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Serological Prevalence of *Helicobacter pylori* Infection in Saxony-Anhalt, Germany, in 2010▽

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Epidemiological studies from different countries have shown a steady decline of the prevalence of *Helicobacter pylori* infection. In order to investigate the current seroprevalence of *H. pylori* infection in the area of Magdeburg, a city of the former East Germany, *H. pylori* antibodies of patients presenting in our emergency wards were analyzed. In total, 2,318 patients (1,181 males and 1,137 females) enrolled between September 2009 and August 2010 were tested for immunoglobulin G (IgG) against *H. pylori* and anti-CagA antibodies by specific enzyme immunoassay (EIA). Patients with either anti-*H. pylori* IgG or anti-CagA antibodies were classified as *H. pylori* positive, whereas the lack of both antibodies led to the assignment of an *H. pylori*-negative status. The overall seroprevalence of *H. pylori* infection was 44.4% (n = 1,029 out of 2,318) and did not differ in relation to sex. The proportion of CagA-positive samples was 43.3% of all *H. pylori*-positive individuals (446 out of 1,029). The seroprevalence showed a birth cohort effect (0 to 20 years of age, 14.6%; 21 to 30 years, 22.4%; 31 to 40 years, 40.6%; 41 to 50 years, 45.5%; 51 to 60 years, 50.8%) up to the age of 60, while it remained between 40.7% and 50.5% for the following decades. Patients younger than 30 years were significantly less *H. pylori* positive (21.1%) than those older than 30 years of age (47.7%; $P < 0.01$), whereas CagA status was similar (44.3 versus 43.3%). Notably, young women (<30 years old) had significantly higher CagA positivity (59.3%) than corresponding men (32.5%; $P = 0.016$). Taken together, seroprevalence of *H. pylori* infection shows a significant drop in subjects born after 1980 in Saxony-Anhalt but still remains in the range of 40 to 50% in subjects born earlier.

Helicobacter pylori infects almost half of the world's population and is associated with various gastroduodenal pathologies including peptic ulcer disease and gastric cancer (1, 2). Epidemiological studies from different countries have shown a steady decline in the prevalence of *H. pylori* infection, with broad variability among different ethnicities. Lowest prevalence rates were reported from Australia and North America (2, 9). European studies reported prevalence rates of *H. pylori* infection between 25 and 60%, whereas the prevalence of the infection in South America and some parts of Asia has been shown to be >80% (2, 7, 9). In the last 15 years epidemiological studies have shown a decline in *H. pylori* infection rates in different industrialized countries including Germany. In studies conducted in the 1980s and early 1990s in the former West Germany including West Berlin, seroprevalence of *H. pylori* infection was 39.2% (for subjects aged 18 to 89 years) (4), 38.2% (age, 17 to 64 years) (25), and 47.2% in adolescents (age, 14 to 18 years) (11). Only one of the cited studies reported the proportion of CagA-positive samples that was 57.6% (4). Studies analyzing active infections by either [^{13}C]urea breath test or antigen stool tests revealed prevalence rates of 34.8% (age, 50 to 85 years) (16) and 21.3% (mean age, 46.6 years) (20). Seroprevalence of *H. pylori* infection was 10% higher in East Germany than in West Germany (48.5% versus 37.9%, respectively) (18). Notably, the largest change in seroprevalence was observed in subjects 60 and 40 years of age in West and East Germany, respectively. The difference between former and new German countries was steady in different age groups but was smallest in young individuals (age, 18 to 29 years), revealing a seroprevalence of 25.4% versus 20.8% (18). Several recent studies have shown a very low prevalence of *H. pylori* infection in young children, adolescents, and young adults (<30 years old) (3, 10, 17, 24). The age-related increase in *H. pylori* prevalence does not represent a steady increase in acquisition but, rather, is a birth cohort phenomenon related to the progressive fall in the rate of acquisition of the infection that has occurred during the past 5 decades.

In order to investigate the current prevalence of *H. pylori* infection in the area of Magdeburg, a city of the former East Germany, we analyzed the seroprevalence of this infection in nonselected patients presenting in our emergency wards with a wide spectrum of disorders. Taking into consideration the proposed role of the CagA pathogenicity island (PAI) in the pathophysiology of this infection (1, 21) as well as the long-lasting persistence of anti-CagA antibodies in serum, two different serological tests (*H. pylori* IgG and CagA antibodies) were applied (i) to allow a comprehensive analysis of the current seroprevalence and (ii) to calculate the proportion of CagA-bearing strains in the infected individuals.

