Paediatric studies	
Bibliographic reference	Alehan, F., Ozcay, F., Erol, I., Canan, O., and Cemil, T. Increased risk for coeliac disease in paediatric patients with migraine. 2008. Cephalalgia 28(9), 945-949. 2008.
quality	NICE case-control quality checklist
	 The study addresses an appropriate and clearly focused question? Yes, question clear Cases and controls from comparable populations? Same exclusion criteria used for both cases and controls? What was participation rate for each group? Cases: controls: N/A; all blood tested. Participants and non-participants are compared to establish their similarities or differences? Yes; baseline characteristics the same between groups. Cases are clearly defined and differentiated from controls: cases are defined in terms of seropositivity, seropositive confirmed with biopsy It is clearly established that controls are not cases? Clear in the fact that cases are seronegative, however this was not confirmed by biopsy Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? Yes, no person was to have had previous suspicion of CD or previous duodenal biopsy Exposure status is measured in a standard, valid, and reliable way? Yes; serological testing for CD was standard Main potential confounders are identified and taken into account in the design and analysis? Only single predictive factor considered other factors not taken into consideration Have confidence intervals been provided? No; calculated from raw data
Study aim and type	To determine the prevalence of coeliac disease in paediatric patients with migraine UK
Patient characteristics	 Study Population: attending child neurology outpatient clinic; May 2004 to January 2006 Control Population: with minor respiratory illness, no history of recurrent headache or gastrointestinal problems N=73, study group; n=41 female, age 12.01±3.07yrs, n=30 had migraine with aura N=147, control group; n=85 female, age 11.82±3.25yrs

	Inclusion: fulfilling the criteria for migraine according to the International Headache Society (all examined by the same child neurologist; complete physical and neurological examination; structured interview concerning characteristics of headache Exclusion: previous suspicion of coeliac disease
Sign/Symptom	Migraine
Investigations	 Serum samples for tTGA antibody and IgA analysis assay (Organtec Diagnostica GmbH ORG 540A; cut off level for a positive result, 10U/mL) Positive tTGA – endoscopic duodenal biopsy for confirmation of coeliac disease
Results	All participants and controls had normal serum IgA levels Positive tTGA antibodies; - N=4/73 (5.5%) study group, N=1/147 (0.7%) control group, p=0.043 Biopsy; - N=3/3 study group, all considered to show potential coeliac disease (N=1 in the study group and N=1 in the control group declined a biopsy)
Funding	Research grant from Baskent University
Other comments	

Bibliographic reference	El-Hodhod, M., El-Agouza, I., Abdel-Al, H., Kabil, N., and Bayomi K. Screening for celiac disease in children with dental enamel defects. 763783, 2012
quality	 NICE case-control quality checklist The study addresses an appropriate and clearly focused question? question clear Cases and controls from comparable populations? Yes - matched for baseline characteristics. Same exclusion criteria used for both cases and controls? No - 1482 children presented with DED- not clear why only 140 enrolled in study What was participation rate for each group? All recruited participants from both groups reported to have participated Participants and non-participants are compared to establish their similarities or differences? Yes Cases are clearly defined and differentiated from controls: yes; seropostivity It is clearly established that controls are not cases? Yes, however no biopsy Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? All patients recruited in same way with no prior knowledge of coeliac status Exposure status is measured in a standard, valid, and reliable way? Yes Main potential confounders are identified and taken into account in the design and analysis? No- other factors that contribute to DED I.e diet, socio economic status, not accounted for. Have confidence intervals been provided? No - calculated from raw data
Study aim and type	To detect the frequency of coeliac disease among patients with dental enamel defects Egypt
Patient characteristics	 Study Population: with dental enamel defects, recruited from attendees of general and dentistry paediatric clinics who showed any abnormality in teeth structure or shape Control Population: age and sex matched, recruited among normal children coming for routine check-up in children's hospital in the well child clinic N=140, study group; n=68 (48.6%) female, age range 4-12yrs, mean age 8.33±1.73yrs N=720, control group; n=349 (48.5%) female, age range 4-12yrs Inclusion: with dental enamel defects, aged between 4 and 12yrs

