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## ***Helicobacter pylori* in out-patients of a general practitioner: prevalence and determinants of current infection**

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### **SUMMARY**

Data on prevalence and determinants of *Helicobacter pylori* infection in well-defined populations are scarce. We investigated the prevalence and determinants of active *H. pylori* infection in a population of out-patients attending a general practitioner in Southern Germany. Infection status was determined by [<sup>13</sup>C]urea breath test. In addition, information on potential risk factors and medical history was collected.

Five hundred and one of the 531 eligible patients participated in the study (response rate of 94·4%). In total, 117 of the 501 patients had a positive [<sup>13</sup>C]urea breath test (23·4%). Prevalence of *H. pylori* infection increased with age from 10·8% (95% CI 5·7–18·1%) in the age group 15–29 years to 30·8% (95% CI 22·1–40·6%) in the age group 60–79 years and was 20·3%, 30·4% and 28·2% for the age groups 30–39, 40–49 and 50–59 years, respectively. Education and childhood living conditions, especially the number of siblings, were identified as additional independent determinants of infection.

### **INTRODUCTION**

*Helicobacter pylori* is one of the most common causes of infection in humans. Acquisition of *H. pylori* infection seems to occur in early childhood and to persist throughout life [1]. Infection with *H. pylori* has been recognized as a major cause of gastric and duodenal ulcers [2, 3] and gastric malignancy [4–7]. The prevalence of infection shows strong regional differences. It is highest in developing countries and it increases with age in most populations [8]. For example, seropositivity in the Eurogast study, a population-based study of 17 geographically defined populations in Europe, North Africa, North America and Japan, was shown to be between 34·9% in the age group 25–34 years and 62·4% in the age group 55–64 years and varied considerably among the various populations [9].

In most previous epidemiological studies infection status has been determined by serological tests which do not allow a clear distinction between current and past infection. Although serological tests show high sensitivity, their specificity is lower than that of tests measuring active infection, such as the [<sup>13</sup>C]urea breath test [10]. Furthermore, serological testing may lead to a falsely positive result in patients who previously received antimicrobial drugs with activity against *H. pylori* for other indications, or in older subjects with atrophic gastritis who may already have lost active infection [11].

The objectives of this study were to determine the prevalence of, and determinants for *H. pylori* infection by means of the [<sup>13</sup>C]urea breath test in an unselected out-patient population attending a general practitioner in Southern Germany.

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## METHODS

### Study population and study design

All out-patients aged 15–79 years who visited the surgery of a general practitioner (GP) at fixed week days from June to September 1996 were invited to participate. The office of the GP was located in a suburban community with approximately 15000 inhabitants near the city of Ulm in Southern Germany. Patients were recruited during the usual office hours, regardless of the reason for their visit. The study was approved by the Ethics Board of the University of Ulm. Informed consent of the patient was obtained in each case.

### Data collection

#### *[<sup>13</sup>C]urea breath test*

Infection status was determined by [<sup>13</sup>C]urea breath test which indicates current infection with *H. pylori*. Breath samples were collected before and 30 minutes after administration of 75 mg non-radioactive labelled [<sup>13</sup>C]urea (Mass Trace, Woburn, USA) in 200 ml of apple juice (pH 2.2–2.4). Breath samples were analysed with an isotope selective non-dispersive infrared spectrometer (NDIRS; Wagner-Analytical-Systems, Worpswede, Germany). A change of the <sup>13</sup>CO<sub>2</sub>:<sup>12</sup>CO<sub>2</sub> ratio over baseline of more than 5‰ was considered positive.

The accuracy of the [<sup>13</sup>C]urea breath test in adults is well documented [12]. Recently, it has been demonstrated that this test shows a perfect concordance with culture and rapid urease test and is therefore ideal for the diagnosis of infection with *H. pylori* [10].

#### *Self-administered questionnaire*

Participating patients were asked to fill out a standardized questionnaire during the office visit. In addition, medical information was taken from the patient's record. In the questionnaire information was sought regarding demographic and socioeconomic factors, medical history including family history and history of medication as well as housing and living conditions. Questionnaire data were checked for completeness and plausibility by trained research assistants.

#### *Statistical analysis*

The proportions of infected patients and 95% confidence intervals were calculated for various age

categories. The bivariate association of variables concerning family demographics, socioeconomic status, housing and living conditions with infection status was assessed after stratification for age and tested for significance using the Mantel–Haenszel  $\chi^2$  test [13]. Furthermore, we assessed the independent effects of various determinants of current *H. pylori* infection by means of multivariate statistical modelling (unconditional logistic regression). The following covariates which had been identified as risk factors for infection in previous studies or which were associated with infection status in our bivariate analyses were included in the initial model: age (in five categories), sex, marital status (single, married, separated/widowed), education ( $\leq 9$  years, 10–11 years,  $\geq 12$  years), number of siblings (0, 1 or 2,  $\geq 3$ ), nationality (German, other), working in the health sector (yes, no). Covariates that did not contribute significantly to the prediction of infection status at a significance level of 0.05 were removed from the model using a stepwise backward elimination strategy.

