Undiagnosed coeliac disease at age seven: population based prospective birth cohort study

Polly J Bingley, Alistair J K Williams, Alastair J Norcross, D Joe Unsworth, Robert J Lock, Andrew R Ness, Richard W Jones, on behalf of the Avon Longitudinal Study of Parents and Children Study Team

Division of Medicine, University of Bristol, Southmead Hospital, Bristol BS10 5NB
Polly J Bingley
reader
Alistair J K Williams
research associate
Alastair J Norcross
research assistant

Department of Immunology, North Bristol NHS Trust, Southmead Hospital, Bristol BS10 5NB
D Joe Unsworth
consultant immunologist
Robert J Lock
principal clinical scientist

Unit of Paediatric and Perinatal Epidemiology, Division of Child Health, University of Bristol, Bristol BS8 1TQ
Andrew R Ness
deputy director (epidemiology), ALSPAC
Richard W Jones
head of biological collections, ALSPAC

Correspondence to: P J Bingley
polly.bingley@ bristol.ac.uk

Coeliac disease is uncommon in childhood and diagnosed in fewer than 1 in 2500 children in the United Kingdom.[1] Subclinical disease is, however, common in adults, and can be detected by testing for serum IgA antiendomysial antibodies (IgA-EMA).[2] We aimed to establish the prevalence of undiagnosed coeliac disease in the general population at age seven, and to look for associated clinical features.

Participants, methods, and results

We studied children aged 7.5 years participating in the Avon Longitudinal Study of Parents and Children (ALSPAC), a population based birth cohort study established in 1990.[3] Two stage screening included a sensitive initial radioimmunoassay for antibodies to tissue transglutaminase (endomysial antigen) with further testing of positive samples for IgA-EMA by indirect immunofluorescence.[4] Children with tTG antibodies below the 97.5th centile were defined as antibody negative. Height, weight, and haemoglobin levels were measured at dedicated study clinics. Details of gastrointestinal symptoms and special diets were collected by routine questionnaire at age 6.75 years.

Of 5470 children tested, 54 tested positive for IgA-EMA (1.0%; 95% confidence interval 0.8 to 1.4). IgA-EMA were more common in girls (odds ratio 2.12; 1.20 to 3.75). IgA-EMA positive children were shorter and weighed less than those who tested negative for tTG antibody (P<0.0001 for all comparisons). 4324 (79%) returned questionnaires, and 50% of IgA-EMA positive children reported diarrhoea compared with 34% of tTG antibody negative (odds ratio 1.96; 1.06 to 3.59). Only one IgA-EMA positive child had consulted a doctor about diarrhoea. There was no overall difference in the number of episodes of diarrhoea. Vomiting, abdominal pain, and constipation were not associated with EMA, but more IgA-EMA positive children reported multiple symptoms. Only four children (0.09%; 0.1 to 0.32) were on a gluten-free diet. Of these, three were tTG antibody negative, consistent with effective treatment, and one was IgA-EMA positive (table).

Comment

At age 7, 1% of children were IgA-EMA positive and likely therefore to have subclinical coeliac disease, though less than 0.1% were reported to be on a gluten-free diet. The prevalence of coeliac disease in these children is therefore comparable to that in UK adults.[5] The benefit of early diagnosis of subclinical coeliac disease remains unproven, but long term follow up of this cohort may help to resolve this. If screening is worth while, it should be started in childhood.

Since ALSPAC is an observational study based on analysis of anonymous samples,[3] confirmatory biopsy was not possible. IgA-EMA have however repeatedly been shown to have high sensitivity and specificity for coeliac disease, and in a recent general population study the combination of IgA-EMA and tTG antibodies that we used was associated with diagnostic histological changes in 83% of those subsequently biopsied, with abnormal intestinal γ/δ T-lymphocyte density in a further 12%.[2] Our strategy may even miss some affected children, as individuals with high levels of tTG antibodies without IgA-EMA may have coeliac disease.[2]

Reported clinical features were similar to those in adults with coeliac disease identified by screening.

Coeliac antibody status and height, weight, haemoglobin concentration, and gastrointestinal symptoms. An additional 137 children were tTG antibody positive but IgA-EMA negative

	tTG antibody negative controls	IgA-EMA positive	
	Median (interquartile range) (n=5333 children)	Median (interquartile range) (n=54 children)	P value
Measurements taken at age 7.5 years			
Height (cm)	126 (122.4 to 129.6)	122.1 (118.25 to 125.33)	<0.0001
Weight (kg)	25.2 (22.8 to 28.0)	23.4 (21.35 to 25.4)	<0.0001
Standard deviation score for height	0.23 (−0.43 to 0.88)	−0.53 (−1.01 to −0.00)	<0.0001
Standard deviation score for weight	0.18 (−0.45 to 0.86)	−0.36 (−1.01 to 0.28)	<0.0001
Haemoglobin concentration (g/l)	125 (120 to 130)	123 (118 to 127)	0.062
	No (%) (n=4285 questionnaires)	No (%) (n=42 questionnaires)	Odds ratio (95% CI)
Symptoms reported at age 6.75 years			
Any diarrhoea	1450 (34)	21 (50)	1.96 (1.06 to 3.59)
Any vomiting	1933 (45)	23 (55)	1.47 (0.80 to 2.71)
Any stomach pains	2557 (60)	28 (66)	1.35 (0.71 to 2.57)
Any constipation	435 (10)	6 (14)	1.48 (0.62 to 3.52)
≥3 gastrointestinal symptoms	931 (22)	17 (40)	2.45 (1.33 to 4.5)

