	40.6	4.7
b–c rc R	25.6	3.9	27.3	4.8	26.9	5.5
c–d rc R	36.0	5.8	37.6	4.9	36.1	7.8
atd R	47.7	12.5	46.5	12.6	44.7	10.4
Left hand						
FRL 1	15.1	7.0	15.7	5.5	14.9	6.6
FRL 2	10.3	6.8	8.5	5.9	10.8	7.7
FRL 3	9.7	5.7	11.8	6.0	13.0	7.7
FRL 4	12.5	6.5	12.6	6.1	17.1	7.0
FRL 5	12.1	6.8	11.5	5.0	16.2	6.2
a–b rc L	38.5	4.9	38.7	4.3	39.3	5.0
b–c rc L	24.0	2.9	29.4	4.5	29.2	7.1
c–d rc L	31.1	5.0	37.1	4.8	35.2	6.8
atd L	46.7	14.1	44.1	10.5	45.0	10.2

relatives. For FRR3, statistically significant difference has been found between male patients and phenotypically healthy population ($p<0.01$), while differences between patients and their family members significance was lower ($p<0.05$). Differences between family members and phenotypically healthy population are not statistically significant. For FRL3, differences are statistically significant between patients and the sample of phenotypically healthy population ($p<0.01$) and between patients and their family members ($p<0.05$). There is no significant difference between immediate relatives and phenotypically healthy population. In the palmar a–b rc right, there is statistically significant difference ($p<0.01$) between patients and phenotypically healthy population, but not among other groups. In the c–d rc left, there is statistically significant difference between patients and their family members ($p<0.01$) and among patients and phenotypically healthy population ($p<0.01$), while patients' family members have not shown statistically significant difference from phenotypically healthy population.

It can be seen from Table 5 that there are statistically significant differences ($p<0.01$) among examined female groups on fingers for FRR1 between females patients with POAG and phenotypically healthy population. No statistically significant differences were found between female patients and members of their families, nor between the two control groups. There has been statistically significant difference on FRR4 and FRL4 between female patients and phenotypically healthy population, and between healthy population and members of patients' family ($p<0.05$). Between female patients and members of their families there was no statistically significant difference. Statistically significant difference ($p<0.01$) on FRR5 were found only between female patients and phenotypically healthy population ($p<0.05$), but not among other groups. There has been statistically significant difference on FRL5 between female patients and phenotypically healthy population ($p<0.05$) and between healty population and members of PAOG family ($p<0.01$). Between female patients and members of their families there has been no statistically significant difference. On palmar dermatoglyphs the a–b ridge count right, shows statistically significant differences ($p<0.01$) among examined female patients with POAG and phenotypically healthy population. No statistically significant differences were found between female patients and members of their families, nor between the two control groups. For b–c rc left, there is a significant difference on the relevance level ($p<0.01$) between female patients and phenotypically healthy population, as well as between female patients and their family members. There was no statistically significant difference between two control groups. For c–d rc left, there was a significant difference at the relevance level ($p<0.05$) between female patients and phenotypically healthy population and between POAG patients and their family members ($p<0.01$). There was no statistically significant difference between two control groups.

TABLE 3
ANALYSIS OF VARIANCE ANOVA FOR ALL EXAMINED GROUPS IN MALES AND FEMALES

	Males F	Females F
Right hand		
FRR 1	9.69**	4.86**
FRR 2	0.14	0.88
FRR 3	6.22**	0.28
FRR 4	0.00	6.92**
FRR 5	14.25**	3.75*
a–b rc R	5.03**	6.90**
b–c rc R	0.17	0.78
c–d rc R	1.62	0.44
atd R	0.16	0.65
Left hand		
FRL 1	3.07	0.11
FRL 2	1.13	0.94
FRL 3	5.70**	1.81
FRL 4	0.27	5.94**
FRL 5	0.32	6.65**
a–b rc L	0.33	0.26
b–c rc L	0.79	7.00**
c–d rc L	8.94**	5.75**
atd L	0.01	0.32

