Increasing incidence of coeliac disease in Sweden

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Abstract

Changes in the incidence of coeliac disease was studied among children born in Göteborg, Sweden, between 1970 and 1988. A total of 188 patients with coeliac disease were found. Of these, 83% were less than 2 years old at the time of their first duodenal biopsy and 74% of them have so far been verified according to the criteria of the European Society for Gastroenterology and Nutrition (ESPGAN). The cumulative incidence at 2 years of age/1000 liveborn infants increased significantly from 0.31 in the first birth cohort to 2.93 in the last. This increase could only partly be explained by improvements in detection. Weight for age at diagnosis was generally considerably below the reference value, but was slightly less affected towards the end of the period. The increase in incidence of coeliac disease is the first reported since the middle 1970s and makes the disease one of the most common chronic diseases among Swedish children.

Since the middle of the 1970s, coeliac disease in childhood has been reported to be decreasing in England,¹⁻⁴ Scotland,⁵ and Ireland.⁶ The incidence and clinical picture have remained unchanged in Italy.⁷ In Finland a decrease in the number of cases diagnosed, together with a changing clinical pattern of a late start and mild course, led to the conclusion that the real incidence was probably unchanged.⁸

In this study we report the changes in the incidence of childhood coeliac disease during the last 20 years in Göteborg, the second largest city in Sweden, which had 435 842 inhabitants in 1979 (the middle of the study period) and a computer based population register. The city, like Sweden in general, has a comprehensive child health service with child health centres attended by 98% of all infants and young children.⁹

Patients and methods

All children with coeliac disease who were attending the Department of Paediatrics, University of Gothenburg, at East Hospital, Göteborg, Sweden were investigated retrospectively. The hospital has the only paediatric department in the city and is the only place where small intestinal biopsy is done. All children with coeliac disease born between 1970 and 1988 were identified. Those born outside the city were excluded. The starting year 1970 was chosen because small intestinal biopsy was not a routine investigation before that.

To confirm the diagnosis of coeliac disease, at least three small intestinal biopsy specimens

were taken when the child was eating different diets according to the criteria of the European Society for Gastroenterology and Nutrition (ESPGAN).^{10 11} Four children, born in 1971, 1972, 1973, and 1980 (the first of them being more than 2 years old at the time of the first small intestinal biopsy) were regarded as verified according to the ESPGAN criteria, although they had not had a small intestinal biopsy specimen taken while on a gluten free diet. Children with typical symptoms, an initial flat mucosa, and a distinct clinical response to a gluten free diet but who had not yet fulfilled all the criteria, were also included in the study. Children with suspected coeliac disease but with a less convincing clinical course or histopathological changes were excluded.

The small intestine was biopsied under fluoroscopic control with a Watson capsule, paediatric size. The histopathological picture was classified according to a five point scale by a pathologist who specialised in gastroenterological pathology.¹²

The age at diagnosis, defined as the time of the first small intestinal biopsy, was determined. Cases diagnosed before the age of 2 years were identified. The number in each birth cohort was divided by the number of liveborn infants in Göteborg of that year, giving the cumulative incidence at the age of 2 years for each birth cohort. For each patient who was less than 2 years old at the time of diagnosis, the weight for age at the first biopsy expressed as SD scores of the reference population was calculated.¹³ Weight for age, onset of symptoms, and time from onset to diagnosis, were consecutively recorded and extracted.

To analyse the significance of differences between proportions we used the χ^2 test. Linear regression was used to assess time trends.

Results

Altogether 188 children with coeliac disease born between 1970 and 1988 were investigated and treated at the department of paediatrics up to 1 June 1990. Of the total, 134 (71%) have been verified according to the ESPGAN criteria.^{10 11}

Between 1971 and 1975, a mean of five new cases of coeliac disease were diagnosed each year. This number increased to 18 for the years 1985-9 (fig 1). At the time of diagnosis 156 children (83%) were less than 2 years old. Of these, 116 (74%) have been verified according to the ESPGAN criteria so far (table). Only 10 of the 188 children (5%) were more than 7 years old. Between 1970 and 1977 only children less than 2 years old were diagnosed as having coeliac dis-

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Figure 1 New cases of coeliac disease by age group and year of first small intestinal biopsy.

