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Prevalence of minor congenital anomalies in diabetic children

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The prevalence of 52 minor congenital anomalies (MCAs) was determined in 111 children with insulin dependent diabetes mellitus (IDDM), and in 111 healthy matched control subjects. The average MCA per person was 1.60 in diabetic children and 0.86 in the controls ($p < 0.001$). The difference was exclusively due to the significantly higher proportion of subjects with 3 or more MCAs in the diabetic group (27.0 versus 9.9%; $p < 0.001$). No specific MCA characteristic of IDDM was found.

Minor congenital anomalies (MCAs) are infrequent structural variations of no medical or cosmetic importance to the affected person. Their diagnostic value rests in their multiple occurrence in the same individual, which points to a prenatal disturbance of morphogenesis in the broadest sense [7, 9]. This is why the study of MCAs has gained increasing interest in teratogenecity research, in mental disorders, and in syndrome identification.

Here we report on a survey of MCAs in diabetic children.

Subjects and Methods

A total of 111 children (50 girls and 61 boys) with insulin dependent diabetes mellitus (IDDM; type I) of the Paediatric Departments of the County Hospitals Győr and Szombathely, and of the University Medical School, Pécs, were examined. Their age varied from 2 to 18 years; duration, course, and therapy were disregarded in this study. An equal number of healthy controls of the same ethnic origin were consecutively matched to the patients by sex and age.

In each subject the presence or absence of 52 MCAs, listed in Table II, was recorded. The diagnostic criteria of Smith [10], Méhes [7], and Holmes (personal communication) were applied. Where possible, objective measurements were performed with tape and caliper [5, 7]. These were made on both sides of paired organs, but when no significant differences were obtained, only the values of the right side were considered at final evaluation. Two standard deviations above or below the mean were regarded as cut-off points for features that were measured. No distinction between unilateral and bilateral occurrence of qualitative features (simian crease, etc.) was made.

Fisher's exact four-field test was used for statistical analysis.

Results

No major malformations or syndromes associated with an unduly high number of MCAs were found in this material, thus all the 111 pairs of children could be included.

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The proportion of subjects with one or more MCAs was 62.2% among the diabetic children and 50.4% among the controls (Table I). This difference was not significant, because the number of subjects with 1 or 2 MCAs was nearly equal in the two groups. At the same time, the occurrence of 3 or more MCAs was significantly more common among the diabetic children (27.0 *vs* 9.9%). This resulted in a high average MCA per subject ratio of 1.60 among the diabetics, in contrast to the 0.86 value of the healthy controls. Although slightly higher frequencies were found in boys, the sex differences were not significant.

The prevalence of individual MCAs is summarized in Table II. The results were first evaluated for boys and girls separately, but since no significant sex difference was found, only the cumulative data are given. As shown by the figures, nearly all MCAs were somewhat more common in diabetic children. However, only epicanthic folds and diastasis recti were significantly more frequent in IDDM. In addition, a moderate but not significant preponderance in diabetic children of clinodactyly and supernumerary nipple may be mentioned.

Discussion

A significant increase in the prevalence of both major malformations and MCAs in infants of diabetic mothers has been firmly established [3, 6]. This is generally attributed to

Table I

Occurrence of MCAs in diabetic children and in matched controls

No. of MCAs		Diabetic children			Controls		
		Girls n = 50	Boys n = 61	Total n = 111	Girls n = 50	Boys n = 61	Total n = 111
0		22	20	42	28	27	55
1		9	18	27	11	19	30
2		5	7	12	6	9	15
3		4	5	9	5	4	9
4		6	5	11	—	1	1
5		3	3	6	—	1	1
6		1	1	2	—	—	—
7		—	2	2	—	—	—
8		—	—	—	—	—	—
Total affected	n	28	41	69	22	34	56
	%	56.0	67.2	62.2	44.0	55.7	50.4
Subjects with 3 or more MCAs	n	14	16	30	5	6	11
	%	28.0	26.2	27.0[a]	10.0	9.8	9.9
Total No of MCAs		76	102	178[a]	38	58	96
MCA per subject		1.52	1.67	1.60[a]	0.76	0.95	0.86

