Impact of migration on helicobacter pylori seroprevalence in the offspring of Turkish immigrants in Germany

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SUMMARY: Porsch-Özcürümez M, Doppl W, Hardt PD, Schnell-Kretschmer H, Tuncay M, Akıncı A, Bilgin Y, Klör H-U. Impact of migration on Helicobacter pylori seroprevalence in the offspring of Turkish immigrants in Germany. Turk J Pediatr 2003; 45: 203-208.

Helicobacter pylori (H. pylori) infection rates differ markedly between distinct populations. Consistent with previous findings of high seroprevalences in less developed countries, Turkish people have been reported to constitute a high-risk population. H. pylori prevalence rates have tended to be lower in Turkish individuals living in Germany for more than one generation.

We conducted a seroepidemiological study to determine the impact of ethnicity, environmental setting, and sociodemographic factors on H. pylori seropositivity. Three subgroups were recruited encompassing 675 Germans (402 males, 273 females), 260 Turkish people born and raised in Germany (145 males, 115 females) and 148 Turkish people living in Turkey (91 males, 57 females), Ages ranged from newborn to a maximum of 30 years in all subgroups. H. pylori immunoglobulin G serum antibodies were determined by a commercial ELISA.

H. pylori age-adjusted overall seroprevalence clearly differed between Germans (13.1%) and Turkih subgroups, with prevalences of 30.4% (Turks in Germany) and 44.5% (Turks in Turkey) seropositive individuals ($p<0.001$). Infection occurred at a younger age in Turks independent of country. Besides age, ethnicity was the only independent and significant predictor of H. pylori seropositivity using multiple logistic regression analysis (odds ratio 2.5; 1.3-5.0 95% confidence interval CI). Place of residence and number of children tended to influence H. pylori seroprevalence but without achieving statistical significance.

Our data suggest that high H. pylori seroprevalence in Turkish people depends on factors that are only insignificantly influenced by migration. The causal environmental factors within this cohort and/or sociocultural practices that perpetuate and encourage the spread of infection remain to be identified.

Helicobacter pylori (H. pylori) was cultured for the first time by Warren and Marshall in 1983[1]. Since that time, it has been recognized as one of the most common infections in the world and it is accepted as a cause of type B gastritis and duodenal and gastric ulcer as well as a risk factor for gastric cancer[2]. The route of H. pylori transmission, its natural history after initial infection, and factors defining disease severity are currently being investigated. A wide geographical variety of H. pylori prevalence has been reported, with high levels in developing countries and lower rates in developed countries[3], in particular between different ethnic groups[4]. Reasons for the ethnic predilection are not entirely clear. Genetic factors may account for these differences[5]. Ethnic differences may also be a surrogate marker for different environmental exposures within the community. Low socioeconomic status and crowded living conditions commonly associated with poor hygienic conditions have

been suggested as major risk factors facilitating H. pylori infection in less developed countries. However, the high variations within and between these countries implies that certain sociocultural practices influence infection to some extent.

Turkish people have been reported as a high-risk population for H. pylori infection[6,7]. Prevalence rates of more than 80% before the age of 40 make H. pylori infection an important health problem in Turkey[6]. However, no longitudinal epidemiological data are available investigating H. pylori prevalence over a longer period. Thus, the kinetics of H. pylori prevalence in a defined cohort as a function of improved socioeconomic conditions are unknown. An alternative approach to assess the impact of westernized living conditions might be to study Turkish people who migrated to more industrialized countries. Since the early sixties there has been a significant migration of Turkish people to Germany. Most of these individuals remained in Germany, so that three generations presently comprise more than 2,000,000 individuals. As a consequence of modified living conditions we observed unfavorable changes in lipid profiles and an increased prevalence of coronary heart disease in this population[8].

The aim of the present study was to determine the impact of different environmental settings on H. pylori seroprevalence, comparing the offspring of Turkish immigrants with Turkish people living in Turkey and with Germans.

