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AN AETIOLOGICAL STUDY ON 6 TO 14 YEARS-OLD CHILDREN WITH SEVERE VISUAL HANDICAP IN HUNGARY

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A population-based aetiological study was carried out on 6 to 14 years-old severely visually handicapped children in Hungary. Of the 547 recorded cases 491 (90 %) were included in the analysis. Eleven aetiological groups were separated: isolated cataracts (16.7 %), congenital abnormalities of the eye (15.1 %), high myopia ± retinal detachment and other cases (13.4 %), retinopathy of praemature (11.0 %), choroidoretinal degenerations (10.0 %), syndromes (9.6 %), nystagmus and/or hypermetropia (9.0 %), isolated and complicated optic atrophy (6.7 %), postnatal causes (4.9 %), retinoblastoma (1.8 %), praenatal causes (1.8 %). A significantly higher rate of previous induced abortions was found in the group of retinopathy of praemature. Perinatal damage syndrome and Mendelian monogenic defects are the two most common aetiological categories in the origin of severe visual handicaps in Hungary.

INTRODUCTION

In Hungary the recorded prevalence of primary school age (6-14) children with severe isolated visual handcap shows a nearly permanent rate about 0.42 per 1000 (0.40 and 0.45 between 1974 and 1987). However, this figure may be an underestimate of the true prevalence for two reasons: (i) it is lower than the well-established rates (0.5-1.3 per 1000) in industrialised countries /8, 9/ and (ii) the territorial distribution of prevalences shows significant differences /4/. The two highest rates were recorded in Hajdu-Bihar county (0.79 per 1000) and Budapest (0.58 per 1000) where the three institutions of these handicapped children exist while the lowest rate of 0.12 was in

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three territorial units. The difference between the highest and the lowest rate is 6.6-fold. The higher figures may reflect the true prevalence, however, lower figures can be explained mainly by the lack of children with low vision.

The present epidemiological study was undertaken to examine the aetiological factors in severe visual handicaps and to compare, to the extent possible, the results with those of Fraser and Friedmann /5/ in the U.K. The severe visual handicap includes blindness (categories 3,4 and 5 of the WHO /10/) and low vision (categories of 1 and 2 of the WHO /10/). The study samples comprised children from the three educational institutions in which mainly "isolated" visual handicap occurs. Thus, those with multihandicaps, e.g., the combinations of mental retardation and visual handicap were excluded.

MATERIALS AND METHODS

Of 547 recorded 6-14 year-old cases, 491 (89.8 %) were included in the study. The reasons for the exclusions of 56 cases were (i) appropriate ophthalmological data were not available in 33 cases of the Institute of Blind Children, Budapest; (ii) the ophthalmological examination could not be performed due to the lack of cooperation of cases and anesthesia was not allowed (8 cases); (iii) lack of parental permission (2 cases) and (iv) acute illness during the study period (13 cases).

Following initial visits to the institutions, the available personal, medical (mainly ophthalmological) and educational data were obtained and recorded in the individual files of index cases. The technical facilities for the study were then organized. Invitation letters were sent to the parents of cases requesting them to give permission for the examination of cases, to take part personally in the study with the sibs of cases and to bring all available medical documents of cases to us.

In the second stage, cases with low vision from two special schools were examined:

1. Complete ophthalmological examination (E.T.) involving all parts of the eye. Unfortunately, the director of the Institute of Blind Children did not allow the ophthalmological examination within the study. Thus, for these cases only data made available to us were used. It explains some obvious difference in the aetiological categories (Table I).
2. Paediatric examinations (J.K.). There were two main purposes: (i) to separate children with suspected or confirmed syndromes, i.e., multimalformed children with extraocular congenital anomalies; the so-called complicated cases where

TABLE I

The main aetiological groups of severe visual handicaps in the Hungarian and English /5/ study samples

Main aetiological groups	School for children with low vision, Budapest		School for children with low vision, Debrecen		Institute of Blind Children, Budapest		Hungarian cases together		English cases	
	No.	%	No.	%	No.	%	No.	%	No.	%
Choroido-retinal degenerations	26	15.4	19	14.4	4	2.1	49	10.0	116	15.0
Retinoblastoma	0	0.0	0	0.0	9	4.7	9	1.8	43	5.5
Optic atrophy	11	6.5	10	7.6	12	6.3	33	6.7	56	7.2
High myopia ± retinal detachment, etc.	23	13.6	34	25.7	9	4.7	66	13.4	47	6.1
Cataract	33	19.5	21	15.9	28	14.7	82	16.7	107	13.8
CAs of eye	21	12.4	17	12.9	36	18.9	74	15.1	94	12.1
Syndromes	22	13.0	12	9.1	13	6.9	47	9.6.	42	5.4
Nystagmus and/or hypermetropia	17	10.1	11	8.3	16	8.4	44	9.0	-	-
Praenatal agents	1	0.6	2	1.5	6	3.2	9	1.8	17	2.2
Retinopathy of premature	8	4.7	3	2.3	43	22.6	54	11.0	177	22.8
Postnatal causes	7	4.2	3	2.3	14	7.4	24	4.9	77	9.9
Total	169	100.0	132	100.0	190	100.0	491	100.0	776	100.0