	Exclusion: chronic illness other than gastrointestinal symptoms, on inhalation therapy for bronchial asthma
	NS differences between groups for age or gender. Higher percentage of consanguinity in the study group (42.86%) compared with the control group (23.47%), p<0.0001
Sign/Symptom	Dental enamel defects
Investigations	 Oral examination for hard tissue changes by a paediatric dentist; evaluated under good artificial light using dental mirros, dental probes and sterile gauze without excess drying. Dental examination in accordance with FDI criteria. A single defect measuring less than 1mm in diameter was not recorded. In case of doubt about the existence of a defect it was scored as normal. Opacities were differentiated from white spot carious lesions, based on colour, texture, demarcation, and relationship to gingival margin. The enamel defects affecting deciduous and permanent teeth were graded 0 to IV according to Aine's classification.
	They were followed up for oral hygiene and problematic defects were treated.
	 Coeliac disease; IgA and IgG tTGA; ELISA (Orgentec) According to manufacturer instructions a value above 10U/mL was used as a cutoff value Total serum IgA was measured Positive serology – oesophagogastroduodenoscopy and intestinal biopsy from the second part of the duodenum (minimum 4 biopsies) assessed histopathologically for features of coeliac disease
Results	 (this study included a 1-yr follow-up of dental care and gluten free diet – data not reported in this evidence table) Coeliac disease; Dental enamel defects group, n=25 (17.9%) Control group, n=7 (0.97%)
	 X² 36.95, p<0.0001 Recurrent gastrointestinal symptoms; Dental enamel defects group, n=25 (17.9%) Control group, n=146 (20.3%) NS difference

	Underweight; - Dental enamel defects group, n=45 (32.1%) - Control group, n=41 (5.7%) - X ² 57.94, p<0.0001
Funding	Not reported
Other comments	

Bibliographic reference	Inaloo, S., Dehghani, S. M., Farzadi, F., Haghighat, M., and Imanieh, M. H. A comparative study of celiac disease in children with migraine headache and a normal control group. 20110823. Turkish Journal of Gastroenterology 22(1), 32-35. 2011.
Study aim and type	To assess the prevalence of coeliac disease in children with migraine headache Iran
quality	NICE case-control quality checklist
	 The study addresses an appropriate and clearly focused question? question clear Cases and controls from comparable populations? Yes - matched for baseline characteristics. Same exclusion criteria used for both cases and controls? Unclear; no clear exclusion criteria. Uncelar whether consecutive recruitment What was participation rate for each group? All recruited participants from both groups reported to have participated Participants and non-participants are compared to establish their similarities or differences? Yes Cases are clearly defined and differentiated from controls: yes; seropostivity It is clearly established that controls are not cases? Yes, however no biopsy Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? All patients recruited in same way with no prior knowledge of coeliac status Exposure status is measured in a standard, valid, and reliable way? Yes Main potential confounders are identified and taken into account in the design and analysis? No confounding factors taken into account Have confidence intervals been provided? No - calculated from raw data
Patient characteristics	 Study Population: paediatric neurology clinic Control Population: participating in another study for detection of the prevalence of coeliac disease N=100, study group; n=41 (41%) female, mean age 10.6±2.8yrs, range 5-18yrs, 30% migraine with aura, < x3/mth in 63% of cases, duration 3-72hrs (60% of participants), 75% had a history of migraine headache in first-degree relatives N=1500, control group; n=675 (45%) female, mean age 9.5±1.3yrs Inclusion: diagnosis of migraine according to the HIS criteria

Appendix D: Evidence Tables

Sign/Symptom	Migraine
Investigations	General and neurological physical examinations by paediatric neurologist
	Serum IgA and IgA tTGA (Diagnostocs GmbH), tires above 18U/mL considered to be positive Positive serology – duodenal biopsy, definite diagnosis based on histologic criteria
Results	Positive tTGA antibodies; - N=2/100 study group, N=30/1500 (2%) control group
	Biopsy; - N=2/2 study group – confirmed the diagnosis of coeliac disease
Funding	Not reported
Other comments	