Eleven patients who had reported *H. pylori* infection in the past and whose infection had been successfully eradicated were excluded from the analysis of current *H. pylori* infection. All statistical procedures were carried out with the SAS statistical software package [14].

## RESULTS

Overall, 501 of the 531 eligible patients participated in the study (response rate of 94.4%). The sociodemographic characteristics of the participants are listed in Table 1.

The main reasons for the self-referred presentation in the GP's office (as recorded by the GP) were chronic back pain or pain of the musculoskeletal system (including myalgia) in 35.4% of the patients. Further medical reasons were utilization of a screening examination in 16.0%, acute infections (mainly of the respiratory system) in 11.4%, allergic diseases or gastrointestinal diseases, both in 6.5% of patients. Overall, 32 patients reported a history of peptic ulcer at some time in the past (6.4%) and 19 patients reported a previous diagnosis of *H. pylori* infection with successful eradication in 11.

In total, 117 of the 504 patients had a positive [<sup>13</sup>C]urea breath test (23.4%, 95% CI 19.7–27.3). The prevalence was 23.9% (95% CI 20.2–27.9%) when the 11 patients whose infection had already been successfully eradicated were excluded. Table 2 shows

Table 1. Sociodemographic characteristics of the study population by sex

Characteristic	Male	Female	All
<i>n</i>	188 (37.4)	313 (62.6)	501
Age (years)			
Mean (s.d)	43.2 (16.0)†	43.1 (15.7)†	43.2 (15.8)†
Range	15–79	15–79	15–79
School education			
≤ 9 years	98 (52.7)	140 (44.7)	238 (47.7)
10–11 years	44 (23.7)	112 (35.8)	156 (31.3)
≥ 12 years	44 (23.7)	61 (19.5)	105 (21.0)
Occupation			
Housekeeping	1 (0.5)	101 (32.3)	102 (20.4)
Employed	114 (60.6)	153 (48.9)	267 (53.3)
Retired	41 (21.8)	24 (7.7)	65 (13.0)
Others	32 (17.0)	35 (11.2)	67 (13.4)
Family situation			
Single	57 (30.3)	79 (25.2)	136 (27.1)
Married	123 (65.4)	196 (62.6)	319 (63.7)
Divorced/widowed	7 (3.7)	38 (12.1)	45 (9.0)

\* Percentages are shown in parentheses unless indicated otherwise.

† s.d.

Table 2. Prevalence of *H. pylori* infection in 501 consecutive patients of a general practitioner according to age

Age (years)	Birth cohort	<i>n</i>	<i>H. pylori</i> positive		
			( <i>n</i> )	(%)	95% CI*
15–29	1967–81	111	12	10.8	5.7–18.1
30–39	1957–66	123	25	20.3	13.6–28.5
40–49	1947–56	92	28	30.4	21.3–40.9
50–59	1937–46	71	20	28.2	18.1–40.1
60–79	1911–36	104	32	30.8	22.1–40.6
Total		501	117	23.4	19.7–27.3
Total†		490	117	23.9	20.2–27.9

\* Denotes 95% confidence interval for proportion of *H. pylori* positive.

† Without *n* = 11 patients whose infection has already been eradicated.

the prevalence of infection in the various age categories. Prevalence of infection was lowest in the age category 15–29 years (10.8%; 95% CI 5.7–18.1) and highest in the age groups above 40, where it was close to 30% with little variation between age groups. An intermediate level of prevalence (20.3%, 95% CI 13.6–28.5%) was seen in the 30–39 year old patients.

Table 3 shows the association of various personal and sociodemographic factors with *H. pylori* infection after stratification for age. No difference was found

for *H. pylori* infection by gender and marital status. The number of children was not significantly associated with infection status whereas the number of siblings the patients had grown up with showed a clear association with infection status in that the proportion of infected subjects increased with the number of siblings ( $P = 0.012$  after stratification for age). This pattern was most obvious in the age group 15–39 years.

Patients with a higher school education showed a tendency towards a lower prevalence of infection ( $P = 0.051$ ). Current housing density (m<sup>2</sup> per person living in household) showed no consistent association with *H. pylori* infection in the various age groups. Foreign patients had a significantly higher prevalence of infection (43.8% vs. 23.2%,  $P = 0.006$ ) although the number of foreign out-patients was very small ( $n = 16$ ).