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TABLE 1. Seroprevalence of *H. pylori* infection and CagA-specific IgG in the study cohort

Cohort (age in yr)	No. of subjects	No. of *H. pylori*-positive subjects (%)[a]	No. of CagA-positive subjects (% of *H. pylori*-positive subjects)
All	2,318	1,029 (44.4)	446 (43.3)
0–20	48	7 (14.6)	5 (71.4)
21–30	241	54 (22.4)	22 (40.7)
31–40	185	75 (40.6)	29 (38.7)
41–50	268	122 (45.5)	67 (54.9)
51–60	329	167 (50.8)	72 (43.1)
61–70	371	167 (45.0)	69 (41.3)
71–80	497	251 (50.5)	100 (39.8)
81–90	352	175 (49.7)	77 (44.0)
>91	27	11 (40.7)	5 (45.5)
<30	289	61 (21.1)	27 (44.3)
>30	2,029	968 (47.7)	419 (43.3)

[a] Subjects were considered *H. pylori* positive based on the presence of *H. pylori*-specific IgG (≥30 EIU) and/or the presence of anti-CagA IgG.

MATERIALS AND METHODS

Study design and subjects. The study was approved by the ethical committee of the Otto von Guericke University, Magdeburg, Germany, as an anonymous epidemiological study (number 2009-86). Therefore, the only data of recruited patients available for statistical analyses were age and sex. According to a new standard operating procedure, all patients who were seen in our emergency wards between September 2009 and August 2010 and from whom a blood sample was taken as part of the routine medical workup were included in the study. No further exclusion and inclusion criteria were applied. If laboratory tests were needed, an aliquot of the serum sample sent to the Central Laboratory of the hospital was obtained and separately stored at −30°C until analysis. From September 2009 until August 2010, 2,479 serum samples were collected. Due to multiple recruitments, missing data, or unclear assignment, 161 serum samples were excluded. Finally, serum samples of 2,318 patients (1,181 males and 1,137 females) were available for analysis. Mean age of the study cohort was 60 ± 20.2 years (range, 1 to 103 years; median, 64 years).

Determination of *H. pylori* status. Anti-*H. pylori* IgG and anti-CagA antibodies were analyzed using an *H. pylori* IgG enzyme-linked immunosorbent assay ([ELISA] catalog number 601040; Biohit, Rosbach, Germany) and a CagA IgG kit (GD33; Genesis Diagnostics Ltd., London, United Kingdom), respectively, according to manufacturers' instructions. Based on the presence of *H. pylori*-specific IgG (≥30 enzyme immunounits [EIU]) and/or the presence of anti-CagA IgG (>6,25 U/ml), patients were classified as *H. pylori* positive, whereas the lack of both antibodies led to the assignment of an *H. pylori*-negative status.

Two out of 2,318 patients revealed anti-CagA antibody levels within the gray zone (6.23 to 6.28 U/ml); they were classified based on the cutoff level of 6.25 U/ml. The proportion of CagA-positive infections was calculated on the basis of the *H. pylori*-infected subjects.

Statistical analysis. All data were entered into a database using the MicroCal Origin, version 8.0G, program package (Northampton, MA). Age is shown as means and standard deviations and was analyzed by an unpaired Student's *t* test. Categorical data (e.g., gender or distribution of *H. pylori* status) are presented as frequencies; comparisons were performed using a chi-square test.

RESULTS

Overall, 1,029 individuals out of 2,318 had a positive *H. pylori* status, resulting in a seroprevalence of *H. pylori* infection of 44.4% for the complete cohort (Table 1). The prevalence rates of anti-*H. pylori* IgG in males (533/1,183, or 45.1%) and females (496/1,137, or 43.4%) were similar and did not significantly differ (Table 2). The *H. pylori* seroprevalence showed a rather weak birth cohort effect until the age of 60 years, with a remarkable increase in patients between 30 and 40 years of age (Table 1). While individuals between 21 and 30 years old showed a seroprevalence of 22.4%, patients of the next age group (31 to 40 years) revealed almost a 2-fold increase in seroprevalence (40.6%).

