Seroepidemiological study of *Helicobacter pylori* infection in infancy

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Abstract

The incidence of *Helicobacter pylori* infection in very young children was determined, based on the emergence of specific IgG antibodies in sequential serum samples from birth to 2 years of age. The risk of acquiring *H pylori* infection in infancy as a result of maternal exposure to the organism was also assessed, based on the determination of maternal cord-blood antibodies. Serum IgG class *H pylori* antibodies were analysed in the cord blood samples of 195 newborns and in their follow up samples until the age of 2 years. Maternal antibodies were detected in the cord-blood samples of 21 children (10.6%). These antibodies disappeared in all but one child before 7 months of age and no new seroconversions occurred in these children. Ten originally cord-blood negative children seroconverted up to the age of 2 years (5.1%).

It is concluded that a major proportion of *H pylori* infections observed in young adults in Finland are acquired during the first two years of life. Maternal seropositivity is not a straightforward risk factor for acquiring *H pylori* infection in infancy. (Arch Dis Child 1996; 74: F141-F142)

Keywords: *Helicobacter pylori*, cord-blood antibodies, maternal seropositivity.

Helicobacter pylori infection occurs all over the world, and more than 50% of adults are infected with this pathogen.¹ The prevalence of infected children varies greatly depending on the socio-economic status of the country concerned. In developing countries children are colonised at an early age.² In these countries the prevalence of gastritis is high and the long term consequences of *H pylori* infection, such as gastric cancer, are more common than in developed parts of the world.³ Based mainly on studies in adult populations, it has been suggested that *H pylori* infection is also acquired during childhood in developed countries.^{4,5} Relevant data about *H pylori* colonisation in infants and young children are, however, scarce. As *H pylori* infection tends to concentrate in families,⁶ our interest was also to find out whether maternal exposure to *H pylori*, as reflected by cord-blood antibodies, increases the risk of acquiring *H pylori* infection in infancy.

Methods

One hundred and ninety five consecutive sera

from a serum pool of 741 sera were selected for study. The samples had originally been collected from term infants born at Tampere University Hospital between October 1984 and July 1985 for a study on childhood diarrhoea.⁷ *H pylori* antibodies were determined in the cord-blood samples and in follow up samples taken as follows: at the age of 28 days and at 7, 12, and 24 months after birth. An additional blood sample taken at the age of 18 months was available from 66 children. Only three follow up specimens were available from 18 children and only two from 19. The sera had been stored at -20°C until analysis.

IgG class *H pylori* antibodies were determined by an enzyme immunoassay (EIA) using acid glycine extract antigen derived from *H pylori* strain ATCC 43504 (NCTC 11637).⁸ The sequential serum samples from each child were analysed in parallel to minimise the interassay variation. Antibody titres were expressed as relative EIA units (EIU). The cut-off for seropositivity was determined as 20 EIU, based on the distribution of antibodies in culturally confirmed *H pylori* positive and negative children.⁹

In the statistical analysis proportions with 95% confidence intervals (CI) were calculated for the annual incidence.

Results

Maternal antibodies to *H pylori* were detected in the cord-blood samples of 21 (10.6%) children. These antibodies disappeared in the later specimens of all but one child during the follow up until 7 months of age. Thus only one infant born seropositive remained so throughout the follow up period. No new seroconversions occurred in these 21 children.

During the first two years of life seroconversions from negative to positive were registered in 10 (5.1%) children, all of whom were cord-blood negative (fig 1). The median age for seroconversion was 18 months. Three seroconversions took place during the first year and seven during the second. The annual incidence of *H pylori* infection was calculated to be 1.5% (95% CI 0.32, 4.43) during the first year of life and 3.7% (95% CI 1.48, 7.37) during the second. The other 164 (84.1%) children remained seronegative. The total incidence of *H pylori* infection in Finnish children from birth to 24 months of age was 5.6%.

Discussion

The *H pylori* antibody positivity registered in the cord-blood samples reflects the maternal antibody status of other similar infections. The

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Time course of the serum IgG antibody response to *Helicobacter pylori* in children from whom sequential samples had been obtained as newborns and up to 24 months of age. Results are only shown for those subjects who exceeded the cutoff for seropositivity during follow up.

amount of seropositive mothers, 10.6%, agrees with a study of Finnish children and blood donors.^{8,9} Therefore, our study indicates that half of the *H. pylori* infections occurring in young adults in Finland are acquired during the first two years of life. We have already shown that seropositive children usually remain so until adolescence, indicating the long term course of the infection.⁹ The slight fluctuations in the antibody titres seen in some children can probably best be explained by the temporary effect of antibiotics so commonly used in this age group.

Based on current observations and on our earlier results showing that over 6% of 3 year old children had measurable *H. pylori* antibodies,⁹ it seems that the risk of infection is very low after reaching toddler age. Thus the incidence of *H. pylori* infection in children after the first years of life is likely to be similar to that of adults in developed countries.^{5,10}

It could be speculated that the incidence figures obtained here might have been different if sera from children born in the 1990s had been studied. A recent cohort study on the prevalence of gastritis in Finland from 1918 to 1957 suggested that the rate of acquisition of *H. pylori* has declined quite rapidly during the past decades in this country.¹¹ This change is most probably attributable to an improvement in socioeconomic conditions in Finland, as has been shown to be the case elsewhere.¹² Over the past 10 years the conditions have, however, remained basically the same and therefore our material can be considered representative even for today.

In earlier studies seropositivity to *H. pylori* was more common in parents of *H. pylori* infected children than in parents of non-infected children.¹³ A strong association has been found between infection of the mothers and the *H. pylori* colonisation of their children.⁶ According to our results, however, maternal seropositivity to *H. pylori* was not a straightforward risk factor for acquiring *H. pylori* infection in infancy and early childhood. We have no additional data, other than the seropositivity and verification (the breath test) of bacterial colonisation of the mothers. Moreover, the mothers were not retested, which means that the mothers could have become infected during the follow up period. In one recent study, however, where mothers with positive IgG titres against *H. pylori* were

confirmed to be colonised using the breath test, none of the 35 infants studied became infected during follow up until the age of 1 year.¹⁴ Other earlier serological studies have also shown that seropositivity in the IgG class is a highly specific indicator of active *H. pylori* infection.¹⁵ Considering the low annual incidence of *H. pylori* infection in adults in western countries,¹⁰ it is unlikely that more than one of the mothers of the seroconverting infants would have harboured *H. pylori* during the follow up.

Our results lead us to conclude that instead of increasing the risk of *H. pylori* infection, maternal seropositivity seems, in fact, to protect the infants from early infection. In Gambian children this was confirmed, when IgA antibodies secreted via breast milk turned out to have protected the infants from *H. pylori* infection.¹⁶ This could also be the explanation for our results, especially because in Finland the duration of breast feeding is generally long (in this study 71% of the infants were breastfed for seven months or longer).⁷ We have been unable to determine the source of the infection among the infants studied. Neither is it possible to extend the results obtained here to other paediatric populations, where infected mothers may well have a different role in transmitting the bacteria to their children. In terms of prevention, risk groups have to be determined within each population separately.

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