ocular defect associated with the symptoms of central nervous system and "isolated" ocular cases; (ii) to refer cases for further necessary special medical (e.g., neurological) or laboratory examinations.

3. Oto-laryngeal and speech examination (G.Sz.) because eye disorders may associate with partial deafness.

4. Anthropometric examinations (M.V.). Body weight, height, head circumference, head maximum length and wideness, cranial index, face length and width, facial index were measured and calculated. (These data are not included in the present paper.)

5. Laboratory examinations. Urine test for aminoacidurias and kidney function, and special examinations (e.g., chromosome) in selected cases.

Participating parents and sibs were also examined by the ophthalmologist. The data of epidemiological questionnaire were obtained through personal interview by social workers and parents were asked to fill in a sociological data sheet.

Further necessary data were obtained by correspondance. In data analysis, 11 aetiological groups were distinguished (L.G.D.).

RESULTS

Overall findings

The percentages of cases with blindness and low vision were 61.3 and 38.7 %, respectively. There is a general male preponderance in the study sample but the sex ratio differs in aetiological groups (Table II). The proportions of low and very low birth weight and preterm births indicate an important role in the origin of some aetiological groups (Table III). The analysis of maternal and paternal age, furthermore, the socioeconomic status of parents did not show significant deviation from the data of population at large. The rate of consanguinity (first cousin) in the parents of cases was 1.9 %.

Aetiological aspects

The distribution of 11 aetiological groups in three institutions is shown in Table I.

The criteria for choroido-retinal degenerations were (i) characteristic ophthalmological findings, e.g., limited peripheral pigmentary change, confirmed to slight "dappling" with limited or no macular change in the type 1 of retinal aplasia /5, 7/, (ii) family history and (iii) case history including the onset of disorder. The proportion of this

TABLE II

Sex ratio and proportion of familial cases and affected sibs

Main aetiological groups	Sex		Sex ratio	Familial (F)	Non-familial (NF)	Ratio (NF/F)	Sibs		Segregation (A/A+N)
	Male	Female					Normal (N)	Affected (A)	
Choroido-retinal degenerations	25	24	0.510	13	36	2.8	49	12	0.20
Retinoblastoma	3	6	0.333	1	8	8.0	3	0	-
Optic atrophy	17	16	0.515	11	22	2.0	24	1	0.04
High myopia ± retinal detachment, etc.	38	28	0.576	21	45	2.1	70	15	0.18
Cataract	45	37	0.549	31	51	1.6	72	9	0.11
CAs of eye	33	41	0.446	13	61	4.7	46	6	0.12
Syndromes	28	19	0.596	4	43	10.8	49	6	0.11
Nystagmus and/or hypermetropia	26	18	0.591	8	36	4.5	51	4	0.07
Praenatal causes	4	5	0.444	0	9	-	15	0	-
Retinopathy of premature	28	26	0.519	4	50	12.5	46	3	0.07
Postnatal causes	15	9	0.625	2	22	11.0	17	0	-
Total	262	229	0.534	108	383	3.5	442	56	0.13

TABLE III

Mean birth weight and gestational week, the rate of low and very low birth, and preterm birth

Main aetiological groups	Average birth weight (g)	<2500 g %	<1500 g %	Average gestation time (week)	<37 week %
Choroido-retinal degenerations	3003	19.2	1.9	39.7	11.5
Retinoblastoma	3350	0.0	0.0	40.2	0.0
Optic atrophy	3076	13.6	0.0	40.2	0.0
High myopia ± retinal detachment, etc.	2718	32.1	13.2	38.2	28.3
Cataract	2821	25.4	6.8	39.2	13.6
CAs of eye	2952	19.1	6.4	39.7	17.8
Syndromes	3153	5.9	2.9	40.2	8.8
Nystagmus and/or hypermetropia	3176	17.6	5.9	40.3	11.8
Praenatal causes	2530	14.3	14.3	39.1	14.3
Retinopathy of premature	1275	94.4	83.8	31.1	89.2
Postnatal causes	3390	0.0	0.0	39.9	0.0
Total	2783	27.3	14.1	38.8	21.8

aetiological group was 10 % however, it is worth stressing here that the majority of cases were diagnosed by the ophthalmological examination within study in the two schools for children with low vision (Table I). The distribution of different types was as follows: retinal aplasia (type I-III) 30; macular lesions ± peripheral involvement, e.g., Stargardt's juvenile macular dystrophy, "central" retinitis pigmentosa, retinitis pigmentosa with macular dystrophy 8; choroideremia 1; choroido-retinal degeneration of uncertain classification 10 cases.