Gastrointestinal symptoms were not prominent, and the excess in girls mirrors that seen in affected adults. The most striking observation was that children with IgA-EMA were shorter by more than 0.76 standard deviation scores and lighter by 0.54 standard deviation scores than antibody negative children matched for date and place of birth. This equates to about 9 months' growth and weight gain in an average child around this age. These features were independent of gastrointestinal symptoms and anaemia and presumably unrelated to malabsorption.

Occult coeliac disease seems to start in childhood, even in those who are subsequently diagnosed as adults. The search for the trigger resulting in the breakdown of immune tolerance to gluten therefore needs to focus on infancy and intrauterine life.

1 Hawkes ND, Swift GL, Smith PM, Jenkins HR. Incidence and presentation of coeliac disease in South Glamorgan. *Eur J Gastroenterol Hepatol* 2000;12:345-9.
2 Maki M, Mustalahti K, Kokkonen J, Kulmala P, Haapalahti M, Karttunen T, et al. Prevalence of celiac disease among children in Finland. *N Engl J Med* 2003;348:2517-24.
3 Golding J, Pembrey M, Jones R, ALSPAC study team. ALSPAC: the Avon longitudinal study of parents and children. I. Study methodology. *Paediatr Perinat Epidemiol* 2001;15:74-87.
4 Bazzigaluppi E, Lampasona V, Barera G, Venerando A, Bianchi C, Chiumello G, et al. Comparison of tissue transglutaminase-specific antibody assays with established antibody measurements for coeliac disease. *J Autoimmun* 1999;12:51-6.
5 West J, Logan RF, Hill PG, Lloyd A, Lewis S, Hubbard R, et al. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. *Gut* 2003;52:960-5.

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Use of tobacco products as dentifrice among adolescents in India: questionnaire study

D N Sinha, P C Gupta, M S Pednekar

In India legislation prohibits the use of tobacco as an ingredient in dental care products.[1] Such products, in the form of powder or paste, are applied most commonly with the index finger to teeth and gums. Various tobacco products are used as dentifrice in different parts of India.[2 3] We are not aware of any reports covering such a use of tobacco products (in contrast to chewing and smoking) especially among adolescents.[4 5]

Participants, methods, and results

The global youth tobacco survey focuses on school students aged 13-15 and uses standardised methods.[4] In India the survey is being conducted independently in each state. We report on the prevalence of the use of tobacco products as dentifrice in 14 states listed in the table, with sample sizes ranging from 2067 to 5245 students.

We selected a two stage probability sample of students in grade 8-10 (which corresponds to 13-15 years in age) in each state and conducted a survey among students with an anonymous, self administered, close ended questionnaire. Participants were asked to include a maximum of five products, which could differ from state to state. A pilot tested questionnaire for India contained a specific question on application of tobacco products (in addition to chewing), and a positive response identified the use of a tobacco product as dentifrice. We defined current use as use within 30 days preceding the survey.

The overall response rate was over 80% except in Bihar (70%) and Maharashtra (79%). The proportion of boys was between 50% and 55% in the different states.

The use of tobacco products as dentifrice varied from 6% (Goa) to 68% (Bihar). The prevalence among boys was notably higher than among girls in Orissa and Uttaranchal, marginally higher in nine states, and marginally lower in three states. Of the specific products, tobacco toothpaste (creamy snuff) and tooth powder (*lal dant manjan*) were common in all states (table). *Gul* (a pyrolysed tobacco product) was used in eight states. Other dentifrice products containing tobacco were: *mishri* (roasted and powdered tobacco) and dry snuff (*bajjar* or *tapkir*) in Goa and Maharashtra; *gudakhu* (paste of tobacco and molasses) in Bihar, Orissa, Uttar Pradesh, and Uttaranchal; and tobacco water (*tuibur* or *hidakphu*, manufactured by passing tobacco smoke through water) in Manipur, Mizoram, Sikkim, and Tripura. It is used for gargling, not drinking.

Comment

Many students in India use tobacco products as dentifrice. Differences between the sexes were minimal and similar to those reported globally.[5]

In India the misconception is widespread that tobacco is good for the teeth. In a study reported from Ernakulam district in Kerala 92% (3013) of 3261 female

School of Preventive Oncology, A127 Anandpuri, Boring Canal Road, Patna 800001, India
D N Sinha
chairman

Tata Institute of Fundamental Research, Homi Bhabha Road, Colaba, Mumbai 400 005, India
P C Gupta
senior research scientist

Epidemiology Research Centre, Tata Memorial Centre, Ernest Borges Marg, Parel, Mumbai 400012, India
M S Pednekar
senior statistician

Correspondence to: P C Gupta
pcgupta@tifr.res.in