*p<0.05, **p<0.01

TABLE 4
RESULTS OF TUKEY HSD POST HOC TEST FOR QUANTITATIVE DERMATPGLYPHIC TRAITS FOR ALL EXAMINED GROUPS IN MALES

Variable	Groups		p	95% confidence interval for mean	
				Lower bound	Upper bound
FRR 1	G	F	<0.01	–10.05	–2.41
	G	O	–	–5.74	3.67
	O	F	<0.01	–9.23	–1.17
FRR 3	G	F	<0.01	–8.14	–1.56
	G	O	–	–7.01	1.09
	O	F	<0.05	–5.36	1.58
FRR 5	G	F	<0.01	–7.90	–2.34
	G	O	–	–3.45	3.40
	O	F	<0.01	–8.03	–2.17
a–b rc R	G	F	<0.01	–8.38	–1.19
	G	O	–	–7.82	1.04
	O	F	–	–5.19	2.39
FRL 3	G	F	<0.01	–8.96	–1.40
	G	O	<0.05	–9.67	–0.36
	O	F	–	–4.15	3.82
c–d rc L	G	F	<0.01	–8.48	–1.97
	G	O	<0.01	–10.18	–2.15
	O	F	–	–2.49	4.37

G – patients with glaucoma, males, O – first degree relatives, males, F – healthy population, males

TABLE 5
RESULTS OF TUKEY HSD POST HOC TEST FOR QUANTITATIVE DERMATPGLYPHIC TRAITS FOR ALL EXAMINED GROUPS IN FEMALES

Variable	Groups		p	95% confidence interval for mean	
				Lower bound	Upper bound
FRR 1	G	F	<0.01	–9.10	–1.22
	G	O	–	–8.21	1.17
	O	F	–	–5.58	2.30
FRR 4	G	F	<0,05	–8.12	–0.59
	G	O	–	–3.79	5.18
	O	F	<0,05	–8.82	–1.29
FRR 5	G	F	<0,05	–7.97	–0.49
	G	O	–	–6.71	2.19
	O	F	–	–5.71	1.77
a–b rc R	G	F	<0.01	–6.95	–1.49
	G	O	–	–5.45	1.10
	O	F	–	–4.78	0.72
FRL 4	G	F	<0.05	–8.62	–0.71
	G	O	–	–4.84	4.57
	O	F	<0.05	–8.49	–0.58
FRL 5	G	F	<0.05	–7.72	–0.53
	G	O	–	–3.71	4.84
	O	F	<0.01	–8.29	–1.10
b–c rc L	G	F	<0.01	–8.57	–1.67
	G	O	<0.01	–9,46	–1.24
	O	F	–	–3.22	3.68
c–d rc L	G	F	<0.05	–7.74	0.42
	G	O	<0.01	–10.36	–1.64
	O	F	–	–1.74	5.58

G – patients with glaucoma, females, O – first degree relatives, females, F – healthy population, females

Discussion

Glaucoma is the second leading cause of blindness in the world after cataract. Quigley's report[16] from 1996 has pointed out that 66.8 million patients in the world are affected by primary glaucoma, while the World Health Organization has mentioned that there are 105 million glaucoma suspects in the world and 6.7 million patients affected with a primary glaucoma suffer from bilateral blindness. Recent studies[16] have showed that 7.6 million patients suffer from bilateral blindness and that blindness was caused by primary glaucomas. Etiopathogenesis of glaucoma remains unclear, although findings on the hereditary base of this disease have greatly facilitated its understanding[17]. The discovery of specific gene loci responsible for predisposition to glaucoma has confirmed the family occurrence of the disease[5,6]. Various epidemiological studies have confirmed family occurrence of this disease and the positive family history as a relevant risk factor for its appearance.

Many authors successfully applied dermatoglyphics of digito-palmar complex to estimate the hereditary base of some common malignant diseases: Basauri et al.[18] and Croatian authors, Rudan et al.[19], and Miličić et al.[20] analyzed quantitative traits of breast cancer, leiomyomas and fibromyomas uteri, cervical cancer, colorectal cancer, and cancer of the thyroid gland. Živanović-Posilović et al.[21] studied quantitative traits in patients with gastric cancer, and Rudić[22] performed similar analysis in patients with larynx cancer.