[a] as compared to controls $p < 0.001$

TABLE II

Occurrence of individual MCAs of different pathogenesis in the children examined

	Diabetic children n = 111	Controls n = 111	
Mild malformations			
Preauricular skin tag	0	1	
Preauricular fistula (sinus)	2	1	
Double whorle of the hair	8	10	
Frontal whorle (upswap) of the hair	5	5	
Bifid uvula	1	1	
Alveolo-buccal frenula	2	0	
Cleft lip microform (lip pits)	0	0	
Bifid xiphoid process/short sternum*	7	2	
Supernumerary nipples	7	3	
Umbilical hernia	4	1	
Inguinal hernia	5	3	
Moderate diastasis recti	10	3	$p < 0.05$
Total mild malformations	51	30	$p < 0.005$
Minor deformations			
Prominent forehead	2	1	
Flat occiput	4	1	
Prominent occiput	4	0	
Primitive shape of the ear	5	1	
Earlobe crease	3	1	
Simian crease	6	3	
Sydney line	1	1	
Single flexion crease on finger 5	0	1	
Clinodactyly	7	2	
Sole crease ("vertical")	6	4	
Total minor deformations	38	15	$p < 0.001$
Minor dysplasias			
Haemangioma	2	2	
Large pigmented naevi	3	3	
Café-au-lait spots	11	6	
Total minor dysplasias	16	11	$p > 0.30$
Minor anomalies (phenogenetic variants)			
Small mandible	3	1	
Extra posterior cervical skin	0	0	
Epicanthus (inner epicanthic folds)	8	1	$p < 0.05$
Upward (mongoloid) slant of the palpebral fissures	7	6	
Downward (antimongoloid) slant	0	1	
Short palpebral fissure*	1	0	
Hypertelorism*	3	1	
Hypotelorism*	2	0	
Ptosis	1	0	
Small ears*	0	0	
Asymmetrical size of the ears*	2	0	
Low-set ears*	6	4	
Severe slanting away of the ear from the eye*	2	2	
Short philtrum*	2	0	
Long philtrum*	1	0	

TABLE II (continued)

	Diabetic children n = 111	Controls n = 111	
Small oral opening*	2	0	
Large tongue	0	0	
High-arched palate	7	3	
Wide-set nipples*	3	5	
Sacral dimple	5	6	
Wide distance between toes 1—2	6	2	
Partial syndactyly of toes 2—3	0	0	
Broad and/or dorsiflected hallux	5	6	
Small, hypoplastic hallux	0	0	
Hypoplastic nails	1	1	
Prominent heel	1	0	
Shawl-like scrotal fold	5	1	
Total phenogenetic variants	73	40	$p < 0.001$

* = based on measurements

the teratogenic effect of the impaired maternal glucose homeostasis. However, except for some dermatoglyphic features [1, 2], the occurrence of malformations and MCAs in diabetic children has not been studied, and it is not known whether a familial increase of these features was associated with IDDM. In other words, it is not clear whether the presence of MCAs, and especially of multiple ones, may reflect a certain predisposition to IDDM, similarly to the preliminary findings obtained in families with childhood malignancy [8].

The present results showed an increased prevalence of multiple MCAs at least in some diabetic children. This was due not only to a higher frequency of extreme variants, minor dysplasias, and deformations, but also to that of "malformation-type" minor anomalies or "mild malformations" such as supernumerary nipples. Could this be confirmed on a larger material, it would be necessary to reconsider our present view on the relation of metabolic disorders to dysmorphology [11]. It should, however, be stressed, that neither a specific individual MCA nor a typical combination characteristic of IDDM was found in this material.

We think that our findings deserve reexamination in other genetic/demographic settings. In particular, detailed family investigations would be needed to determine how far the occurrence of multiple MCAs was related to susceptibility to IDDM, and which individual MCAs or which combinations of them are of predictive or diagnostic significance.

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