Perinatal Determinants Among Children Who Later Develop IDDM

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OBJECTIVE — The aim of this study was to investigate whether children who develop insulin-dependent diabetes mellitus (IDDM) differ in some aspects from a matched control group at the time of birth.

RESEARCH DESIGN AND METHODS — We studied all children who were born in Denmark during the period 1973–1977 and admitted to a Danish hospital with a diagnosis of IDDM during 1978–1989. The study was conducted by combining two nationwide registries, The National Patient Registry and The Birth Registry.

RESULTS — The criteria were fulfilled by 837 children. Data regarding the age of the parents, the number of previous pregnancies of the mother, the month of birth, and the birth weight and length of the children who developed IDDM were compared with the data of an age- and sex-matched control group of 837 children without IDDM. We did not detect any significant differences between the two groups with respect to the parameters studied.

CONCLUSIONS — No differences in perinatal determinants could be demonstrated among Danish children who develop IDDM compared with children without diabetes.

Insulin-dependent diabetes mellitus (IDDM) is an autoimmune disease in which the pancreatic β-cells are destroyed by the immune system. Genetic predisposition as well as environmental factors are believed to be of etiological importance (1). Because IDDM can develop at any age, including in very young children, it seems relevant to investigate whether children who later develop IDDM differ in some aspects from a matched control group at the time of birth. In this study, we investigated the perinatal factors among Danish children who later developed IDDM using a nationwide registry-based method.

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IDDM, insulin-dependent diabetes mellitus; NPR, National Patient Registry; BR, Birth Registry.

RESEARCH DESIGN AND METHODS

— The subjects in this study were people who were born in Denmark between 1 January 1973 and 31 December 1977 and admitted to a hospital in Denmark between 1 January 1978 and 31 December 1989 with a diagnosis of IDDM. It is generally believed that all new cases of IDDM in Denmark, especially among children, are admitted to a hospital. Thus, the group studied consists of all patients who were born in Denmark during 1973–1977 and *1*) developed IDDM during 1978–1989 or *2*) developed IDDM before 1978 but were admitted to a hospital during the period 1978–1989.

The National Patient Registry (NPR) is owned by the Danish Board of Health. The registry was started in 1977 and contains data of all admissions to Danish hospitals with few (and, for this purpose, unimportant) exceptions (2).

The Birth Registry (BR) is also established by the Danish Board of Health and contains data on all the deliveries by women living in Denmark from 1 January 1973 onward (3).

In this study, we aimed to investigate the people fulfilling the two abovementioned criteria by combining these two registries. Initially, the NPR was searched for patients born between 1 January 1973 and 31 December 1977 and hospitalized in a Danish hospital within the period 1978–1989 with a diagnosis of IDDM. These patients were thereafter identified in the BR, from which an age- (same day of birth) and sex-matched control group were randomly drawn. The following data were obtained from the registries:

1. Maternal and paternal (if possible) ages (years) at delivery of child
2. Place and date of birth and sex of the child
3. The number of the mother's previous pregnancies
4. The birth weight (in groups of 250 g) and length (in centimeters) of the child
5. Date and place of first hospitaliza-

tion with a diagnosis of IDDM (diabetes group only).

Those children in the diabetes group who had a mother with IDDM at the time of birth were identified from records from the hospital at which the birth took place.

To assess the validity of the procedure used, we compared the finding of cases in the registries with the actual identifiable hospital records in Roskilde County, which is inhabited by 4.3% of the Danish population. The hospital records were, independent of the registries, searched systematically for patients fulfilling the inclusion criteria. A total of 45 patients were identified, of which six previously had been admitted to a hospital in another county with a diagnosis of IDDM. The search in the registries identified 40 cases from Roskilde County, and 39 of these were included among the 45 patients identified from the hospital records. The six patients previously admitted to a hospital in another county with a diagnosis of IDDM were all identified in the register. The one patient registered as having IDDM who was not identified in the search of hospital records was identified as a 10-year-old boy with weight loss, glucosuria, and hyperglycemia, but who went normoglycemic during hospitalization and was discharged without insulin treatment. As this patient does not fulfill the conventional criteria for IDDM, the ascertainment in this random sample of the population studied was 97.8%.

