

# HELICOBACTER PYLORI COLONIZATION IN INFANTS AND ITS RELATION TO CHILDHOOD MORBIDITY



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## Abstract

*Helicobacter pylori* infection is universally reported from all over the world including both developed and developing countries [1]. The prevalence of *Helicobacter pylori* infection in Pakistan is unknown. Although a few studies [2,3] have been done in adults, there are no studies looking at the prevalence of *Helicobacter pylori* colonization especially in children. In addition, a number of symptoms such as nonspecific abdominal pain [4], diarrhea and malnutrition [5] etc. are attributed to it though most cases of *Helicobacter pylori* colonization remain asymptomatic. The association between *Helicobacter pylori* and gastrointestinal symptoms however, remains controversial. Hence in order to determine the prevalence of *Helicobacter pylori* infection, its time of acquisition and to look at its correlation with diarrhea-associated morbidity, we proposed to do the present study.

*In this study we will look for the evidence of Helicobacter colonization in infants with the non-invasive techniques using <sup>13</sup>C urea breath test and stool ELISA for Helicobacter pylori every at three month interval in a cohort of infants from a periurban community in Karachi Pakistan.*

## 1. SCIENTIFIC BACKGROUND OF THE PROJECT

*Helicobacter pylori* infection is universally reported from all over the world including both developed and developing countries [1] but its prevalence in Pakistan is unknown. It is also recognized that low socioeconomic conditions, close living conditions and overcrowding are predisposing factors for its colonization. Breast feeding has also been reported to be protective due to presence of kappa-casein in the human breast milk [6] It is recognized as the commonest cause of gastritis and gastro duodenal ulcers both in adults and children [2-7]. However, most cases of *Helicobacter pylori* colonization remain asymptomatic though a number of symptoms such as nonspecific abdominal pain [4], diarrhea and malnutrition [5] etc. are attributed. The reason for the reported associations between *Helicobacter pylori* colonization and enteric disease is perhaps due to the decreased acidity of stomach [5], which allows the bacterial pathogens reach lower gut easily, leading to diarrhea and malnutrition. This association between *Helicobacter pylori* colonization and the gastrointestinal disease has not been confirmed in other studies. No difference in prevalence of abdominal pain in children with and without *Helicobacter* colonization was found in population based study among preschool children in Southern Germany [8]. Similarly studies from Bangladesh [9] and Thailand [10] have also not confirmed any association between *Helicobacter pylori* and diarrhea. Thus, the association between

*Helicobacter pylori* and gastrointestinal symptoms remain controversial. It was difficult to do epidemiological studies previously due to the non-availability of reliable noninvasive tests for the diagnosis of *Helicobacter pylori* infection.

The gold standard for its diagnosis has always been gastroscopy, antral biopsy and identification of the organisms in gastric mucosa. Though detection of antibodies against *Helicobacter* by ELISA [2,11] is a relatively noninvasive technique, it is commonly used for diagnosis in association with gastroscopy. The <sup>13</sup>C Urea breath test (UBT) using stable isotope (<sup>13</sup>C) is a new non-invasive and reliable test for the diagnosis of *Helicobacter* colonization [12,13]. Its sensitivity and specificity has been reported between 90 to 100% [12] and can be easily used in community for epidemiological studies. The basis of UBT is the property of *Helicobacter* to split urea into CO<sub>2</sub> (Carbon dioxide) and NH<sub>3</sub> (Ammonia). The <sup>13</sup>C labeled carbon dioxide is exhaled in the breath, which is collected and analyzed using mass spectroscopy.

A large prospective cohort study is being done at AKUH to evaluate different complementary feeding regimen and their relationship to micronutrient status and growth supported by UNICEF and other agencies. Using this unique opportunity, we will evaluate risk factors such as *Helicobacter pylori* colonization longitudinally, with its relationship to intervene morbidity patterns. The aims of the study are:

- a) To determine the prevalence of *Helicobacter pylori* infection in a well defined cohort of infants in a peri-urban area of Sindh, Pakistan, by mean of longitudinal surveillance.
- b) To determine the age of infants at the time of acquisition of *Helicobacter pylori* infection and risk factors for colonization.
- c) To evaluate the correlation between *Helicobacter pylori* infection and diarrhea associated morbidity.
- d) To evaluate the independent correlation between *Helicobacter pylori* infection and growth rate and malnutrition.

## 2. METHODS

A peri-urban village i.e. Rehri Goth in Karachi with a population of 28000 has been selected for the study. The entire households in the selected area are registered. A baseline survey of these houses has been done. All the pregnant women at present have been identified and their expected date of delivery noted. These households are visited and will continue to visit once a month for identification of newly pregnant women. The information about the birth of babies is obtained with the help of local Traditional Birth Attendants (TBAs). All the newborn babies are visited within 72 hours and thereafter every fortnight by a team of research medical officer (RMO) and community health nurses selected for the study. The RMO takes a detailed history about the birth of the baby and the mother. He also examines the baby and records the anthropometric measurements. These babies will be visited every fortnight for next eighteen months. The RMO will reexamine the baby and record anthropometric measurements on each visit. He will also obtain the history about feeding, the number of episode of the diarrhea and other illnesses such as ARIs (acute respiratory infection) etc and the treatment given for these illnesses. A stool sample will be collected on each visit and stored at  $-70^{\circ}\text{C}$  for detection of *Helicobacter pylori* antigen using a recently developed ELISA (Meridian Diagnostics USA). Parental consent will be obtained for conducting  $^{13}\text{C}$  urea breath test. The test will be performed as follows.

### $^{13}\text{C}$ Urea Breath Test

After a two to four hour fasting period these babies will be given 50mg  $^{13}\text{C}$  urea in citrus fruit juice such as orange drink or clean drinking water.

Breast feeding or formula feed as the case may be, will be given one hour after administering the  $^{13}\text{C}$  urea. The exhaled air will be collected slowly in a twenty ml syringe using an oxygen facemask over a period of two minutes. The air so collected will be transferred to a vacutainer tubes and labeled accordingly. The air samples will be collected at 15, 30, 45 and 60 minutes. Once the samples are collected, these will be stored at  $-20^{\circ}\text{C}$  and analyzed using mass spectroscopy at University Department of Child Health Glasgow U.K. An increase of 4 delta over base line after 30 minutes of  $^{13}\text{C}$  urea administration will be taken as positive test.

## 3. RESULTS

Since the award of the contract, we have been conducting the survey of the proposed population and registering the pregnant women. Forms have been developed to collect the baseline data of the registered population and the neonatal examination. However no infant has yet undergone Urea breath test. The statistics till 30<sup>th</sup> April 1999 are:

Total population:	23000
Total number of household	1612
Number of pregnant women registered so far	169
Number of non-pregnant women	2326
Number of babies delivered during last two months	82

## 4. PLAN FOR FUTURE WORK

In 2001-2002 we have to continue the present work, as the babies registered at the end of the first year will have to be followed up during the next year. However after validation of the results of Stool ELISA and UBT, an effort will be made to establish these tests at the Aga Khan University for management of patients with *Helicobacter* infection.

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