The percentage of subjects with CagA-positive infection in the complete cohort was 43.3% (446 out of 1,029 *H. pylori*-positive individuals) (Table 1) and did not significantly differ between men (41.2%) and women (44.0%) (Table 2). CagA status was rather similar among the different age groups except for the groups of subjects aged 0 to 20 years and 41 to 50 years, which had a high proportion of CagA-positive infections. Notably, a higher prevalence of anti-CagA IgG (54.9%) in the group of subjects aged 41 to 50 years was observed in both genders (male, 53.6%; female, 56.6%). However, the difference in the prevalence of anti-CagA IgG between this and other age subgroups of this cohort did not reach statistical significance. Stratification of individuals according to sex in the different age groups did not reveal significant differences for seroprevalence of *H. pylori* and CagA-positive infections between men and women (Table 2).

Taking into consideration the significant change in *H. pylori* seroprevalence between the groups of subjects aged 21 to 30 years and 31 to 40 years, patients were further stratified in two groups using an age of 30 years as a cutoff. Based on this

TABLE 2. Seroprevalence of *H. pylori* infection and CagA-specific IgG stratified to sex and age

Cohort (age in yr)	*H. pylori* infection prevalence			CagA positivity		
	No. of positive subjects/total no. of subjects (%)		*P* value (χ^2 test)[a]	No. of positive subjects/no. of *H. pylori*-infected subjects (%)		*P* value (χ^2 test)[a]
	Male	Female		Male	Female	
All	533/1,181 (45.1)	496/1,137 (43.6)	NS	228/533 (41.2)	218/496 (44.0)	NS
0–20	4/21 (19.0)	3/27 (11.1)	NS	2/4 (50.0)	3/3 (100)	NS
21–30	30/115 (26.1)	24/126 (19.0)	NS	9/30 (30.0)	13/24 (54.2)	0.07
31–40	47/103 (45.6)	28/82 (34.1)	0.11	17/47 (36.2)	12/28 (42.9)	NS
41–50	69/153 (45.1)	53/115 (46.1)	NS	37/69 (53.6)	30/53 (56.6)	NS
51–60	89/189 (47.1)	78/140 (55.7)	0.12	35/89 (39.3)	37/78 (47.4)	NS
61–70	100/217 (46.1)	67/154 (43.5)	NS	46/100 (46.0)	23/67 (30.3)	0.13
71–80	117/242 (48.3)	134/255 (52.5)	NS	43/117 (36.8)	57/134 (42.5)	NS
81–90	76/135 (56.3)	99/217 (45.6)	**0.05**	39/76 (51.3)	38/99 (38.4)	0.09
>91	1/6 (16.7)	10/21 (47.6)	NS	0/1 (0.0)	5/10 (50.0)	NS
<30	34/136 (25.0)	27/153 (17.6)	0.13	11/34 (32.5)	16/27 (59.3)	**0.016**
>30	499/1,045 (47.8)	469/984 (47.7)	NS	217/499 (43.5)	202/469 (43.1)	NS

[a] *P* values of >0.15 are not shown. *P* values of ≤0.05 (bold) are significant (chi-sequare test). NS, not significant.

stratification, patients younger than 30 years old were significantly less *H. pylori* positive (21.1%) than those older than 30 years (47.7%; χ^2 test, $P < 0.01$), whereas the proportion of CagA positivity was almost identical (44.3% and 43.3%) in both of these groups (Table 1). Notably, CagA positivity was significantly higher in younger females (59.3%) than in men of the same age group (32.5%) (Table 2).