Retinoblastoma was diagnosed in 9 cases, only one was familial.

Optic atrophy is a heterogeneous group; here cases affected with isolated, complicated and perinatal optic atrophy were evaluated. Postnatal and syndromatic cases are classified into other groups. Of 33 cases, 11 isolated familial cases had autosomal dominant origin with a male preponderance.

High myopia ± retinal detachment and other high myopia is again a heterogeneous group. The uncomplicated myopia rarely causes sufficient visual handicap in childhood to necessitate certification as blindness or low vision. About one-third of cases affected with high myopia ± retinal detachment might be the consequence of perinatal damage syndrome. The family history indicated autosomal dominant origin in another one-third. However, the retinal detachment may not occur in all affected members of these families indicating a variable expressivity. Congenital and infantile retinal detachment was diagnosed in 3 cases, pseudoglioma in 2 cases and retinoschisis in 1 case.

The group of cataract includes visual defects of heterogeneous origin, here the isolated cases are evaluated. Complex cases are classified into the congenital abnormality (CA) group while some other cases into the syndrome and praenatal groups, respectively. Of 82 cases, the family history indicated an autosomal dominant origin in 31 cases. An important category was the cataract as a symptom of perinatal damage syndrome including about one-quarter of cases. It explains the low mean birth weight and shorter gestational time

(Table III).

CAs of the eye were diagnosed in 74 cases. Isolated, complex and secondary cases were separated (Table IV). The family history indicated obvious genetic origin only in 13 cases. Buphthalmos of autosomal recessive origin occurred in 6 sibs of cases with healthy parents.

The following syndromes were identified: Marfan 13, different types of oculocutaneus albinism 10 including one Hermansky-Pudlak, neuronal ceroid lipofuscinosis 2, Bardet-Biedl 2, Coats 2, Gillespie (oculo-dento-digital) 2, Lowue 1, Loken-Senior 1, Knobloch 1, galactosemia 1 case. A syndrome could not be identified in 12 multimalformed cases.

Cases affected with nystagmus and/or hypermetropia were classified into one group. Of 44 cases, 23, 8 and 12 had congenital nystagmus, congenital nystagmus and hypermetropia, and hypermetropia, respectively.

Praenatal causes were confirmed only in 9 cases. Congenital rubella syndrome was diagnosed in 3 cases. The component CAs of these cases were (i) cataract, patent ductus arteriosus, microcephaly, (ii) cataract-microphthalmos and partial deafness with seroconversion during pregnancy, (iii) cataract-microphthalmos, patent ductus arteriosus, partial deafness with seroconversion during pregnancy. This praenatal cause was suspected in more cases, however, these did not fit the diagnostic criteria. Congenital toxoplasmosis was diagnosed in 6 cases, mainly on the basis of characteristic ophthalmological finding. The consequence of lues and gonorrhoea were not detected. The role of other teratogenic factors (physical, chemical, occupational, etc) could not be confirmed though all kinds were studied.

One of the most important aetiological groups is retinopathy of premature. (The classification of Fraser and Friedmann /5/ used term retrolental fibroplasia.) These cases do not include other ocular consequences of perinatal damage syndrome (e.g., high myopia $\pm$ retinal detachment, cataract, optic atrophy, buphthalmos). Of 54 cases, birth weight did not exceed 2500 gram in 51 cases (94.4 %) and 1500 gram in 45 cases (83.3 %). The mean birth weight was 1275 gram while the mean gestation

TABLE IV

Distribution of isolated, complex and secondary CA-s of the eye

CA-groups	No.	%	%*
Isolated			
An-microphthalmos	7	9.5	1.4
Buphthalmos	18	24.3	3.7
Ectopic lentis	2	2.7	0.4
Aniridia	2	2.7	0.4
Coloboma	8	10.8	1.6
Cong. corneal distrophy	1	1.4	0.2
Microcornea	1	1.4	0.2
Optic nerve hypoplasia	1	1.4	0.2
Cong. ptosis	3	4.1	0.6
Subtotal	43	58.1	8.8
Complex CAs			
Cataract and microphthalmos	11	14.9	2.2
Cataract and aniridia	5	6.8	1.0
Cataract and coloboma	2	2.7	0.4
Cataract and myopia	4	5.4	0.8
Cataract and ectopia lentis	1	1.4	0.2
Cataract and microcornea	2	2.7	0.4
Microphthalmos and coloboma	3	4.1	0.6
Coloboma and myopia	1	1.4	0.2
Subtotal	29	39.2	5.9
Secondary CAs			
Hydrocephaly	2	2.7	0.4
Total	74	100.0	15.1

