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Active infection with *Helicobacter pylori* in healthy couples

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SUMMARY

The mode of spread of *Helicobacter pylori* infection is subject to ongoing debate. Recent studies among patients with gastrointestinal disorders suggest a potential role of conjugal transmission. In this study, the clustering of *H. pylori* infection was assessed among 110 employees of a health insurance company and their partners. Active infection with *H. pylori* was measured by the ^{13}C-urea breath test. Information on potential confounders was collected by a standardized questionnaire. Overall, 16 employees (14·5%) and 24 partners (21·8%) were infected. While only 7% (6/86) of employees with an uninfected partner were infected, this applied to 42% (10/24) of employees with an infected partner. A very strong relation between partners' infection status persisted after control for age and other potential confounders (adjusted odds ratio, 7·0; 95% confidence interval, 1·8–26·7). Furthermore, the risk of infection increased with the number of years lived with an infected partner. These results support the hypothesis of a major role of spouse-to-spouse transmission of *H. pylori* infection.

INTRODUCTION

Infection with *Helicobacter pylori* is common among adults throughout the world [1]. It is a major cause of type B gastritis, and it is strongly associated with the development of gastric and duodenal ulcer and stomach cancer [2, 3]. Although infection status has been found to be more strongly related to childhood risk factors than to risk factors in adulthood [4–6], there is evidence that acquisition and elimination of the infection occurs throughout adulthood [7–9].

Despite extensive research, the mode of transmission of *H. pylori* infection is still subject to debate. The weight of evidence suggests direct transmission from one human to another. Faecal-oral [10], oro-oral [11], and gastro-oral [12] routes of transmission have been proposed.

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Spouse-to-spouse transmission would appear to be an obvious source of infection in adulthood. Several studies have addressed clustering of infection within couples [13–20]. Results were conflicting, but some studies found a strong relation between infection status of index subjects and their spouses [15, 16, 19, 20]. With the exception of one smaller study [15], these studies were carried out among special groups of patients, however, including patients with duodenal ulcer [13, 19, 20], other gastric problems [13, 16, 17], or fertility problems [14], which raises the question of generalizability. Furthermore, most of these studies included small numbers of couples and did not control for covariates [13, 15, 16, 18, 20]. This is of major concern since important risk factors of infection, such as age and childhood living conditions, which strongly cluster within couples, may severely confound the results. In one study from the USA, which took such factors into account, the association between infection

status of partners was entirely explained by age and national origin [14].

In this study, we investigated the relation of active infection with *H. pylori* among healthy employees of a health insurance company in Southern Germany and their partners. Particular care was given to account for the influence of risk factors that might confound the results.

METHODS

Study design and study population

All employees of a health insurance company in the city of Ulm, Germany, and their household members above age 15 were invited to participate in a cross-sectional study. Participation was voluntary and informed consent was obtained in each case. The study was approved by the Ethics Board of the University of Ulm.

Data collection

Employees were enrolled in the study at the headquarters of the health insurance company during work hours. Active infection with *H. pylori* was determined by the ^{13}C-urea breath test (UBT). First, an initial breath sample was collected in a plastic bag. The employees then received 200 ml of apple juice (pH 2·2–2·4) which contained 75 mg of ^{13}C-urea (Mass Trace, Woburn, USA). After 30 min a second breath sample was collected. The breath samples were analysed with an isotope selective non-dispersive infra-red spectrometer (NDIRS; Wagner-Analytical Systems, Worpswede, Germany). A change of the $^{13}CO_2/^{12}CO_2$ ratio over baseline of more than 5% was considered to indicate active infection. Sensitivities and specificities of the ^{13}C-urea breath test close to 100% have consistently been reported suggesting the test to be the gold standard in subjects in whom endoscopy is not indicated [21–23].

Employees filled out a standardized questionnaire between collection of the first and the second breath sample. The questionnaire included questions on sociodemographic factors including current and childhood living conditions and household contacts.

Employees were handed out a UBT kit and a standardized questionnaire for each household member to be handled at home in the same manner as described for the employees above. These materials were collected at the workplace during the following workday.

Table 1. *Basic characteristics of employees in the study sample*

Characteristic	*n*	%
Age		
20–29	47	42·7
30–39	27	24·6
40–49	21	19·1
50–60	15	13·6
Sex		
Female	77	70·0
Male	33	30·0
Own school education		
$\leqslant$ 9 years	24	21·8
10–11 years	67	60·9
$\geqslant$ 12 years	19	17·3
School education of father		
$\leqslant$ 9 years	83	76·9
10–11 years	19	17·6
$\geqslant$ 12 years	6	5·6
Number of siblings		
0	14	12·7
1	41	37·3
2	30	27·3
$\geqslant$ 3	25	22·7

Statistical analysis

The employees were first described with respect to basic sociodemographic factors. We then assessed the prevalence of infection with *H. pylori* among employees by infection status of their partners. The association between infection status of employees and their partners was quantified by crude and adjusted odds ratios and their 95% confidence intervals. Adjustment was made by conditional logistic regression with the employee's infection status as the dependent variable and the partner's infection status and the following potential confounders as the independent variables: age (in years; included as both a linear and a quadratic term to account for potential non-linear relations), school education of father (categories: $\leqslant$ 9 years, $\geqslant$ 10 years), and number of siblings with whom the employees had grown up (categories 0–1, $\geqslant$ 2). The latter two covariates were chosen to account for the influence of childhood living conditions,. Additional analyses were carried out in which the number of years employees had lived with an infected partner were taken into account (categories: 1–15, $>$ 15). All analyses were carried out with the SAS statistical software package [24].