Statistical analysis

The Mann-Whitney *U* test was used to compare the two groups for shifts in the distributions of maternal and paternal ages, birth weight and length, and the number of previous pregnancies. The Kolmogorov-Smirnov two-sample test was used to compare the shape of these distributions. The χ^2 test was used to compare the month-of-birth distributions.

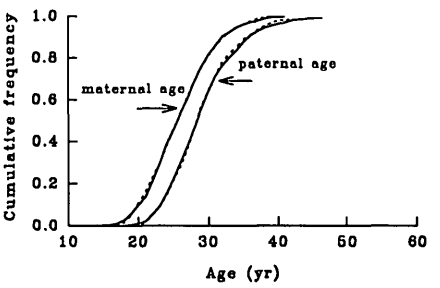

Figure 1—*Parents' ages at delivery of children in the diabetes group (———) and in the control group (• • •).*

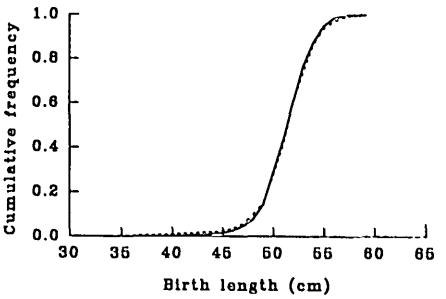

Figure 3—*Birth length among children who later developed IDDM (———) and among children in the control group (• • •).*

Ethics

The study was approved by the Danish Board of Health and the Danish Data Surveillance Agency.

RESULTS— The patient group consisted of 837 patients (451 boys and 386 girls).

Figure 1 shows the age of the parents at the delivery of the child. The average age of the mothers in the diabetes group was 26.4 ± 4.8 years (14–45) [means ± SD (range)] compared with 26.4 ± 4.7 years (16–42) in the control group (z = 0.22, P = 0.83). The age of the fathers was 29.6 ± 5.3 years (18–56) in the diabetes group (n = 692) compared with 29.5 ± 5.0 years in the control group (n = 714, z = 0.14, P = 0.89).

The distributions of the weight and length data are shown in Figs. 2 and 3. The mean weight and length at birth among the children in the diabetes group was 3,381 ± 536 g (880–5,130) and 51.8 ± 2.6 cm (29–60), respectively. The corresponding values in the control group were 3,351 ± 602 g (880–5,130) and 51.7 ± 3.0 cm (35–61). Neither statistically significant differences were found between median birth weight (z = 0.59, P = 0.55) or birth length (z = 0.03, P = 0.97) nor any significant difference among the birth weight (P = 0.98) or length (P = 0.90) distributions in the two groups.

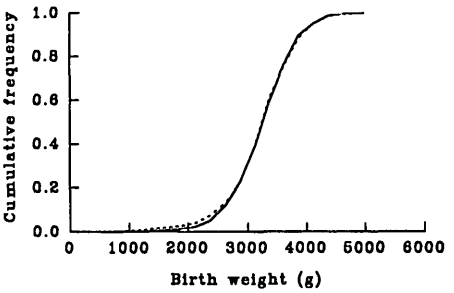

Figure 2—*Birth weight among children who later developed IDDM (———) and among the children in the control group (• • •).*

The group of children in the diabetes group who had a mother with IDDM at the time of birth (n = 17; 7 boys and 10 girls) were excluded from these calculations. The birth weight in this group was 3,144 ± 742 g (1,630–4,630), which was not significantly different from the rest of the diabetes group (z = 1.64, P = 0.10). The birth length was 49.7 ± 2.7 cm, which was significantly less than the rest of the diabetes group (z = 3.2, P = 0.0013).

The distributions of the number of previous pregnancies of the mothers (Table 1) in the diabetes group and in the control group did not differ significantly.

Figure 4 shows the month-of-birth distribution among the children who developed IDDM compared with the expected pattern according to the distribution of the total numbers of deliveries in Denmark during the same months (4). No statistically significant differences were found between the distributions in boys ($\chi^2$2 = 13.4, P = 0.28), in girls ($\chi^2$2

Table 1—*Number of previous pregnancies of the mothers in the two groups*

Number of pregnancies	Diabetes group	Control group
0	293	301
1	286	287
2	149	160
3	74	54
4	25	25
5	6	7
6	3	2
7	1	1
Total	837	837

= 10.2, $P = 0.51$), or for groups combined ($\chi^2 2 = 12.5$, $P = 0.33$). We also did not detect any significant differences when grouping the time of births into four seasons (winter being December-February) between the observed and expected values among the boys ($\chi^2 3 = 1.4$, $P = 0.68$), the girls ($\chi^2 3 = 2.6$, $P = 0.45$), or for the two sexes combined ($\chi^2 3 = 1.4$, $P = 0.71$).

