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Effect of *Helicobacter pylori* infection on growth trajectories in young Ethiopian children: a longitudinal study

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SUMMARY

Background: *Helicobacter pylori* infection has been associated with early childhood growth impairment in high- and middle-income countries; however, few studies have examined this relationship within low-income countries or have used a longitudinal design. The possible effects of *H. pylori* infection on growth trajectories were examined in a cohort of young Ethiopian children.

Methods: In 2011/12, 856 children (85.1% of the 1006 original singletons in a population-based birth cohort) were followed up at age 6.5 years. An interviewer-led questionnaire administered to mothers provided information on demographic and lifestyle variables. Height and weight were measured twice, and the average of the two measurements was used. Exposure to *H. pylori* infection was assessed using a rapid *H. pylori* stool antigen test. The independent associations of positive *H. pylori* infection status (measured at ages 3 and 6.5 years) with baseline height and weight (age 3 years) and height and weight growth trajectory (from age 3 to 6.5 years) were modelled using hierarchical linear models.

Results: At baseline (age 3 years), the children's mean height was 85.7 cm and their mean weight was 11.9 kg. They gained height at a mean rate of 8.7 cm/year, and weight at a mean rate of 1.76 kg/year. *H. pylori* infection was associated with lower baseline measurements and linear height trajectory ($\beta = -0.74$ cm and -0.79 cm/year, respectively), after controlling for demographics and markers of socio-economic status. However, the positive coefficient was associated with quadratic growth in height among *H. pylori*-infected children ($\beta = 0.28$, 95% confidence interval 0.07 to 0.49, $p < 0.01$), and indicated an increase in height trajectory as the child increased in age. A non-significant difference in baseline and trajectory of weight was observed between *H. pylori*-infected and non-infected children.

Conclusions: These findings add to the growing body of evidence supporting that *H. pylori* infection is inversely associated with childhood growth trajectory, after controlling for a range of factors associated with reduced growth and *H. pylori* status. Further follow-up will be important to confirm possible catch-up in height trajectory among *H. pylori*-infected children as they grow older.

1. Introduction

There is now good evidence that infection with *Helicobacter pylori* is the principal cause of acute and chronic gastritis and atrophic gastritis.[1–3] More recently, however, there has been interest in the effects of *H. pylori* in extra-gastroduodenal diseases.[4–7] This interest has led researchers to investigate the effects of *H. pylori* in a wide range of growth outcomes. Evidence for an association between *H. pylori* and childhood growth impairment has arisen from a range of epidemiological studies.[8–12] Delayed growth,[11,12] short stature,[13] and growth retardation[8,9,12,14] appear to be related to *H. pylori* infection.

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Several mechanisms by which *H. pylori* infection causes growth impairment have been proposed.[15,16] One hypothesis that has attracted attention is that since infection with *H. pylori* is accompanied by hypochlorhydria, this facilitates the acquisition of other enteropathogens due to impairment of the gastric acid barrier. This then results in diarrheal disease, iron-deficiency anaemia, and growth impairment.[15,16] This is likely to occur most frequently in developing regions where the prevalence of *H. pylori* infection is disproportionately high and multiple enteric co-infections are common.[15,17] *H. pylori* infection has also been associated with impaired absorption of nutrients and vitamins,[18] and reduced food intake as a result of dyspepsia,[19] which in turn impairs childhood growth. Although these hypotheses seem biologically plausible, whether growth impairment occurs as a direct effect of the *H. pylori*-induced inflammation, or as a consequence of indirect effects (such as infection-induced anorexia,[20] *H. pylori*-associated intestinal permeability changes,[21] and/or malabsorption or diarrheal disease[22]) is unclear. It has been suggested that direct and indirect effects may both contribute to growth impairment.[4]

Whilst the role of *H. pylori* in childhood growth impairment is intriguing, possible bias due to potential confounding variables such as socio-economic status, which may contribute both to occurrences of childhood growth impairment and to *H. pylori* infection, are difficult to exclude. If *H. pylori* can be proved to negatively affect childhood growth, it can then be considered a treatable cause of diminished growth and a potential target for nutritional intervention. In Ethiopia, childhood undernutrition continues to be a major public health problem,[23] and is associated with complex socio-demographic and economic factors.[24] Few studies have examined the possible link between *H. pylori* infection and childhood growth outcomes within low-income countries or have used a longitudinal design. It appears that no study has attempted to investigate this relationship in Ethiopia. In this study, data from a detailed Ethiopian birth cohort were used to assess the effect of *H. pylori* infection on growth trajectories, using two-level hierarchical linear models.