Number of patients and cumulative incidence of coeliac disease at 2 years of age/1000 liveborn infants

Year of birth	Total No	Verified according to ESPGAN criteria	Two small intestinal biopsy specimens taken	One small intestinal biopsy specimen taken	Cumulative incidence
1970	2	2	0	0	0.31
1971	4	3	0	1	0.60
1972	9	8	0	1	1.44
1973	6	5	0	1	1.01
1974	4	4	0	0	0.67
1975	3	3	0	0	0.54
1976	8	7	0	1	1.53
1977	10	10	0	0	1.96
1978	5	5	0	0	1.02
1979	6	4	2	0	1.18
1980	5	3	1	1	0.99
1981	6	4	0	2	1.22
1982	8	8	0	0	1.57
1983	10	10	0	0	2.06
1984	8	7	0	1	1.54
1985	17	15	2	0	3.19
1986	14	9	2	3	2.58
1987	13	7	4	2	2.21
1988	18	2	6	10	2.93
Total	156	116	17	23	

ease. Not until 1979 was the diagnosis applied to children over 7 years of age (fig 1). Of the 188 patients, 131 (70%) were girls, which is significantly more than the expected number ($p<0.001$). The preponderance of girls did not change during the period of investigation.

The cumulative incidence at 2 years of age for each birth cohort increased from 0.31/1000 liveborn infants in 1970 to 2.93/1000 in 1988 (table, fig 2). The last figure is a minimum, because

not all children in the last cohort had reached the age of 2 years by the end of the study period. A linear regression was fitted to the data. The regression (b), that is the average yearly increase, was 0.12/1000/year ($p<0.0001$, SE 0.02).

In the group in which coeliac disease had been diagnosed before the age of 2 years, the age at the onset of symptoms increased from a mean

Figure 2 Cumulative incidence of coeliac disease at 2 years of age/1000 liveborn infants by birth cohort.

Figure 3 Weight attained at the time of first small intestinal biopsy in children with coeliac disease <2 years of age related to their birth year.

Figure 4 Age at diagnosis of coeliac disease related to birth cohort (fields within oblique lines) and year of diagnosis. Solid circles indicate patients with coeliac disease.

of 6.7 months in the first half of the observation period to 8.2 months in the second half ($p < 0.0004$, $b = 0.17$, $SE\ 0.05$).

The age at diagnosis increased from a mean of 12.4 months in the first half of the observation period to 13.4 in the last five months ($p < 0.05$, $b = 0.14$, $SE\ 0.07$). The mean time between onset and diagnosis did not change significantly, being 5.3 months for the whole period.

Weight at the time of diagnosis among children with coeliac disease diagnosed before the age of 2 years was generally far below the reference mean (fig 3). When a linear regression was fitted to the data, a slight but significant increase was found ($p = 0.0001$, $b = 0.06$, $SE\ 0.02$), but variations in weight increased during the second half of the 1980s.

Discussion

We have retrospectively studied the incidence of coeliac disease in birth cohorts born in Göteborg from 1970 to 1988, and found a threefold increase over the period. Of the 188 children studied, 83% were less than 2 years old at the time of the first small intestinal biopsy.

The first Swedish studies of children using the same diagnostic criteria as we used showed an incidence of between 1.02 and 1.16/1000 liveborn infants.^{14 15} Later reports showed that the incidence was unchanged.^{16–18} In another Swedish study 1866 healthy blood donors were tested with antigliadin antibodies and those with increased titres were offered a small intestinal biopsy.¹⁹ An incidence of coeliac disease of 3.7/1000 was found.

