**Objective:** To determine whether *Helicobacter pylori* is associated with infantile colic.

**Design:** Case-control study.

**Settings:** Local tertiary hospital in rural Gizan, Saudi Arabia.

**Participants:** A total of 55 patients with infantile colic who were 2 weeks to 4 months of age and who fulfilled modified Wessel criteria (ie, crying and fussy behavior) and a total of 30 healthy controls with no history of colic who were matched by country of origin, age, sex, and ethnicity to the 55 colicky infants.

**Main Outcome Measure:** *Helicobacter pylori* infection determined by *H pylori* stool antigen testing.

**Results:** Of the 55 patients presenting with infantile colic, 45 (81.8%) tested positive for *H pylori*; of the 30 healthy controls, 7 (23.3%) tested positive for *H pylori* (odds ratio, 15.3 [95% CI, 17.9-29.8]).

**Conclusion:** *H pylori* infection is associated with infantile colic and may be a causative factor.


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**METHODS**

Approval of the present study was received from the administration of Alemeis National Hospital in Sabia, Saudi Arabia. Cases were recruited from the local tertiary hospital in rural Gizan, Saudi Arabia, from May to September 2009. Cases admitted for routine outpatient clinical care, for vaccination, or for medical services were selected. A questionnaire was administered to the mothers of infants 2 weeks to 4 months of age and included questions about maternal health behaviors, demographic characteristics, and the current source of infant nutrition (whether the infant was ex-
clusively breast fed, exclusively formula fed, or fed both breast milk and formula). Standardized measures (the 6-item state scale of the Spielberger State–Trait Anxiety Inventory, the Support Behaviors Inventory, and Anticipatory Guidance) that assessed maternal anxiety, postnatal depression, and social support were incorporated into the first questionnaire because these constructs have been suspected to play a role in the development of colic.15 Mothers were also asked to complete a short questionnaire based on the Ames cry score, which is composed of 3 questions, each with its own 4 response categories that are scored from 0 to 3. This short questionnaire asks about the frequency and the average and maximum duration of an infant’s cries during the past week. Overall scores, calculated by summing the scores of individual items, range from 0 to 9, with a score of 3 or greater indicating colic.12 Ninety-two participants were categorized into 2 groups (ie, case and control groups), and allocations were concealed from the participants’ parents until after pretesting was complete. Of the 92 participants, 85 completed the study. There were no statistically significant differences in baseline sociodemographic between the 7 participants who dropped out of the study and the 85 participants who completed the study. There were 55 case infants aged 2 weeks to 4 months who fulfilled modified Wessel criteria for infantile colic, which criteria meant that a well, thriving infant cried for 3 hours daily for more than 3 days every week for more than 3 weeks,4,12,13 excluding other causes of crying. The results of a detailed examination of the infant were recorded to rule out any underlying causes of excessive crying (eg, central nervous system abnormalities, infections, trauma, foreign body in the eye, fractured bone, or other gastrointestinal dysfunctions).14 Eligible controls were selected from the same population and matched to case infants by country of origin, age, sex, and race. The study controls were identified as having no colic or no history of colic, and no severe distressing illness or abnormalities.

The case and control groups were investigated for *H pylori* using a stool antigen test. This one-step test is a chromatographic immunoassay for the qualitative detection of *H pylori* infections (Alcon Laboratories Inc). It is a relatively simple, reliable, more applicable, and noninvasive test of infection.14 Although the result of this test is recognized as being highly sensitive, specificity, and positive and negative predictive values.16

All analyses were performed using SPSS (SPSS Inc). The demographic characteristics of cases and controls were compared using the Fisher exact test, and odds ratios and 95% CIs were calculated.

### RESULTS

There were 28 boys and 27 girls enrolled in the case group and 17 boys and 13 girls enrolled in the control group. The 2 groups were similar in terms of age, sex, race, prematurity, insurance status, maternal education, and maternal depression (Table). Of the 55 case infants, 45 (81.8%) tested positive for *H pylori*, and 10 (18.2%) tested negative. Of the 30 controls, only 7 (23.3%) tested positive for *H pylori*, and 23 (76.7%) tested negative (odds ratio, 15.3 [95% CI, 7.9-29.8]).

### COMMENT

Numerous studies have elucidated the pathogenesis, immunology, and *H pylori* gastrointestinal–related disorders (in addition to the extraintestinal manifestations) associated with *H pylori* infection, but, to my knowledge, none of these studies have investigated the role of *H pylori* in infantile colic. The present study found a strong association between *H pylori* infection and infantile colic.