Table 4 shows the association of other potential risk factors with *H. pylori* infection. Working in the health service sector showed a weak but not significant positive association with *H. pylori* infection ( $P = 0.087$ ). A proxy marker of current hygienic behaviour (sharing a towel with other household members given that more people lived together) showed no significant association with infection status. A history of a stay abroad exceeding 3 months, contact with pets in general, or more specifically contact with dogs or cats were likewise not associated with infection status.

Table 3. Prevalence of *H. pylori* infection (H.p. +) according to personal and family characteristics and living conditions after stratification by age

Risk factor	Age group (years)								*P-value
	15–39		40–59		60–79		All		
	n	H.P. + (%)	n	H.p. + (%)	n	H.p. + (%)	n	H.p. + (%)	
Sex									
Male	85	15.3	57	28.1	41	28.8	183	21.9	
Female	143	16.8	103	31.1	61	34.4	307	25.1	0.405
Marital status									
Single	121	10.7	11	36.4	3	33.3	135	13.3	
Married	102	22.6	128	28.1	80	32.5	310	27.4	
Widowed/separated	5	20.0	20	40.0	19	26.3	44	35.4	0.186
Number of children									
0	139	9.4	26	42.3	7	28.6	172	15.1	
1	29	24.1	31	29.0	24	25.0	84	26.2	
2	39	18.0	70	28.6	39	28.2	148	25.7	
> 2	18	50.0	30	26.7	22	40.9	70	37.1	0.094
Number of siblings grown up with									
0	17	0	25	24.0	10	30.0	52	17.3	
1	88	10.2	38	31.6	21	19.1	147	17.0	
2	62	12.9	38	31.6	14	35.7	114	21.9	
3	29	24.1	17	23.5	16	18.8	62	22.6	
> 3	32	40.6	42	33.3	41	41.5	115	38.3	0.012
School education									
≤ 9 years	75	24.0	92	31.5	70	38.6	233	30.5	
10–11 years	82	14.6	42	33.3	27	18.5	151	20.5	
≥ 12 years	71	9.9	25	20.0	8	37.5	104	14.4	0.051
Occupation									
Housekeeping	24	29.2	37	18.9	38	31.6	99	26.3	
Employed	147	15.6	106	33.0	7	28.6	260	23.1	
Retired	0	0.0	9	55.6	55	32.7	64	35.9	
Others	57	12.3	8	12.5	2	0.0	67	11.9	0.326
m <sup>2</sup> per person living in household									
≤ 21	91	22.0	32	21.9	14	50.0	137	24.8	
> 21–37.5	57	8.8	40	27.5	19	31.6	116	19.0	
> 37.5–50	55	18.2	49	30.6	35	22.9	139	23.7	
> 50	25	8.0	39	38.5	34	32.4	98	28.6	0.418
Nationality									
German	214	14.5	158	29.8	102	31.4	474	23.2	
Other	14	42.9	2	50.0	0	0.0	16	43.8	0.006

\* P-value of Mantel–Haenszel  $\chi^2$  test of general association (pooled over categories of age groups).

Table 5 shows the result of the multivariate analysis. Odds ratios (OR) and 95% confidence intervals (CI) for the relation with *H. pylori* infection were calculated for each variable after adjustment for the others by multiple logistic regression. Only age, nationality and the number of siblings significantly contributed to the prediction of *H. pylori* infection and were retained in the model. As in the bivariate analysis the odds ratio for infection increased up to the age group 40–49

years (OR = 4.1, 95% CI 1.8–9.0) when compared with the age group 15–29 years and levelled off in the age groups 50–59 years (OR = 3.3, 95% CI 1.4–7.8) and 60–79 years (OR = 3.6, 95% CI 1.6–8.0).

The OR for *H. pylori* infection for foreign patients was 4.2 (95% CI 1.4–12.8) when compared with German outpatients. Again, as in the bivariate analysis, the number of siblings showed a statistically significant association with *H. pylori* infection. The

Table 4. Prevalence of *H. pylori* infection (H.p. +) according to various potential risk factors by age

Risk factor	Age group (years)								*P-value
	15-39		4-59		60-79		All		
	n	H.p. + (%)	n	H.p. + (%)	n	H.p. + (%)	n	H.p. + (%)	
Working in the health service sector									
No	191	14.7	148	29.1	102	31.4	441	23.4	
Yes	37	24.3	12	41.7	0	0.0	49	28.6	0.087
Sharing towel with other household members (if more than one person per household)									
Yes	44	15.9	21	14.3	4	25.0	69	15.9	
No	150	17.3	119	31.9	82	32.9	351	25.9	0.199
More than 3 months abroad									
No	200	15.0	149	30.2	93	30.1	442	23.3	
Yes	28	25.0	11	27.3	9	44.4	48	29.2	0.217
Pet in the household									
No	63	20.6	53	32.1	52	38.5	168	29.8	
Yes	165	14.6	107	29.0	50	24.0	322	20.8	0.085
Dog in the household									
No	174	16.1	117	29.1	78	34.6	369	24.1	
Yes	53	15.1	42	31.0	23	21.7	118	22.0	0.596
Cat in the household									
No	154	15.6	107	30.8	80	33.8	341	24.6	
Yes	74	17.6	53	28.3	22	22.7	149	22.2	0.670

\* P-value of Mantel-Haenszel  $\chi^2$  test of general association (pooled over categories of age groups).