*Calculated for the total study sample

time was 31.1 weeks. Thus, the proportion of preterm babies was 89 %. In agreement with these findings, the rate of twins was 13 % instead of expected 2 % based on the Hungarian population figure. Our study showed three interesting correlations.(i) Retinopathy of premature were connected relatively frequently with "CA-association of low birth weight" /3/. (ii) Of 54 cases, 3 had affected sibs. This "familial" cluster may indicate an aetiological role of permanent maternal factors. It is important to know them in order to prevent sib-occurrences. (iii) There was a significantly higher rate of induced abortion in the previous pregnancies of mothers in this aetiological group ($X^2_1 = 4.33$; $p<0.05$) Table V). Another significantly higher rate of induced abortion in previous pregnancies in the group of retinoblastoma was explained by two induced abortions in the familial case. The higher induced abortion rate is a well-known phenomenon after the affected child.

The majority of cases with postnatal origin had optic atrophy. Their aetiological types were: trauma 8, infections 3, uveitis 8, keratitis 1, tumours 4.

DISCUSSION

This first Hungarian population-based epidemiological study designed to detect causes, faced some technical difficulties. (i) The majority of ophthalmologists are satisfied with clinical diagnosis and make no effort to achieve a nosological-aetiological one. (ii) The ophthalmological examination within the study was not allowed in the cases of the Institute of Blind Children (38.7 %), thus only the available ophthalmological data could be evaluated in these cases. (iii) At the time of school age it is difficult to diagnose the primary pathological process due to the progression of the condition and/or medical treatment (e.g., surgery).
However, in general, available previous medical documents helped us to establish the diagnosis of primary disease.

A comparison between the distribution of aetiological groups in the English and Hungarian studies shows a similarity in the

TABLE V

The number of previous and subsequent pregnancy outcomes in the mothers of cases and the proportion of induced abortions

Main aetiological groups	No. of previous pregnancies	Induced abortion		No. of subsequent pregnancies	Induced abortion	
		No.	%		No.	%
Choroido-retinal degenerations	43	10	23.3	43	10	23.3
Retinoblastoma	11	4	36.4	3	2	66.7
Uptic atrophy	21	5	23.8	27	9	33.3
High myopia ± retinal detachment, etc.	63	14	22.2	43	12	27.9
Cataract	33	22	26.5	67	21	31.3
CAs of eyes	53	15	28.3	39	11	28.2
Syndromes	45	7	15.6	33	12	36.4
Nystagmus and/or hypermetropia	63	14	22.2	52	12	23.1
Praenatal causes	15	1	6.7	2	0	0.0
Retinopathy of praemature	95	34	35.8	44	20	45.5
Postnatal causes	15	2	13.3	16	8	50.0
Total	507	128	25.2	369	117	31.7

group of praenatal causes, optic atrophy and choroidoretinal degeneration (in the latter if one excludes cases of the Institute of Blind Children) (Table I). The differences are small in the groups of cataract and CAs of the eye. The deviation in other groups can be explained mainly by the differences of diagnostic criteria and classification.

The purpose of this study was the delineation of causes in the origin of Hungarian childhood visual handicaps. In general, our findings confirm those available in the literature on the aetiology of blindness and low vision in childhood. To our knowledge, our study was the first one which detected the role of previous induced abortion in the origin of retinopathy of praemature. In Hungary the classical D+C method was used for the termination of pregnancy and it may cause cervical insufficiency /1/. The latter may mediate the preterm birth with low birth weight causing a predisposition for this cause of visual handicap. The second case of Knobloch and Layer /6/ syndrome was found in the study sample.

Obviously the two most common general aetiological categories are the perinatal damage syndrome and the monogenic Mendelian inheritance. The former category involved retinopathy of praemature, several cases with high myopia $\pm$ retinal detachment, cataract, optic atrophy, buphthalmos. The existence of latter category could be demonstrated by the pattern of familial cases and the consanguinity. The 1.9 % occurrence of cousin parents is 6-times higher than the general Hungarian figure /2/. Chromosome aberrations were not detected in these children affected with severe isolated visual handicap. The knowledge of causes may help us in the prevention of severe visual handicaps in the future.

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