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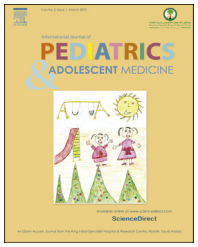

ORIGINAL RESEARCH ARTICLE

Is *Helicobacter pylori* infection a risk factor for childhood periodic syndromes?

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KEYWORDS
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Abstract *Background and objectives: Helicobacter pylori (H. pylori)* infection has been assumed to have roles in various extra-digestive diseases. The current study was designed to evaluate the incidence of *H. pylori* infection in patients with cyclic vomiting syndrome and its possible role in the etiology of this disease.
Design and setting: In this case-control study, 120 cases with diagnoses of cyclic vomiting or abdominal migraine who were registered at the Gastroenterology Clinic at Shiraz University of Medical Sciences from 2010 to 2013 were enrolled.
Materials and methods: Primarily information regarding the patients' diseases were collected with a data gathering sheet, and fresh morning stool samples were collected from the patients and examined for *H. pylori* stool antigen with the *H. pylori* Ag EIA test kit. The results were compared with those of healthy children from the control group.
Results: A total of 120 patients with cyclic vomiting (47.5%) and abdominal migraine (52.5%) with a mean age of 7.1 ± 3.4 (range 2–16 years) and a male-to-female ratio of 1.6 were included. The HPs Ag tests were positive in only 7 (5.8%) patients in our case group, and the HPs Ag tests were positive in 13 (13%) of the children in the control group; this difference was statistically insignificant.
Conclusion: Our study did not support *H. pylori* infection as an etiological factor in CV or AM.

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1. Introduction

Within several years of its discovery in approximately 1982, the association of *Helicobacter pylori* (*H. pylori*) infection with antral gastritis was completely accepted [1]. However, in recent years, in addition to its gastrointestinal functions, the roles of *H. pylori* infection have been assumed to extend to various extra-digestive diseases [2].

The pathogeneses of these extra-intestinal manifestations seem to be related to the chronic nature of the infection and the persistent inflammation it causes. It has been proposed that this chronic inflammation can have direct (i.e., the effects of the infectious agent on the vascular wall) and indirect (i.e., the production of inflammatory mediators) effects, which likely explain the association of these extra digestive diseases with *H. pylori* infection [3].

Different studies have revealed the involvement of this infection within vascular [4—7], autoimmune [8,9], and skin diseases [10]. Lately, many studies have implicated the relationship between *H. pylori* infection and migraine headaches in both children and adults [11—14]. The basis of these studies is related to the fact that migraine headaches seem to have a vascular pathogenesis [15]; moreover, previous investigations have revealed the relation of *H. pylori* infection with diseases of vascular origin, such as atherosclerosis and the Raynaud phenomena [16,17]. As previously explained, the probable pathogenic role of chronic *H. pylori* infection in these cases is based on the relationship between the host immune response against the bacterium and the chronic release of vasoactive substances [13].

The link between cyclic vomiting (CV) and migraine headaches was first expressed in 1904 [18]. Due to similarity of the stereotypical clinical presentations, the progression of CV to migraine headaches, and the frequent occurrence of CV in children with family histories of migraine, later in 1933, Wyllie and Schlesinger described a term called childhood periodic syndrome that included abdominal migraine (AM), cyclic vomiting syndrome, and benign paroxysmal vertigo that persists into adult life as migraine attacks [19]. In the recent years, this syndrome has been accepted as a migraine variant in children [20]. The cause of CV is still unknown; however, due to the resemblance of their clinical presentations, it has been speculated that migraine headaches and CV share similar mechanisms [21]. Other hypotheses that have been described for the pathogenesis of these diseases include autonomic instability, disturbances in the hypothalamic-pituitary-adrenal axis, mitochondrial disorders, and abnormalities in ion channels [22].

Based on these facts, the current study was designed to evaluate the incidence of *H. pylori* infection in patients with CV as a possible etiologic factor in the pathogenesis of the disease that has not previously been proposed elsewhere.

2. Materials and methods

One hundred twenty cases with diagnoses of CV or AM according to the IHC_ Classification ICHD_II (Table 1) [23] who were registered at the Gastroenterology Clinic at Shiraz University of Medical Sciences from 2010 to 2013 were enrolled in this study. Moreover, a control group consisting of healthy children who were referred to the out-patient clinic affiliated with the Shiraz University of Medical Sciences for routine health care visits was considered. These children were matched to the case group in terms of age and sex.

All patients and their parents were informed of the aims of the study, and written consent was attained. This study was approved by the ethical committee of our institution.

Prophylactic treatment with propranolol (1 mg/kg/day) had been initiated for all of the patients following the diagnoses of CV or AM, and this treatment had been gradually tapered in the patients group (50.8%) who had been symptom free for at least 6 months on prophylactic medication.

Primarily information regarding the patients' diseases was collected on data-gathering sheets and included

Table 1 Diagnostic criteria for abdominal migraine and Cyclic vomiting.[a]

Abdominal migraine	Cyclic vomiting
A- At least 5 attacks fulfilling criteria B-D	A- At least 5 attacks fulfilling criteria B and C
B- Attacks of abdominal pain lasting 1—72 h (untreated or successfully treated)	B- Episodic attacks that are stereotypical in the individual patient and include intense nausea and vomiting lasting from 1 h to 5 days
C- Abdominal pain with all of the following characteristics:	C- Vomiting during attacks occurs at least 4 times/hour for at least 1 h
1. Midline location, periumbilical or poorly localized	D- Symptom-free between attacks
2. A dull or only sore quality	E- Not attributable to any other disorder
3. Moderate or severe intensity	
D- During abdominal pain at least 2 of the following occur:	
1. Anorexia	
2. Nausea	
3. Vomiting	
4. Pallor	
E- Not attributable to any other disorder	

[a] IHC_ Classification-ICHD_I.