Table 5. Adjusted odds ratios (OR) for significant predictors of *H. pylori* infection

Factor	Adjusted OR† (95% CI)
Age (years)	
15-29	*1
30-39	2.3 (1.0-4.9)
40-49	4.1 (1.8-9.0)
50-59	3.3 (1.4-7.8)
60-79	3.6 (1.6-8.0)
Nationality	
German	*1
Other	4.2 (1.4-12.8)
Number of siblings	
0	*1
1	1.2 (0.5-2.7)
2 or 3	1.5 (0.7-3.4)
4 over	2.7 (1.2-6.1)

\* Reference category.

† Adjusted for all variables listed in the table by multiple logistic regression.

OR increased from 1.2 (95% CI 0.5-2.7) in patients with one sibling to OR = 2.7 (95% CI 1.2-6.1) in the category four or more siblings when compared with subjects without siblings (P-value for trend < 0.001).

## DISCUSSION

This study describes the prevalence of *H. pylori* infection as determined by a [<sup>13</sup>C]urea breath test in a sample of 501 consecutive patients visiting the practice of a general practitioner in Southern Germany. Overall, the prevalence of *H. pylori* infection was 23.4%, but there was considerable variation in the various age groups. A clear increase was evident from 10.8% in the age group 15-29 years to 30.4% in the age group 40-49 years. Beyond that age, however, no further increase was seen. In addition, factors reflecting childhood living conditions, such as the number of siblings and nationality, were independent determinants of *H. pylori* infection status.

In contrast to this study, a higher overall level of prevalence and a continuous increase of seropositivity with age was seen in a representative sample of the

German population from three study regions of the Eurogast [9, 15] and in most other studies from European countries [16–20]. The rise of seroprevalence with age most likely reflects a cohort effect resulting from improved childhood living conditions in younger birth cohorts [8, 21].

Differences in demographic and socioeconomic characteristics and geographic variation of *H. pylori* prevalence may explain partly the lower prevalence among older persons in our study population. Alternatively, the lower prevalence of *H. pylori* infection in older age groups found in our study sample may be attributable to the measurement of infection status by [<sup>13</sup>C]urea breath test rather than serologically.

Older patients often suffer atrophic gastritis. It has been shown that positive serology can persist despite the lack of detectable *H. pylori* on histological examination in persons with atrophic gastritis [11]. While *H. pylori* infection is a risk factor for the development of atrophic gastritis [22], there are indications that the prevalence of current *H. pylori* infection may lessen once atrophy has developed [23]. However, this hypothesis requires further study. The possibility that *H. pylori* infection of some older patients may have been incidentally eliminated (and hence be undetected by [<sup>13</sup>C]urea breath test) due to antibiotic treatment for other infections seems unlikely since the effect of monotherapy in adults is very limited [24].

In agreement with previous studies, we found a clear relationship between living conditions in childhood and infection status. Residential crowding may play a key role for transmission within families [25]. Close physical contact in early childhood may promote spread of infection [26] which is further associated with a low level of socioeconomic status and poor living and housing conditions [27, 28].

Other factors characterizing present household conditions, present family size, an occupation in the health service sector, a history of being abroad for more than 3 months, or contact with pets were not relevant determinants of *H. pylori* infection status in this study. Although an occupational risk for *H. pylori* has been described for gastroenterologists [29] and nurses [30], an excess risk for persons working in the health sector in general was not seen in our study. However, the number of subjects working in the health sector and hence the power of our study to detect such an association was very limited.

Although a zoonotic pathway for *H. pylori* infection

has been suggested and some animals harbour other *Helicobacter* species (31) a natural animal reservoir for *H. pylori* has not been identified to date. We did not find an association between contact with pets and *H. pylori* infection.

This study is one of the first to report the prevalence of an out-patient population consulting a general practitioner. The strengths of the study include the very high response rate and the use of the [<sup>13</sup>C]urea breath test to determine infection status. The high sensitivity and specificity of this test allow estimation of the prevalence of current *H. pylori* infection with high accuracy. Although the study population is not representative of the general population, the results should be applicable to patient populations with similar sociodemographic and medical characteristics.

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