Table 2. *Employee's infection with* H. pylori *by infection status of partner and duration of living together*

Partner infected	Years living with infected partner		Employee infected	Odds ratio (95% confidence interval)		
				Crude	Adjusted*	Adjusted†
No‡	0	$n = 86$	6 (7%)	1·0	1·0	1·0
Yes	> 0	$n = 24$	10 (42%)	9·2 (2·9–29·2)	7·1 (1·8–27·4)	7·0 (1·8–26·7)
				$P < 0{\cdot}001$§	$P = 0{\cdot}004$§	$P = 0.004$§
	⩽ 15 years	$n = 12$	3 (25%)	4·4 (0·9–20·3)	5·6 (1·0–30·1)	5·3 (1·0–28·5)
	> 15 years	$n = 12$	7 (58%)	17·8 (4·4–72·0)	9·4 (1·5–59·3)	9·8 (1·5–62·2)
				$P < 0{\cdot}001$‖	$P = 0{\cdot}008$‖	$P = 0{\cdot}007$‖

* Adjusted for age.
† Adjusted for age and, additionally, for school education of father and number of siblings with whom employees have grown up.
‡ Reference group.
§ *P*-value for difference between employees with and without infected partner.
‖ *P*-value for linear trend.

RESULTS

Overall, 211 among 276 eligible employees (76·5%) participated in the study. Among these, 189 employees (89·6%) supplied information on their household members; 140 employees (74·1%) lived with a partner. In 114 cases (81·4%), the partner also participated in the study. To avoid confounding by nationality, which was found to be a strong risk factor of infection in another study from the same region (25), three foreign employees and their partners were excluded from the analyses. We further excluded one couple due to use of antibiotics by one partner at the time of the examination as this may lead to a false negative result of the UBT. After these exclusions, there remained a final number of 110 couples for the analysis.

Table 1 shows basic characteristics of the employees in the study sample. About two-thirds of the employees were between 20 and 40 years old. Mean age was 35·1 years (range 20–60 years). Seventy percent of the employees were female, and about 60% had a medium level of school education (10–11 years). School education of employees was considerably higher than school education of their fathers, which reflects secular trends in educational levels in Germany. A minority of one out of eight employees had grown up without siblings, and half of the employees had grown up with two or more siblings.

Overall, 16 employees (14·5%) were infected with *H. pylori*. Prevalence of infection was somewhat higher among partners, of whom 24 (21·8%) were infected. Employees' infection was strongly related to infection status of their partners (see Table 2). While only 7% (6/86) of employees with an uninfected partner were infected, this applied to 42% (10/24) of employees with an infected partner, resulting in a crude odds ratio (OR) (95% confidence interval) of 9·2 (2·9–29·2). This relation was partly due to confounding by age, but it remained strong (OR = 7·1) and clearly statistically significant ($P = 0{\cdot}004$) even after age adjustment. Additional adjustment for indicators of childhood living conditions (school education of father and number of siblings with whom employees had grown up) did not materially alter the results (OR = 7·0).

Furthermore, the prevalence of infection strongly increased with the number of years employees had lived with an infected partner. Although this relation was again strongly confounded by age, a clear monotonic increase of risk with the time lived with an infected partner persisted even after control for age and indicators of childhood living conditions.

DISCUSSION

In this study among healthy couples, we found a strongly increased prevalence of *H. pylori* infection among individuals whose partner was infected. The risk of infection increased with the number of years employees had lived with an infected partner. The relation between partners' infection status remained strong even after control for potential confounders, including age and factors reflecting socioeconomic conditions in childhood. The association can likewise not be due to confounding by nationality, which is strongly related to *H. pylori* infection in Germany

[25], since only employees of German nationality were included in the analysis.

These results among healthy individuals confirm and extend previous evidence of clustering of the infection among couples, which was mainly based on studies among individuals with gastrointestinal problems [16, 19, 20], and which was limited by the fact that most of these studies did not control for potential confounders [15, 16, 20].

In theory, the clustering of *H. pylori* infection among couples may be due to several mechanisms. Firstly, it may be due to clustering of other potential risk factors of the infection which were not controlled in the present analysis, such as lifestyle habits including smoking, alcohol consumption or nutritional factors. Findings concerning the importance of these factors are inconsistent, however [1], and it is unlikely, that these factors could produce as strong a relation as we found between partners' infection status. Secondly, there may be common sources of infection of both partners, or partners may have infected each other. Given that no environmental source of *H. pylori* has been recognized with certainty to date, and that contacts with partners are typically much more intensive than contacts with other individuals, the latter explanation appears to be most plausible.

While direct evidence for spouse-to-spouse transmission is limited in our study in the absence of DNA typing data, clustering of identical or similar *H. pylori* strains within families has repeatedly been reported [20, 26–28]. In particular, a recent study found reinfection after eradication of two patients with the same *H. pylori* strain that was also found in their partners (who had not undergone eradication) [28]. A high concordance of strains was also found in a recent study among infected couples from Greece [20]. Considering the genomic diversity of *H. pylori*, the most likely explanation for these findings is conjugal transmission.

Despite increasing evidence of the occurrence of conjugal transmission, no certain conclusions on the mode of spread can be drawn at present. A plausible possibility would be that mouth secretions may be contaminated from *H. pylori* in gastric juice, and that the micro-organism may be transferred through the oral–oral contact of the couple [11, 12]. However, other modes of spread, such as faecal–oral transmission cannot be ruled out [10].

Further longitudinal studies are needed to assess the rate of conjugal transmission. Should they corroborate the increasing evidence of a major role of conjugal transmission, this may have important clinical implications. In that case, concurrent eradication of *H. pylori* in the partner may have to be considered among patients treated for peptic ulcer. This may help to prevent both reinfection of the patients as well as development of peptic ulcer disease among the partners, who may be at increased risk by carrying the same, potentially particularly ulcerogenic *H. pylori* strain.

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