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Qualitative Analysis of Dermatoglyphics of the Digito-Palmar Complex in Children with Severe Recessive Perceptively Impaired Hearing

Nada Šikić¹, Jasna Miličić², Anđelko Vrca³, Adinda Dulčić⁴ and Nađa Runjić⁴

¹ Croatian Pension Insurance Institute, Zagreb, Croatia

² Institute for Anthropological Research, Zagreb, Croatia

³ Department of Neurology, University Hospital Dubrava, Croatia

⁴ Polyclinic SUVAG, Zagreb, Croatia

ABSTRACT

The possible hereditary indicated differences in the ascending family tree was investigated in children with severe recessive perceptively impaired hearing, their parents, and healthy controls, using qualitative analysis of dermatoglyphics of the digito-palmar complex. The χ^2 test was performed and biological distance was investigated by means according to Hiernaux Δg methods, and presented using Ward's method for the examined groups. The results show that the healthy control group differs from the groups of boys and girls with impaired hearing and also from their fathers mostly in palmar variables. The mothers were biologically more distant from the examined groups of patients, and more similar to the control group of randomly selected healthy female controls. The results indicate polygenic inheritance of sporadic sensoneurial hearing loss.

Key words: qualitative analysis, dermatoglyphics of the digito-palmar complex, recessive impaired hearing, heredity

Introduction

Recessive sensorineural impaired hearing results from damage to the inner ear or the auditory nerve. The most common type is caused by the outer hair cells not functioning correctly. The person has trouble hearing clearly, understanding speech, and interpreting various sounds. This type of hearing loss is permanent. Recessive perceptively impaired hearing is genetically determined. The responsible gene or genes have been confirmed in the studies of other investigators¹. Dermatoglyphs are cutaneous ridges on fingers, palms and soles, formed in the course of early intrauterine life, from the 7th to the 21st week. During this period genetic and environmental factors have a chance to greatly influence their formation. Therefore dermatoglyphs are used as easily accessible in the study of genetically influenced diseases. The studies of inheritance of dermatoglyphics are based on the polygenetically determined and are probably under the total effect of a larger number of non-dominant genes^{2,3}. As it has been proved that a great number of dermatoglyphic traits have a hereditary base, their analysis was used for the examination of diseases with unknown aetiology. The dermatoglyphic analysis of the digito-palmar complex ware used for some time to observe differences in the patterns of fingers and palms in persons with diseases with predicted hereditary transmission (insufficient mental development^{4,5}, breast carcinoma⁶, multiple sclerosis⁷, autism⁸, other mental disorders^{9,10,11} etc.) from groups of healthy, randomly selected controls. For this reason we have attempted to use this method to differentiate boys and girls with impaired hearing and also to determine differences in the ascending family tree.

The aim of this study was to analyze the qualitative dermatoglyphic traits in boys and girls with impaired hearing and their mothers and fathers in order to find the possible differences between the affected and their parents as well as with the healthy control groups.

Material and Methods

Subjects

All the subjects included in this investigation were diagnostically treated and rehabilitation carried out in the Polyclinic for Rehabilitation of Hearing and Speech

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SUVAG, Zagreb, during the period 2001–2004. The selection of subjects for the group with severely peripherally impaired hearing was based on a detailed family history anamnesis and the following subjects were excluded from the investigation:

- 1. Subjects who had a member of the family with impaired hearing and all subjects with complications during birth or pregnancy, retarded in psychomotor development, past disease or head trauma, and antibiotic therapy which could result in impaired hearing.
- 2. Assessment of psychomotor development of the subjects was performed by a psychologist using psychological tests, depending on the age of the subject. All subjects retarded in psychomotor development were excluded from the investigation.
- 3. All subjects with another focal neurological deficit besides auditory-speech impairment were excluded from the investigation. In this way we separated 54 subjects.

Hearing was examined by an audiologist by means of tonal audiometry and auditory evoked potentials. In this study 51 patients (24 girls and 27 boys) with average trifrequency level above 93 dB were included in the investigation. Mothers (N=40) and fathers (N=28) of children with severe peripherally impaired hearing were also tested for hearing and used as a control group. The healthy control group of subjects included in the investigation of qualitative traits of dermatoglyphics of the digito-palmar complex consisted of 200 males and 200 females) from Zagreb area. For this group the results of qualitative analysis of dermatoglyphics of the digito-palmar complex were obtained from the Institute of Anthropological Research, Zagreb¹².