Other studies have suggested that this association might be causal. Recently, strains of lactobacilli bacteria, selected for their capability of promoting the production of interleukin 10 (IL-10) and, consequently, the proliferation of CD4+CD25+ T-cell receptors have been used for the treatment of infantile colic.17-19 A recent study by Savino et al20 has found that a daily dose of a probiotic helps improve colic symptoms. The more recent research conducted by Zhou et al21 demonstrated the role of lactobacilli in treating *H pylori*–related diseases, and the results indicated that viable lactobacilli prevented the development of *H pylori* Sydney strain 1 (SS1) lipopolysaccharide (LPS)–activated Toll-like receptor 4 (TLR4) pathways in SGC-7901 cells, leading to the inhibitory effects of lactobacilli on IL-8 production stimulated by *H pylori* SS1 LPSs.21

Some studies have demonstrated that *H pylori* stimulates the release of IL-8 from gastric epithelia, which initiates inflammatory damage to gastric mucosa as the basis of the pathogenesis of *H pylori* infections. *H pylori* LPS is the major initiator in *H pylori*–induced IL-8 production. Considering the novel finding that *H pylori* is an indigenous biota in gastric microflora, including lactobacilli, and the hypothesis that the disturbance of the microecosystem plays a more important role in the pathogenesis of *H pylori*, the restoration of the gastric

### Table. Demographic Characteristics of 85 Participants With or Without Infantile Colic

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case Group (n = 55)</th>
<th>Control Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant age, mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>13 (23.6)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>2-3</td>
<td>27 (49.1)</td>
<td>14 (46.7)</td>
</tr>
<tr>
<td>4</td>
<td>15 (27.3)</td>
<td>9 (30.0)</td>
</tr>
<tr>
<td>Male infant</td>
<td>33 (60.0)</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td>Infant race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saudi Arabian</td>
<td>48 (87.3)</td>
<td>27 (90.0)</td>
</tr>
<tr>
<td>Non–Saudi Arabian</td>
<td>7 (12.7)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>37 (67.3)</td>
<td>20 (66.7)</td>
</tr>
<tr>
<td>Private, cash</td>
<td>18 (32.7)</td>
<td>10 (33.3)</td>
</tr>
<tr>
<td>&lt;High school education</td>
<td>34 (61.8)</td>
<td>19 (63.3)</td>
</tr>
<tr>
<td>for caregiver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal depression</td>
<td>7 (12.7)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Prematurity (&lt;36 wks’ gestation)</td>
<td>47 (85.5)</td>
<td>27 (90)</td>
</tr>
<tr>
<td>No</td>
<td>8 (14.6)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total annual outcome, $</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 000</td>
<td>33 (60.0)</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td>30 000-50 000</td>
<td>10 (18.2)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td>51 000-100 000</td>
<td>7 (12.7)</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>&gt;100 000</td>
<td>5 (9.1)</td>
<td>3 (10)</td>
</tr>
</tbody>
</table>

*Socioeconomic status is based on parental occupation, and education was nearly balanced among participants’ parents, particularly when considering the rural nature of this community.*

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microecosystem by the therapeutic effects of lactobacilli on *H pylori*-associated diseases has been demonstrated.22

Christensen et al22 suggested that different species of lactobacilli exert very different dendritic cell activation patterns, and at least one species may be capable of inhibiting the activities of other species. Thus, there is potential for \( T_{51}/T_{52} \)-driving capacities of the gut dendritic cell to be modulated according to the composition of gut microflora. Moreover, Kao et al23 suggested that dendritic cells participate in the host immune response against *H pylori* and that their suppression by *H pylori*-secreted factors may explain why infected hosts fail to prevent bacterial colonization.

In a recent study,21 2 soluble proteins with molecular sizes of 75 and 40 kDa were purified from supernatant of *Lactobacillus rhamnosus* and named P75 and P40, respectively, which ameliorated apoptosis of intestinal epithelium treated with tumor necrosis factor, interferon \( \gamma \), or IL-1α and promoted cell growth. Similarly, it could intervene in *H pylori* SS1-LPS–activated TLR4 signaling through modulating other pathways in SGC-7901 cells.21

In short, the interaction between the host immune factors and the *H pylori* virulence factors determines the outcome of *H pylori* infection (ie, the development of infant colic after the second week of life). Gradually, the microecosystem and other gastrointestinal flora did come into action to dominate and modulate (*H pylori* vs host) immune responses in order to drive the interactive pathways toward the relief of colic symptoms after 3 to 4 months of age.

I did not find any significant difference between severity of infantile colic and concentration of *H pylori* stool antigen that was compatible with the findings in Madani et al24 and Bahut et al25; both of those studies24,25 found no correlation between severe gastritis and marked bacterial colonization. *Helicobacter pylori* infections may be considered the etiologic pathogenic organism of infantile colic.

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REFERENCES