Since dermatoglyphs are considered to show changes in the early embryonic development, their analysis may be used in the etiologic research of some other diseases for which there has been a doubt that have a genetic predisposition. Šupe et al.[23] examined patients with multiple sclerosis, Jelovac et al.[24] patients with bipolar disorder and schizophrenia. Miličić et al.[25] examined autistic children etc. All these authors found the difference between the group of patients suffering from different type of disease and control groups.

In this analysis, lower number of ridges on fingers was observed for the group of patients affected by POAG in males and females, while greater number of ridges has been noticed at members of their families, and the greatest number has been found in phenotypically healthy population for most variables of fingers and palms. While variables of fingers are considered to have a significant hereditary impact, for variables of the palms it may be said that are influenced by environmental factors, too, but only during the short intrauterine period of life[26]. In males, the number of ridges on the position a–b is more under the influence of environmental factors, than the number of ridges on other positions on the palm. With females, phonotypical expression of the number of ridges in all three interdigital areas on the palm has stronger hereditary component[27].

In groups of male individuals who were examined, there has been statistically significant difference between those affected by the disease and phenotypically healthy population, as well as between family members of those affected by the disease and phenotypically healthy population on FRR1, FRR 5, while on FRR3, FRL 3, a–b arc, c–d arc L there has been a statistically significant difference between patients and phenotypically healthy population. In groups of examined females, it has been noticed that statistically significant differences exist between those affected by the disease and phenotypically healthy population, as well as between family members and phenotypically healthy population on FRR1, FRR4, FRR5, FRL4 and FRL5. These details have confirmed that both males and females with POAG and members of their immediate relatives (unaffected people with at least two POAG affected family members), have significant differences in quantitative traits of dermatoglyphs in comparison to phenotypically healthy population. The results have confirmed a link between digito-palmar dermatoglyphs in patients affected by POAG and traits of dermatoglyphs of their immediate non-affected relatives. We have also determin-

ed the difference, which may discriminate patients from phenotypically healthy population. Although it can be proposed that members of the same family are more similar to each other than to the rest of the population due to certain amount of shared DNA, there is still statistically much lower number of ridges on some finger and palm dermatoglyphic variables, which shows that they are different from healthy population.

The results of this study have mostly confirmed hereditary predisposition of POAG and the relevance of hereditary factors in the etiopatogenesis of this disease. Differences that have been noticed between males and females have confirmed that females more slowly react to environmental factors and thus show greater genetic impact and »selective inertia« on changes[28].

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ANALIZA KVANTITATIVNIH SVOJSTAVA DERMATOGLIFA DIGITOPALMARNOG KOMPLEKSA U BOLESNIKA S PRIMARNIM GLAUKOMOM OTVORENOG KUTA

SAŽETAK

Članovi uže obitelji bolesnika od primarnog glaukoma otvorenog kuta, za koji se zna da imaju nasljednu predispoziciju mogli bi biti nosioci promjena u svojstvima dermatoglifa digito-palmarnog kompleksa budući da se trabekularna mreža razvija u isto vrijeme i iz iste zametne osnove kao i dermatoglifi koji su visoko nasljedna svojstva. Tako su postavljeni ciljevi rada: utvrditi da li postoje razlike u kvantitativnim svojstvima dermatoglifa digito-palmarnog kompleksa između bolesnika od glaukoma i fenotipski zdrave populacije te utvrditi da li njihovi članovi obitelji imaju ta ista svojstva dermatoglifa. U radu su proučavana kvantitativna svojstva dermatoglifa kod bolesnika oboljelih od glaukoma, članova njihove uže obitelji te fenotipski zdrave populacije. Za analizu je korištena deskriptivna statistika, univarijatna analiza varijance (ANOVA) i post hoc (Tukey HSD) metoda. Iz dobivenih rezultata utvrdila se povezanost kvantitativnih svojstava dermatoglifa digito-palmarnog kompleksa kod bolesnika sa svojstvima kod bližih neoboljelih srodnika kao i razlika po kojoj se oboljeli i njihovi bliži srodnici mogu diskriminirati od fenotipski zdrave populacije. Rezultati studije objektiviziraju u većoj mjeri obiteljsku predispoziciju za razvoj primarnog glaukoma otvorenog kuta tj. ukazuju na važnost nasljednih čimbenika u etiopatogenezi ove bolesti.