Methods

Finger and palm prints on both hands were taken by the method of print in colour on paper and analysed by Cummins and Midlo method³. The frequencies of qualitative traits were examined: on fingers ulnar and radial loop, arch, whorl, and on the palm the presence of patterns in II, III, and IV interdigital areas, on thenar and hypothenar, and position of axial triradius »t«. Prints of the fingers and palms were also taken from the other family members. Qualitative analysis of dermatoglyphics of the digito-palmar complex was performed in each investigated groups of subjects^{3,14}. The results obtained were compared with the healthy control group¹².

Data analysis

The relative frequencies of patterns on the fingers and palms for qualitative dermatoglyphics of the digito--palmar complex of the subjects were analysed.

 χ^2 test was used to determine whether significant differences existed between the three examined groups. Hiernaux Dg estimation of biological distances^{15} was used to determine biological differences between the groups, and Ward's method for graphic presentation of examined groups by dendrograms, using Statistica Release 8 progreme.

Results

The relative frequencies of analysed dermatoglyphic traits in the group of boys and girls with severely impaired hearing, their close relatives and healthy controls was presented on the Tables 1 and 2. Table 1 shows the relative frequency of dermatoglyphic patterns on the fingers of girls with severe peripherally impaired hearing,

 TABLE 1

 RELATIVE FREQUENCIES OF DERMATOGLYPHIC PATTERNS ON FINGERS IN GIRLS WITH SEVERE IMPAIRED HEARING (H90), MOTHERS, AND CONTROL FEMALES

Girls H90 N $= 24$					Mothers $N = 40$				Control females $N = 200$			
Right hand	Whorl	Ulnar loop	Radial loop	Arch	Whorl	Ulnar loop	Radial loop	Arch	Whorl	Ulnar loop	Radial loop	Arch
Finger 1	41.67	58.33	0.00	0.00	45.00	55.00	0.00	0.00	45.50	51.50	0.50	2.50
Finger 2	37.50	50.00	0.00	12.50	45.00	37.50	12.50	5.00	38.00	36.50	13.50	12.00
Finger 3	16.67	70.83	4.17	8.33	22.50	75.00	2.50	0.00	18.00	77.00	1.50	3.50
Finger 4	41.67	58.33	0.00	0.00	55.00	45.00	0.00	0.00	50.00	48.00	0.00	2.00
Finger 5	4.17	91.67	4.17	0.00	12.50	87.50	0.00	0.00	15.50	84.00	0.00	0.50
Total Right	28.34	65.83	1.67	4.17	36.00	60.00	3.00	1.00	33.40	59.40	3.10	4.10
Left hand												
Finger 1	37.50	62.50	0.00	0.00	37.50	62.50	0.00	0.00	40.50	54.50	0.50	4.50
Finger 2	41.67	33.33	4.17	20.83	42.50	42.50	10.00	5.00	38.00	32.50	17.50	12.50
Finger 3	25.00	70.83	0.00	4.17	30.00	57.50	5.00	7.50	23.00	70.00	2.00	5.00
Finger 4	29.17	70.83	0.00	0.00	47.50	52.50	0.00	0.00	39.50	58.00	0.00	2.50
Finger 5	4.17	95.83	0.00	0.00	20.00	77.50	0.00	2.50	11.00	87.00	0.00	1.50
Total left	27.50	66.67	0.83	5.00	35.50	58.50	3.00	3.00	30.40	60.40	4.00	5.20
Total	27.92	66.25	1.25	4.59	35.75	59.25	3.00	2.00	31.90	59.90	3.55	4.65

 TABLE 2

 RELATIVE FREQUENCIES OF DERMATOGLYPHIC PATTERNS ON FINGERS IN BOYS WITH SEVERE IMPAIRED HEARING (H90), FA-THERS, AND CONTROL MALES

