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Otitis Media with Effusion and *Helicobacter pylori*

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Abstract

Previous studies reported the presence of *Helicobacter pylori* in middle ear fluid and raised a possible causal role of this bacterium in otitis media with effusion (OME). We investigated 48 children with OME (age, 7 months to 12 years) seen in New Orleans, Louisiana, and found no evidence of *H pylori* presence in any middle ear fluid specimen by amplification of the 16S rRNA gene. One child had *H pylori* detected in a stool specimen, in accordance with the low prevalence in our population. While *H pylori* may be significant in other countries, these findings do not support a role for *H pylori* in OME in our pediatric population in the United States.

Keywords

otitis media with effusion, *Helicobacter pylori*, *H pylori*, OME

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Otitis media with effusion (OME)—defined as the presence of a nonpurulent middle ear effusion (MEE) for ≥3 months with the absence of gross signs of infection—is a common disease in the pediatric population and the leading cause of conductive hearing loss in the developed world.[1] OME is a complex condition with various contributing factors, including bacterial and viral infections, eustachian tube dysfunction, allergens, and gastroesophageal reflux syndrome.[1] In 2005, Karlidag et al[2] detected *Helicobacter pylori* by polymerase chain reaction (PCR) in the middle ear fluid of 9 of 38 children (23.7%) with OME in Turkey, and in 2008, Kariya et al[3] induced inflammation of the middle ear of mice by inoculating *H pylori* whole-cell protein lysate. These findings raised the question whether *H pylori* may play a causative role in OME. To approach this issue, we investigated the presence of *H pylori* in the MEE of our pediatric patients with OME.

Materials and Methods

Institutional review board approval was obtained from the Louisiana State University Health Sciences Center and Children's Hospital, both in New Orleans, Louisiana. A series of consecutive pediatric patients who had OME and were scheduled for myringotomy for tube placement from December 2013 to March 2015 were recruited to participate in the study. Patients with recurrent acute otitis media or acutely infected middle ears at the time of procedure were excluded. MEE samples were collected sterilely from both ears and promptly frozen at –20°C. Stool samples were also collected voluntarily from the participating patients.

MEE specimens were thawed and centrifuged at 15,000 rpm × 10 minutes; DNA was extracted from the supernatant (200 μL) and pellet (resuspended in 180 μL of buffer ATL) with the DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany). DNA extracts were then subjected to PCR amplification of the 16S rRNA gene with primers 5′-CTTGCTA GAGTGCTGATTA-3′ (nt: 69-87) and 5′-TCCCACACTC TAGAATAGT-3′ (nt: 593-611), with annealing at 54°C and extension at 68°C for 40 cycles.[4] The resulting 543-bp amplicon was visualized under ultraviolet light of ethidium bromide–stained agarose gel. Positive control (DNA extracted from *H pylori* strain SS1) and negative control (distilled water) were processed simultaneously. *H pylori* colonization/infection of participants was investigated by a commercial *H pylori* stool antigen test (Premier Platinum HpSA Plus; Meridian Bioscience, Cincinnati, Ohio) following the manufacturer's instructions.

Results

Forty-eight children (27 male and 21 female) met criteria and were included in the study. Their age range was 7 months to 12 years (mean, 42 months; median, 39 months). Of them, 6 males and 7 females provided stool specimens (mean age, 44 months; median age, 27 months). All samples were processed simultaneously following end of enrollment,

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first on March 2015 and then on April 2015 for confirmation. No MEE sample tested positive for *H pylori* DNA. Of the 13 stool samples, 1 from a 5-year-old boy was positive for *H pylori* antigen.

Discussion

Following the original report by Karlidag et al,[2] few additional studies tried to detect *H pylori* in MEE, with variable results: some did not detect any *H* pylori,[5] and some detected a rate as high as 67%.[6] Many studies had methodological limitations, such as observational nature, small number of specimens, inadequate controls, or use of diagnostic tests with poor sensitivity. A systematic review included 6 studies and concluded that there was poor evidence for an association between *H pylori* and OME.[7] A more recent report[8] in Egypt randomized children with OME and *H pylori* (detected by stool antigen) to either standard otitis media treatment (amoxicillin and clavulanate) or *H pylori*–specific triple therapy (clarithromycin, metronidazole, and lansoprazole) and found that those treated for *H pylori* had a better chance of improvement on audiometry and tympanometry (68.7% vs 49.3%, $P = .035$), suggesting a potential role for *H pylori* in OME. Unfortunately, that study did not correlate individual clinical response with *H pylori* eradication.

All of these studies were done in areas of high prevalence of *H pylori*, and their significance is unclear for areas of low prevalence. To our knowledge, the only study in the United States (done in Morgantown, West Virginia) did not focus on MEE but on adenoid tissue, and it detected *H pylori* by PCR in 10 of 45 (22.2%) cases of OME and 6 of 37 (16.2%) controls, a finding that did not support a role for *H pylori* in OME ($P = .49$).[9] Despite the high frequency of OME in our population, none of the MEE specimens tested positive for *H pylori*. As expected, we found a low prevalence of *H pylori* gastrointestinal infection in our population (1 of 13 stool specimens, 7.7%). Hence, our findings do not support a role for *H pylori* in our population with OME; *H pylori* may still have a role in populations of high incidence of this bacterium but not in our population.

Some limitations of our study should be noted. The small sample size (48 patients) limits the power of the study; similarly, with this being a single-center study, its generalizability to other populations in the United States is unclear and would require further studies in other regions and other populations. Stool was not analyzed for all 48 patients, since only 13 provided a sample; their young age likely contributed to the low positivity rate found (1 of 13). Detection of *H pylori* can be difficult; we elected to use PCR to process MEE since most other studies used it. PCR performance is dependent on the target gene, the primers used, and the conditions of the reaction, but in general, it is highly sensitive and specific for 16S rRNA.[10] We did not have independent specimens to validate our assay but used appropriate positive and negative controls, which increase the confidence in our results.

In conclusion, our findings do not support the hypothesis that *H pylori* may have a contributing role in OME in our pediatric population.

Author Contributions

Anita Jeyakumar, study design, specimen collection, manuscript preparation, approval of final version; **Rodolfo E. Bégué**, study design, and execution; data analyses, manuscript preparation, approval of final version.

Disclosures

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