CONCLUSIONS— Previous studies have reported a higher birth weight among children who later developed IDDM (5). In this study, we found no increased birth weight or birth length among these children, which is in agreement with other Scandinavian reports (6–9). The 17 children in the diabetes group who had a mother with IDDM at the time of delivery were significantly shorter than the rest of the diabetes group but were of normal weight, presumably reflecting carefully monitored pregnancies.

A higher maternal age (at delivery) among mothers of patients with IDDM has been suggested (6,10–12). Like Kyvik et al. (9), we did not detect any significant difference in maternal or paternal age among the two groups. The reason for these apparently different results is unknown. Based on the results so far reported, however, it seems reasonable to consider geographical, socioeconomic, racial, and methodological differences as possible explanations.

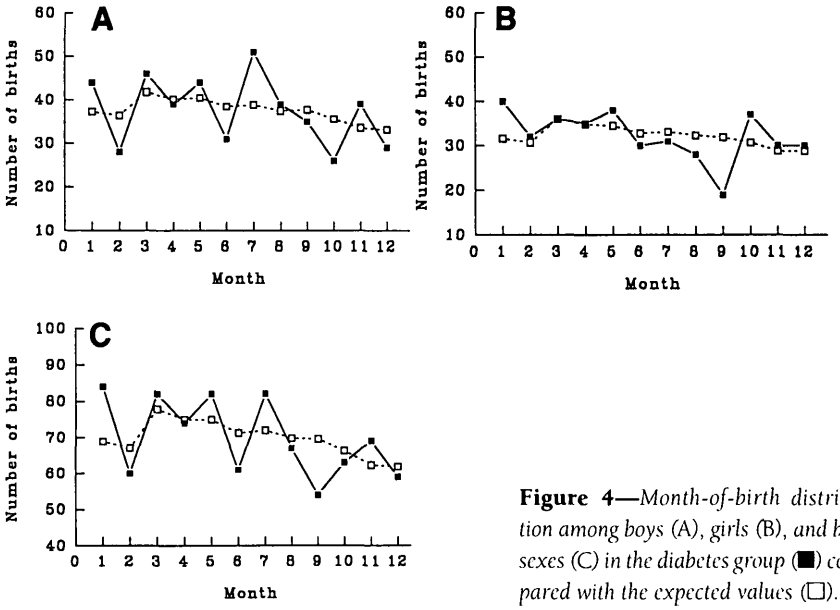

Figure 4—*Month-of-birth distribution among boys (A), girls (B), and both sexes (C) in the diabetes group (■) compared with the expected values (□).*

In this study, we found no relationship between the number of the mother's previous pregnancies and the risk for IDDM of the offspring. Other investigators have reported a birth order effect on the incidence of IDDM (11,13–15). Because the birth order was not a parameter in the BR from the start of the registry (but was included later), we were not able to investigate whether these observations could be confirmed in Danish material.

Previous studies have suggested a relationship between the month of birth and the risk of developing IDDM (16,17). We did not find any difference in the month-of-birth distribution between the two groups.

As previously described, the investigated individuals in this study were children born in Denmark between 1973 and 1977 who had a diagnosis of IDDM before or during hospitalization in Denmark in the period of 1978–1989. One of the strengths when using the present design of this nationwide study is the very high contribution rate, the accurately matched control group, and the well-defined total population. Furthermore, the obtained data, e.g., birth weight, are those originally noted by the medical staff at the hospital or birth clinic. The two nationwide registries used to investigate the perinatal conditions in this study are, as mentioned, rather new in their present forms. We believe that these registries will be very useful for further investigations of epidemiological aspects of IDDM in the future.

In conclusion, we did not detect any significant differences among 837 children who later developed IDDM compared with a matched control group of 837 children with regard to birth weight and length, parents' ages, number of previous pregnancies of the mother, or the month-of-birth distribution.

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