Boys H90 N = 27						Fathers $N = 28$			Control males N=200			
Right hand	Whorl	Ulnar loop	Radial loop	Arch	Whorl	Ulnar loop	Radial loop	Arch	Whorl	Ulnar loop	Radial loop	Arch
Finger 1	40.74	55.56	0.00	3.70	64.29	32.14	0.00	3.57	54.00	54.00	0.00	1.00
Finger 2	37.04	51.85	11.11	0.00	32.14	42.86	10.71	14.29	40.00	26.00	22.50	11.50
Finger 3	7.41	88.89	0.00	3.70	14.29	67.86	3.57	14.29	23.00	68.00	1.00	8.00
Finger 4	59.26	40.74	0.00	0.00	50.00	42.86	0.00	7.14	57.00	41.00	0.50	1.50
Finger 5	18.52	77.78	0.00	3.70	10.71	85.71	0.00	3.57	22.50	76.00	0.00	1.50
Total Right	32.59	62.96	2.22	2.22	31.43	54.29	2.86	8.57	39.30	51.20	4.80	4.70
Left Hand												
Finger 1	40.74	59.26	0.00	0.00	35.71	60.71	0.00	3.57	37.00	59.00	0.50	3.00
Finger 2	25.93	55.56	11.11	7.41	35.71	57.43	3.57	3.57	32.00	36.50	20.50	11.00
Finger 3	11.11	85.19	0.00	3.70	10.71	85.71	0.00	3.57	18.50	70.50	0.50	10.50
Finger 4	55.56	44.44	0.00	0.00	35.71	60.71	0.00	3.57	42.50	55.00	0.00	2.50
Finger 5	18.52	74.07	0.00	7.41	14.29	85.71	0.00	0.00	12.50	85.00	0.00	2.50
Total left	30.37	63.70	2.22	3.70	26.43	70.05	0.71	2.86	28.60	61.20	4.30	5.90
Total	31.48	63.33	2.22	2.96	28.93	62.17	1.79	5.72	33.95	56.20	4.55	5.30

their mothers and the control group of randomly selected healthy females. Table 2 shows the relative frequency of patterns on the fingers of boys with severe peripherally impaired hearing, their fathers and the control group of randomly selected healthy males.

 χ^2 test analysis of frequencies of dermatoglyphic patterns on the fingers between healthy control group of females and girls with severe peripherally impaired hearing, or their mothers and also the control group of males and boys with severe peripherally impaired hearing, or their fathers is presented on Tables 3. We did not found statistically significant differences of randomly selected

 $\begin{array}{c} \textbf{TABLE 3}\\ \textbf{THE RESULTS OF } \chi^2 \text{ TEST FOR FREQUENCIES OF}\\ \textbf{DERMATOGLYPHIC PATTERNS ON FINGERS} \end{array}$

H 90	Controls/ Boys (H90)	Controls/ Girls (H90)	Controls/ Fathers	Controls/ Mothers
R 1	0.306	0.782	0.147	0.895
R 2	0.016^{*}	0.346	0.186	0.581
R 3	0.152	0.527	0.346	0.773
R 4	0.872	0.497	0.203	0.771
R 5	0.535	0.051	0.260	0.718
Total Right	0.724	0.947	0.843	0.858
L 1	0.852	0.707	0.859	0.649
L 2	0.201	0.313	0.042^{*}	0.265
L 3	0.324	0.995	0.304	0.387
L 4	0.356	0.420	0.582	0.631
L 5	0.275	0.420	0.667	0.319
Total left	0.928	0.944	0.724	0.821
-				

healthy females. In boys with severe peripherally impaired hearing and the control group of males statistically significant difference were obtained on the second finger of the right hand (p<0.02), between their fathers and controls on the second finger of the left hand (p<0.05).

Table 4 show the results of χ^2 test for frequencies of dermatoglyphic patterns between boys with severe peripherally impaired hearing and fathers, and mothers, girls with severe peripherally impaired hearing and fathers, and mothers and between boys and girls with severe peripherally impaired hearing. Statistically signifi-

 $\begin{array}{c} \textbf{TABLE 4} \\ \textbf{THE RESULTS OF } \chi^2 \text{ TEST FOR FREQUENCIES OF} \\ \textbf{DERMATOGLYPHIC PATTERNS ON FINGERS} \end{array}$

	Boys	Boys	Girls	Girls	Girls (H90)
	(H90)	(H90)	(H90)	(H90)	/Boys
	/Fathers	/Mothers	/Fathers	/Mothers	(H90)
R 1	0.366	0.863	0.343	0.977	0.929
R 2	0.403	0.473	0.635	0.292	0.287
R 3	0.360	0.243	0.925	0.504	0.474
R 4	0.783	0.921	0.681	0.753	0.562
R 5	0.877	0.753	0.771	0.626	0.315
Total Right	0.916	0.932	0.872	0.845	0.943
L 1	0.970	0.953	0.989	0.988	0.965
L 2	0.598	0.383	0.168	0.220	0.133
L 3	0.999	0.039^{*}	0.593	0.764	0.536
L 3	0.566	0.865	0.924	0.527	0.270
L 3	0.720	0.713	0.674	0.341	0.202
Total Left	0.932	0.917	0.986	0.917	0.942

cant difference was found in frequencies of patterns only on the third finger of the left hand in boys with severe peripherally impaired hearing compared to their mothers (p < 0.05).

