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ORIGINAL ARTICLE

A neglected cause for chronic spontaneous urticaria in children: *Helicobacter pylori*

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Abstract
Background: The aetiology of chronic urticaria is usually considered idiopathic. There is a paucity of research both on the prevalence of *Helicobacter pylori* infection in the aetiology of chronic spontaneous urticaria (CU) in children and also on which patients *H. pylori* should be investigated.
Methods: All paediatric and adult patients who presented to the allergy outpatient clinic due to CU between January 2011 and July 2012 were included in this prospective, randomised study. Stool samples from all patients were examined for the *H. pylori* antigen. Paediatric and adult patients who had a positive stool test for the *H. pylori* antigen were reassessed following eradication therapy.
Results: Thirty-two children with CU and 35 adults with CU were enrolled in the study. Ten of the 32 (31.2%) children and 18 of the 35 (51.4%) adults were *H. pylori* positive ($p = 0.09$). All children with positive-*H. pylori* were older than eight years of age. There was a significant positive correlation between age and the frequency of *H. pylori* infection ($p < 0.001$; $r = 0.61$). The presence of *H. pylori* was not significantly associated with the presence of GI (gastrointestinal) symptoms ($p > 0.05$). Following *H. pylori* eradication, urticarial symptoms recovered in 15 of the adults (83.3%) and 10 of the paediatric (100%) patients ($p = 0.172$).
Conclusion: In the current study we found that *H. pylori* is common among children with CU, particularly after eight years of age. We suggest that CU patients with an unknown aetiology should be routinely screened for *H. pylori* even if they do not present with GI symptoms and that those with *H. pylori*-positive results may receive treatment.

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Introduction

Urticaria is defined as transient, pruritic, variably sized wheals with central pallor and well-defined borders. Urticaria has historically been classified as either acute or chronic based on its duration (acute, lasting fewer than six weeks, and chronic, lasting six or more weeks).[1] While up to 25% of adults are estimated to experience at least one episode of acute urticaria at some time in their lifetime, only around 3% will develop chronic spontaneous urticaria (CU).[2] The prevalence of CU is reported to be around 0.6% in adults.[3] In children, however, urticaria seems to be less common and the incidence of overall childhood urticaria of any form is reported to be around 3.4–5.4%. In the United Kingdom chronic urticaria has been reported to affect 0.1–0.3% of all children.[4]

The aetiology of chronic urticaria is usually considered idiopathic. The rate of children with identified aetiology varies widely, and is reported to be between 21% and 51% [4]. The role of infections in chronic urticaria is well recognised.[5] Data regarding *Helicobacter pylori* infection have primarily been collected from studies conducted on adult chronic urticaria patients. In a recent study, *H. pylori* infection was identified in 22.9% of adult chronic urticaria patients.[6] Studies about the prevalence of *H. pylori* infection among paediatric patients with chronic urticaria, however, are lacking. Current guidelines recommend performing routine blood count, erythrocyte sedimentation rate and C reactive protein testing when screening for CU aetiology and also additional extended parameters including *H. pylori* in patients with clinical suspicion. However, these guidelines do not exactly describe the criteria for clinical suspicion of *H. pylori*, hence leaving a gap of knowledge for the potential patients to be screened for *H. pylori* in the aetiology of CU.[7]

In this study, we aimed to determine the risk factors of *H. pylori* infection and *H. pylori* treatment response in children with CU. We also aimed to determine the prevalence of *H. pylori* infection among children presenting to the paediatric and adult allergy clinics within a given time period and to compare it with the prevalence in the adult population.

Materials and methods

Study subjects

All patients who presented to the paediatric and adult allergy outpatient clinics of Fatih University due to CU between January 2011 and July 2012 were included in this prospective, randomised study. For each children with CU included in the study, we enrolled an adult with CU. Overall 37 children and adults with CU were enrolled. Because five children and two adults did not complete their treatment, they were excluded from the study, leaving 32 children and 35 adults with CU. CU was defined based on the current guideline as urticarial symptoms lasting for six or more weeks.[7] Patients who had any infectious agent (except for *H. pylori*), were excluded from the study. During the study period all adult and paediatric patients with CU were screened for *H. pylori* from stool samples. Self and family history of allergic diseases, the presence of parental consanguinity and gastrointestinal (GI) complaints (epigastric pain, nausea, regurgitation, abdominal distension, etc.) were recorded in paediatric patients. Additionally, extensive aetiological investigations were planned for paediatric patients. Both paediatric and adult patients with a positive stool test for *H. pylori* antigen received eradication therapy [lansoprazole capsules (paediatric dosage 15–30 mg/day; adult dosage 30 mg bid) for 1 month, amoxicillin (paediatric dosage 50 mg/kg/day bid; adult dosage 1 g bid) and 15 mg/kg/day clarithromycin (paediatric dosage 15 mg/kg/day bid; adult dosage 500 mg bid) for 15 days]. All children and adult with CU received oral daily antihistamines (5 mg/day cetirizine or 2.5–5 mg/day desloratadine) for one month. Of these, 11 (4 children and 7 adults) were started on daily oral systemic corticosteroids due to exacerbation of symptoms and were followed by careful dose titration for 3–7 days. Four weeks after the completion of eradication therapy, patients were recalled for control examinations. They were inquired for complaints and retested for *H. pylori* antigen. Remission was defined as being free of symptoms such as wheals and pruritus although not receiving any medical treatment for a minimum of seven consecutive days.[7]

Venous blood samples were collected into Vacuette tubes (Greiner Bio-One, Monroe, NC, USA) and centrifuged at $3000 \times g$ for 15 min at 4 °C. Complete blood count analysis was performed with the LH-780 system (Beckman Coulter Diagnostics, Image 8000, Brea, CA, USA). C reactive protein (CRP) levels were measured by turbidimetric assay method using a Roche P 800 modular system (Hitachi, Tokyo, Japan). Levels of total serum IgE were measured by the ECLIA (electrochemiluminescence immunoassay) method using an ELX-800 system (DIAsource, Nivelles, Belgium). ANA and anti-dsDNA were determined by means of indirect immunofluorescence testing (Euroimmune, Lübeck, Germany). C3 and C4 levels were determined by immunonephelometry (Beckman Coulter Diagnostics, Immage 8000, Brea, CA, USA). Thyroglobulin (Tg, Anti-T) and thyroid peroxidase (TPO, Anti-M) autoantibodies were detected by chemiluminescence immunoassays using the IMMULITE 2000 system (Roche Diagnostics, Integra 800, Mannheim, Germany). *H. pylori* infection was assessed using Hp Rapid Strip Test, based on a lateral flow chromatography with polyclonal antibodies (ACON Laboratories Inc, San Diego, CA, USA).

Atopy in the patients was assessed using a skin prick test (SPT) and specific IgE (sIgE) measurements. We defined a positive SPT test as a wheal with a mean diameter of at least 3 mm greater than that of a saline control. Each child was tested with a core battery of allergens (e.g. dust mite, cockroach, cat, dog, mould, grass, tree, weed, milk, egg, peanut) and a clinic-specific battery of locally relevant allergens (ALK Abelló, Hørsholm, Denmark).

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPPS) for Windows, version 16.0 (SPSS Inc., Chicago, IL, United States). We expressed categorical variables as percentages and continuous variables as mean ± standard deviation (SD). We used the Kolmogorov–Smirnov test to evaluate whether the