DISCUSSION

Here, we determined an overall *H. pylori* seroprevalence of 44.4% in a region of the former East Germany. This proportion of positive *H. pylori*-related seroprevalence is similar to that reported from other European regions. The prevalence of active *H. pylori* infection was reported to be 41.7% for the Czech Republic in 2006 (6). Seroprevalences of 50.5% and 47% were found in Ireland and Italy, respectively (13, 15). The low *H. pylori* infection rate in children and adolescents found in our study is in line with reports from other areas of Germany (Ulm and Würzburg in south Germany, and Leipzig in East Germany, close to Magdeburg), where *H. pylori* prevalence has been shown to be as low as 4 to 9.4% (3, 10, 24). A prospective study conducted between 2000 and 2002 in individuals between 50 and 74 years of age in the Saarland (south Germany) revealed an overall seroprevalence of 52.6% (8) and a proportion of serological CagA positivity of 55.2% (22); both rates are higher than those of this study conducted almost 10 years later. There are no plausible explanations for the observed trend of higher CagA positivity in the group of very young individuals (<20 years old) and the group of subjects 41 to 50 years of age. Whether these findings are caused by low numbers (in particular for the younger individuals) or reflect a pathophysiological phenomenon (e.g., higher infectious rates of CagA-positive strains) cannot be concluded. Since the two serological tests applied in the present study detect different antibodies, both patients with anti-*H. pylori* IgG and anti-CagA antibodies were classified as *H. pylori* positive. As CagA antibodies can persist in serum for a long time also after seroconversion for general anti-*H. pylori* IgG (23), patients were considered *H. pylori* positive also in the case of sole positivity for anti-CagA antibodies. In this cohort, only 97 of the 1,029 patients classified as *H. pylori* positive (9.4%) had anti-CagA antibodies but no anti-*H. pylori* IgG in serum, whereas 91.6% of individuals classified as *H. pylori* positive had anti-*H. pylori* IgG. This aspect needs to be considered if *H. pylori* seroprevalences are compared among various studies. In the present study more than half of the *H. pylori*-positive individuals (about 56%) were found to be infected with CagA-negative strains. In a study from the 1980s conducted in West Germany in a population with similar ages as ours, a much higher prevalence of anti-CagA antibodies (57.6%) was found (4). As the presence of CagA is associated with a more prominent gastric inflammation and an increased risk of developing peptic ulcer gastric adenocarcinoma (1, 21), the decreased prevalence of anti-CagA antibodies may account for a reduced proportion of patients with *H. pylori* infection that will develop a symptomatic outcome of the infection in the future.

In the present study young women were found to be predominately infected with a CagA-positive strain. Since this finding is based on a small group of study participants, a prospective study including a larger number of young subjects is need before general conclusions can be drawn.

Previous reports demonstrated a linear birth cohort effect of *H. pylori* seroprevalence (6, 7, 9, 12–14) in other populations. In our study such an effect was not completely reproducible. Indeed, seroprevalence almost doubled in patients aged between 30 and 40 years compared to rates in those younger than 30 years, while a slight increase in subjects up to the age of 60 years was observed. The steep decrease of *H. pylori* seroprevalence in subjects younger than 30 years of age observed in our study is remarkable and most likely related to the major socioeconomic changes that occurred in the 1970s in the former East Germany. In fact, a comprehensive housing program was initiated in 1972, leading to the construction of large apartment complexes with centralized heating, water supply, and sewage disposal. In line with this program, in the period from 1975 to 1982 the birth rate in the former East Germany strongly increased (from 1.5 children/woman to 1.7 to 1.95 children per woman), whereas in West Germany the number of children/woman was lower, between 1.3 and 1.4 children per woman (19). In general, an inverse association between *H. pylori* transmission and improved housing and general levels of household hygiene has been observed. Taking into account that the primary caregiver (usually the infected mother) (24) is the main source of transmission of *H. pylori* infection, one may speculate that the introduction of the housing program together with the improvement in hygiene led to the strong decline in *H. pylori* seroprevalence in individuals born in this period. Since these changes happened in the whole of East Germany from 1975 to the 1980s, a similar reduction of *H. pylori* prevalence can be expected also in other areas as well; however, no other studies concerning *H. pylori* seroprevalence in former areas of East Germany are currently available. There is no doubt that simultaneously with this housing program other relevant socioeconomic factors affecting the transmission of *H. pylori*, including the improvement of health care systems (e.g., availability of antibiotics), have probably contributed to the decline of *H. pylori* seroprevalence in the group of younger individuals. Notably, for a limited time, the improvement in socioeconomic conditions led to a remarkable increase in the birth rate in the former East Germany. This phenomenon may have further facilitated the decline in *H. pylori* prevalence in this generation.

Furthermore, it should be noted that the seroprevalence of *H. pylori* infection overestimates the rate of current infections as seroconversion after successful eradication of *H. pylori* infection may take several years. A previous study analyzed the concordance between serology (anti-*H. pylori* IgG) and an antigen-based stool test for detecting *H. pylori* infection in patients from Germany with similar ages as our cohort and found that 83% of seropositive individuals had active infections (5). Based on these data, the estimated current prevalence of an active *H. pylori* infection in Saxony-Anhalt might be around 35%.

Due to the study design, an assessment of previous antibiotic therapies as well as other demographic data that are known to be associated with *H. pylori* infection (e.g., education, size of the household, and numbers of siblings) was not possible.

Altogether, we conclude that *H. pylori* infection is still frequent in the area of Saxony-Anhalt, in particular for individ-

uals older than 30 years of age, where it can be detected in about half of the population. The strong decline in *H. pylori* seroprevalence in individuals born in the 1970s and later reflects the major socioeconomic changes that occurred in the former East Germany during this period.

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