Table 5 shows the frequency of patterns on the palms: in the area of the thenar, hypothenar and interdigital areas II, III and IV in all examined groups.

Table 6 shows the results of χ^2 test for frequencies in palmar traits. The results of the analysis did not show any statistically significant differences between the girls with severe peripherally impaired hearing and the control group of healthy subjects. We found statistically significant differences between the boys with severe peripherally impaired hearing patterns and healthy controls in area III (p<0.001) and IV (p<0.02) on the interdigital area of the right hand, and also in II interdigital area of the left hand (p<0.02). Differences were also found between the control group of healthy subjects and fathers of boys with severe peripherally impaired hearing in the II interdigital area of the left hand (p < 0.02) and IV of the interdigital area on both hands (R p<0.001; L p<0.03). The group of examined mothers differed from the control group in the II interdigital area of the right hand (p < 0.007), in III interdigital area of the left hand (p<0.001), and the IV interdigital area on both hands (R p<0.001: L

TABLE 6 THE RESULTS OF χ^2 TEST FOR THE FREQUENCY OF DERMATOGLYPHIC PATTERNS ON THE PALMS

	Controls/	Controls/	Controls/	Controls/
	Boys $(H90)$	Girls (H90)	Fathers	Mothers
Thenar R	0.653	0.978	0.321	0.107
II Right	0.689	0.203	0.669	0.007**
III Right	0.001***	0.983	0.159	0.591
IV Right	0.015^{*}	0.978	0.001***	0.001***
Hypothenar Right	0.997	0.987	0.617	0.001***
Thenar L	0.228	1.000	0.264	0.035^{*}
II Left	0.018^{*}	0.203	0.020*	0.370
III Left	0.430	0.978	0.641	0.001***
IV Left	0.332	0.985	0.026*	0.001***
Hypothenar Left	0.135	0.985	0.887	0.001***

* p< 0.05, ** p< 0.01, *** p< 0.001

 $p\!<\!0.001),$ on the thenar of the left hand $(p\!<\!0.04)$ and on the hypothenar of both hands (R $p\!<\!0.001$: L $p\!<\!0.001$).

Table 7 shows the relative frequency of positioning of axial triradius on the palms of the girls and boys with se-

TABLE 5	
RELATIVE FREQUENCIES OF DERMATOGLYPHIC PATTERNS ON PALMAR	AREAS

Girls H90 N = 24	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	8.3	0	16.7	8.3	33.3
Left	12.5	0	8.3	20.8	20.8
Total	10.4	0	12.5	14.6	27.05
Boys H90 N = 27	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	11.1	7.4	18.5	22.2	37.0
Left	22.2	7.4	18.5	48.1	48.1
Total	16.7	7.4	18.5	35.2	42.6
Mothers $N = 40$	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	0	2.5	10.0	17.5	37.5
Left	0	0.0	17.5	34.5	47.5
Total	0	1.3	13.8	25.0	42.5
Fathers $N = 28$	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	14.3	3.6	39.3	14.3	32.1
Left	21.4	3.6	21.4	35.7	32.1
Total	17.9	3.6	30.3	25.0	32.1
Control M N=200	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	8.5	5.0	56.5	36.5	32.0
Left	13.5	1.0	24.5	47.0	33.5
Total	11.0	3.5	40.5	41.8	33.0
Control F N=200	Thenar	II interdigital area	III interdigital area	IV interdigital area	Hypothenar
Right	10.5	1.0	25.5	58.0	33.5
Left	8.5	5.5	53.5	47.0	37.0
Total	9.5	3.3	39.5	52.5	35.3