In other parts of Europe, coeliac disease was reported to be increasing until the middle of the 1970s.^{1 4 5 7 20 21} This was probably the result

of a more active diagnostic approach, particularly the increased use of small intestinal biopsy in clinical practice. Since the second half of the 1970s, only decreasing^{1–6} or unchanged^{7 8} incidences have been reported, and the figures have varied among populations. Some differences are the result of varying diagnostic criteria, and others of the lack of standardised epidemiological approaches with subsequent difficulties in comparison. Some studies were based on figures without relation to a population.^{4 22}

One important problem of longitudinal epidemiological studies is that of the duration of observation periods of the different birth cohorts (fig 4). To avoid a systematic error with overestimation of the incidence in the older cohorts, it is necessary to maintain the same observation time. A choice must be made between a shorter observation time that will exclude the cases that were diagnosed later, and a longer observation time resulting in a long delay before changes can be identified.

Another problem arises when the total population is divided by the number of cases. The cases must be derived from the birth cohorts which constitute the population at risk. In this study children from the surrounding areas treated in the department, and children who had moved to Göteborg before or after the diagnosis was made, were excluded. Children with coeliac disease who were born in Göteborg but in whom the diagnosis was made after they had moved away from the city were impossible to trace and therefore could not be included in the study. Consequently our cumulative incidence represents a minimum. The number of liveborn children in Göteborg varied between 4845 and 6694/year during the study period.

The migration of the population is yet

another problem in epidemiological studies. The inward migration of cases and population was well controlled in this study. The occurrence of coeliac disease in the population is not likely to differ between the part of the population that stays and the one that migrates out of the city. As we divided the number of cases into the number of liveborn infants, however, and not into the actual number of the cohort who lived in Göteborg, there will be a systematic error that will increase with migration out of the city related to a longer observation time. The number of children with coeliac disease within the birth cohort but in whom the disease was diagnosed after they had moved away from the city will also add to the systematic error with the observation time. There are two ways to adjust for these processes: one is to use a 'life-table' approach, in which the lost part of the cohort is subtracted and the cases are divided into the 'true' denominator. The other approach is to include only the cases in which coeliac disease was diagnosed during a short observation time, for example before 2 years of age, as was done in this study (fig 4). With the last method the problems will be considerably reduced.

Our study is the first to our knowledge to report an increasing incidence in coeliac disease since the beginning of the 1970s. The incidence is one of the highest ever reported, and even higher than those reported from Galway, Ireland 1960–70²³ and from Austria 1969–72,²⁴ making coeliac disease one of the most common of the chronic diseases in Swedish children today.

In the last cohorts a lower proportion of cases have fulfilled the ESPGAN criteria so far. This could not explain the observed increase, however, because the number with transient gluten intolerance is low and has been decreasing in our area, as in other parts of Sweden.¹⁸ In addition, all doubtful cases were excluded from the study.

The increase could consequently not be explained by systematic errors or shortcomings in the methods used. Could it be the result of improved detection? Throughout the study, the same diagnostic criteria were used, and the biopsy specimens were examined by the same two pathologists. The ability to detect and interpret deviations in growth velocity, however, is thought to have improved among physicians and nurses at child health centres. Screening tests for antigliadin antibodies have been in clinical use in the area since the beginning of the 1980s. There is also an increasing awareness of the existence of coeliac disease both among medical staff and the general public. Consequently there has been an increase in the number of small intestinal biopsies done in the department during the study period, and the weight for age at diagnosis has slightly increased (fig 3). All these factors support improved detection as an explanation for the increased incidence. On the other hand, the cases with high weight SD scores could only explain part of the increase (fig 3) and the delay between the onset of symptoms and diagnosis did not change significantly. We also doubt that

a different rate of detection could be the sole reason for the different incidence trends in different countries. This indicates that detection bias could only partly explain the observed increase.

We have found a threefold increase in the incidence of coeliac disease over the last 20 years. Our data indicate that only a small part of this increase may be explained by increased diagnostic activities or improved clinical detection or screening. Other factors that may influence the incidence of coeliac disease, such as feeding patterns and gluten consumption, are currently being investigated.

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