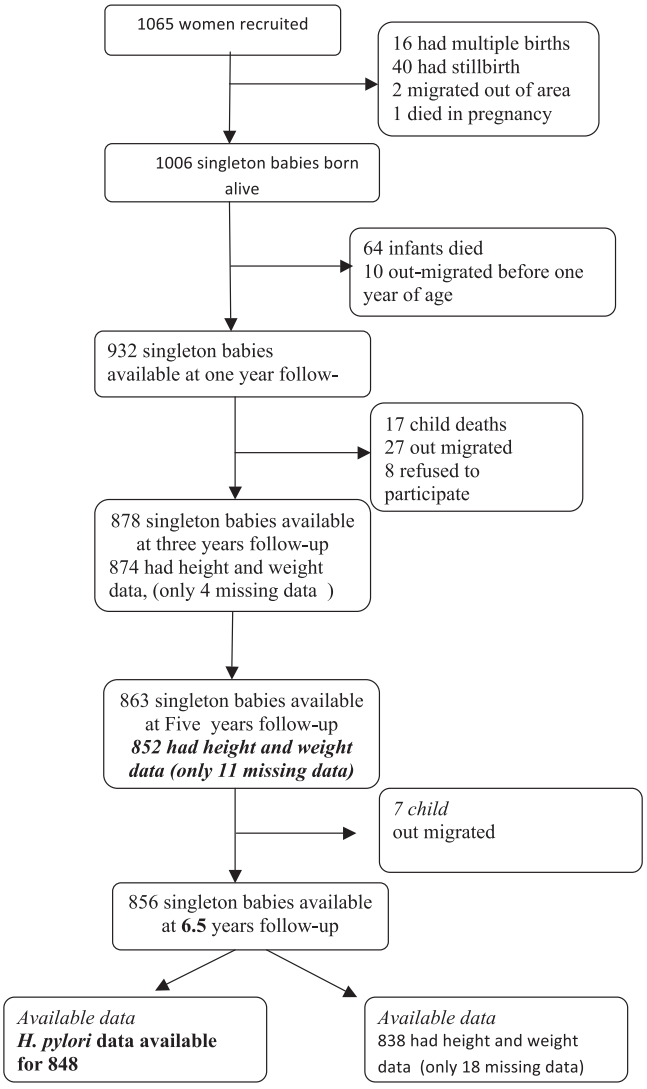

Figure 1. Butajira birth cohort followed at age 6.5 years.

2. Methods

2.1. Study setting and design

A detailed description of the original Butajira Birth Cohort study has been published.[25,26] Briefly, the birth cohort is nested within the Butajira Demographic Surveillance Site,[27] which covers a sample of nine rural and one urban administrative units in and around the town of Butajira in southern Ethiopia,[24] with a total population of approximately 33 393 in 2007. Of the 1234 women eligible in 2005–2006, 1065 were recruited (86% of those eligible); all live singleton babies born to these women ($n = 1006$) were followed-up as a birth cohort (Figure 1).

2.2. Measurement and data collection

After informed consent was given by the mothers, information on demographic and selected lifestyle factors was collected via an interviewer-administered questionnaire during pregnancy, at birth, and during the follow-up visits.

During follow-up visits at ages 3, 5, and 6.5 years, mothers were also asked to collect a faecal sample from their child using a leak-proof plastic container. The samples were then transported to the Butajira Health Centre laboratory for analysis, to ascertain the child's *H. pylori* and intestinal parasite infection status.

2.3. Laboratory analyses

H. pylori status was determined using an *H. pylori* stool antigen test (SD Bioline; Standard Diagnostics, Inc., South Korea). *H. pylori* stool antigen (HP Ag) testing is rapid, non-invasive, easy to perform, and can be used to detect a current infection; it can also be used to monitor the effectiveness of eradication therapy. Tests were performed in accordance with the manufacturer's instructions. A portion of faeces (approximately 50 mg) was swirled with assay diluent solution at least 10 times, until it dissolved. It was then allowed to settle for 5 min at room temperature. One hundred microlitres of the prepared sample was placed on the HP Ag test strip, and the test results were read 15 min later. One red line indicated a negative result, and a double red line indicated a positive result.

All faecal samples were also examined qualitatively using the modified formol–ether concentration method to ascertain the child's intestinal parasite infection status.

2.4. Anthropometric measurements

At each follow-up visit, the child's height and weight were measured in duplicate, and the average of the two measurements