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Girls H90 N = 24	t	ť'	other
Right	54.2	25.0	20.8
Left	45.8	33.3	20.8
Total	50.0	29.2	20.8
Boys H90 N = 27	t	ť	other
Right	51.9	25.9	22.2
Left	40.7	29.6	29.6
Total	46.2	27.8	25.9
Mothers $N = 40$	t	ť	other
Right	75.0	12.5	12.5
Left	62.5	20.0	17.5
Total	68.8	16.3	15.0
Fathers $N = 28$	t	ť'	other
Right	50.0	21.4	28.6
Left	46.4	25.0	28.6
Total	48.2	23.2	28.6
Control M N=200	t	ť'	other
Right	53.0	32.5	14.5
Left	47.0	38.0	15.0
Total	50.0	35.3	14.7
Control F N=200	t	ť'	other
Right	60.0	31.0	9.0
Left	48.5	40.0	11.5
Total	54.2	35.5	10.3

TABLE 7

RELATIVE FREQUENCIES OF POSITIONS OF AXIAL TRIRADIUS

ON PALMS

vere peripherally impaired hearing, their fathers and mothers, and the control groups of both sexes. The χ^2 test is presented in Table 8. The results did not show statistically significant differences in the position of the axial triradius between the control group of healthy subjects and the boys and girls with severe peripherally impaired hearing. However, difference was found between the boys with severe peripherally impaired hear

ing and their mothers in the frequency of t-triradius on both hands (R p<0.02: L p<0.03) and t'-triradius right (p<0.008). Differences were also found for girls with severe peripherally impaired hearing and mothers in the frequency of t'-triradius right (p<0.03) and left (p<0.001). Girls and fathers differ with regard to the position of axial triradius on the left hand (p<0.04). When the results are compared with the control group of healthy subjects only one difference can be found between the healthy male subjects and mothers of boys and girls in the position of axial t'-triradius on both hands (p<0.03).

Hienaux's Δg biological distance was estimated for all fingers and palms of both hands in all subjects and presented in Table 9. Graphic presentation of the obtained values of all examined groups was calculated by means of Ward's method and presented in Figure 1.

From the presented figure it can be seen that the both male and female control group of healthy subjects formed separate dendrogram from the examined groups of boys and girls with severe peripherally impaired hearing and their fathers. Mothers show fewer differences in the

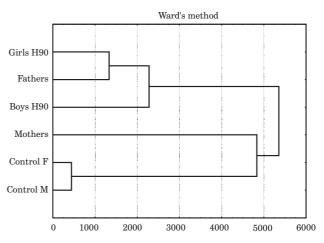


Fig. 1. Graphic presentation of Hiernaux ∆g biological distances for examined groups using Ward's method.

	t Right	t' Right	Other right	t Left	t' Left	Other left
Boys (H90)/ Fathers	0.891	0.937	0.059	0.508	0.485	0.246
Boys (H90)/ Mothers	0.015^{*}	0.001***	0.884	0.030 *	0.365	0.316
Girls (H90)/ Fathers	0.764	1.000	0.036 *	0.312	0.335	0.094
Girls (H90)/ Mothers	0.029*	0.001***	0.825	0.088	0.233	0.756
Girls (H90)/ Boys	0.869	0.940	0.739	0.714	0.776	0.555
Girls (H90)/ Controls	0.990	0.548	0.201	0.949	0.488	0.418
Boys (H90)/ Controls	0.884	0.560	0.501	0.834	0.448	0.125
Mothers/ Controls	0.107	0.029*	0.695	0.149	0.027^{*}	0.432
Fathers/ Controls	0.924	0.334	0.106	0.884	0.339	0.125

TABLE 8 THE χ^2 TEST FOR THE FREQUENCY OF THE POSITION OF AXIAL TRIRADIUS ON THE PALMS

* p< 0.05, ** p< 0.01, *** p< 0.001

	Girls H90	Boys H90	Mothers	Fathers	Control Females	Control Males				
Girls H90	_									
Boys H90	2627.51	-								
Mothers	4119.87	3288.74	-							
Fathers	1333.62	1456.59	4481.64	_						
Control F	3334.61	2474.56	3498.93	2451.66	-					
Control M	3925.37	2880.99	3976.01	2444.55	443.16	_				

occurrence of particular patterns on the fingers and palms in relation to the control group of healthy subjects than the other examined groups.

Discussion

In the present investigation we included the girls and boys with severe peripherally impaired hearing, and their parents to obtain insight into the ascending family tree, and also healthy controls.

From analysis of the data obtained it can be concluded that, the control group of healthy subjects differs from the boys with severe peripherally impaired hearing and also from their fathers only in few variables. Mothers of the girls and boys with severe peripherally impaired hearing do not have dermatoglyphic differences on fingers when compared with the control group of healthy subjects. The only statistically significant difference was found when compared dermatoglyphic patterns on the fingers of boys with severe peripherally impaired hearing, and their healthy mothers.

Analysis of the dermatoglyphic patterns on the palms in boys with severe peripherally impaired hearing and healthy control groups shows differences in III, IV interdigital area right and II left. Their fathers differ with healthy control group in II interdigital area left and IV interdigital area right and left. Arrieta et al.¹⁶ found that in palmar variables in males genetic influence is stronger for a-b and c-d ridge counts, which correspond with interdigital areas II and IV.

Between the mothers of children with severe peripherally impaired hearing and the healthy control group of females we found differences in II, IV interdigital area and hypothenar right and III and IV interdigital area and thenar and hypothenar left.

Using the qualitative analysis of dermatoglyphics of the digito-palmar complex in children with severe perceptively impaired hearing we were not able to clearly differentiate a group of girls because they did not differ statistically significant, from a healthy control group for any of the examined parameters. We did not find statistically significant differences on palms between the girls with severe peripherally impaired hearing and their parents.

By analysing the distances of the examined groups in relation to the control group of randomly selected healthy subjects we concluded that the mothers differ from boys and girls with severe perceptively impaired hearing, and their fathers, and according to the examined traits of the dermatoglyphics of the digito-palmar complex, mothers are more similar to the healthy control group.

This analysis enabled us to determine significant differences with regard to gender, both for children with impaired hearing and their healthy parents. Further investigation should include a quantitative analysis of dermatoglyphics of the digito-palmar complex.

The qualitative dermatoglyphics are more sensitive than quantitative on events which took place during the microevolution of the contemporary populations, and as it was expected from the literature which shows that males are more influenced by environmental factors than females, we found more differences in males. These studies suggest that for successful reproduction, the female phenotype is more canalized and shows greater amonggroup variations than within-group^{17,18}, and the females more represent ancestral population than males^{19,20}.

Analyses of HLA-A24 and HLA-B15 antigen²¹ in patients with sporadic sensorineural hearing loss show statistically significantly less frequency in relation to a healthy control group. In clinical practice to date, the absence of this antigen is not linked with increased risk of the occurrence of sporadic sensorineural hearing loss.

The results indicate polygenic inheritance of sporadic sensorineural hearing loss^{16,21}.

From this and previous analysis²¹ we can conclude that sporadic sensorineural hearing loss indicate polygenic inheritance, and it is more significant in boys. Different genes have been found which are responsible for the occurrence of deafness in certain families²². Modern diagnostic methods, such as genetic testing, will help diminish the number of cases with hearing impairment of unknown etiology, for the benefit of children who receive early and appropriate medical, audiologic, genetic and educational counseling based on the etiology of their hearing²³.

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J. Miličić

Institute for Anthropological Research, Gajeva 32, 10000 Zagreb, Croatia email: jasna.milicic@inantro.hr

KVALITATIVNA ANALIZA DERMATOGLIFA DIGITO-PALMARNOG KOMPLEKSA U DJECE S TEŠKIM RECESIVNIM PERCEPTIVNIM OŠTEĆENJEM SLUHA

SAŽETAK

Kvalitativnom analizom dermatoglifa digito-palmarnog kompleksa u djece s teškim recesivnim perceptivnim oštećenjem sluha, njihovih roditelja i zdrave kontrolne skupine pokušalo se utvrditi postoje li nasljedno indicirane razlike. Koristili smo χ^2 test kako bi utvrdili postojeće razlike te Hiernaux-ovu Δg procjenu bioloških udaljenosti, koju smo grafički prikazali koristeći Wardovu metodu. Iz dobivenih nalaza utvrdili smo da se zdrava kontrolna skupina razlikuje od djece s teškim recesivnim perceptivnim oštećenjem sluha kao i od njihovih očeva, naročito u varijablama dlana. Majke su biološki sličnije kontrolnoj skupini žena nego djeci s teškim recesivnim perceptivnim oštećenjem sluha. Takav nalaz ukazuje na moguće poligenetski uvjetovano nasljeđivanje s većom ekspresijom u muškom spolu.