Material and Methods

Subjects

The study included 675 Germans (402 males, 273 females), 260 Turkish people living in Germany (145 males, 115 females) and 148 Turkish people living in Turkey (91 males, 57 females). Ages ranged from newborn to a maximum of 30 years in all subgroups (Fig. 1).

Subjects living in Germany were recruited and interviewed after presenting to the Central Laboratory of the University Hospital at the University of Giessen for different laboratory tests, while Turkish people living in Turkey were recruited at the Central Hospital in Diyarbakır. All Turkish people recruited in Giessen were born in Germany. Children and adults taking antimicrobial drugs during the last three months before the study, those taking immunosuppressive or chemotherapeutic drugs, and subjects with primary or

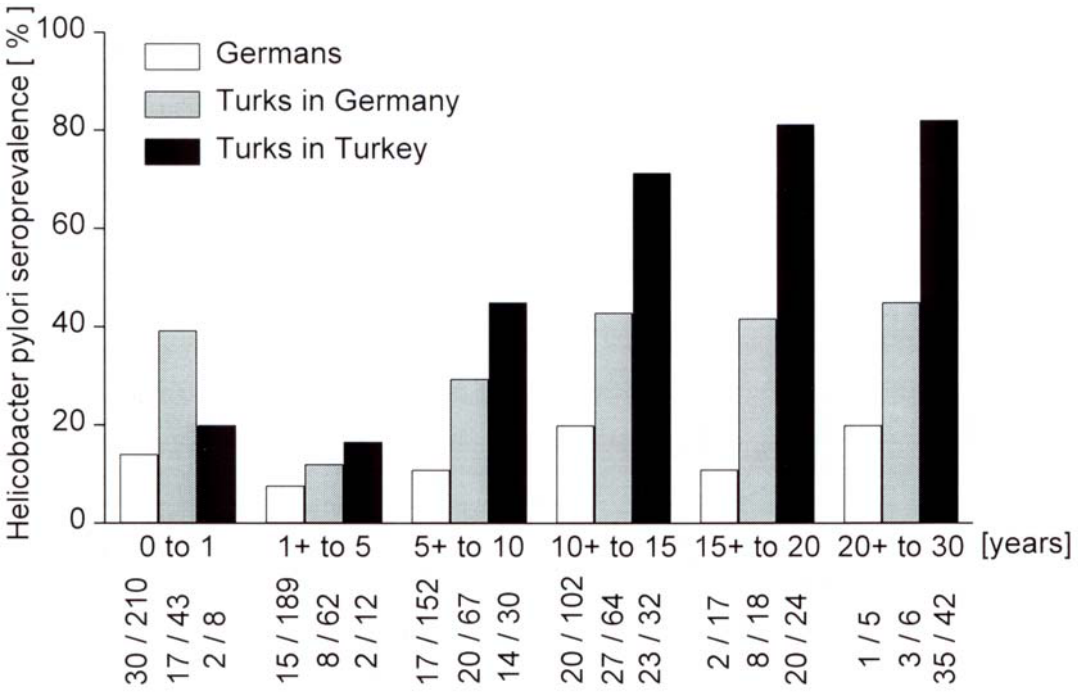

Fig. 1. H. pylori seropositivity comparing Turkish and German individuals stratified by age groups. Numbers under bars indicate positive cases/overall cases in each age group.

secondary immunodepression were excluded. All participatnts' symptoms were unrelated to gastroduodenal disease. Before blood collection parents or responsible persons and/or the recruited individual responded to a questionnaire requesting information about age, sex, use of medication, and their familial situation.

The study was approved by the local Ethics Committees. Informed consent to participate in the study was obtained from the patients, and their parents or guardians.

Laboratory Analysis

Serum samples were stored at –20°C until assayed. Frozen samples from Turkey were sent to Germany for analysis. H. pylori immunoglobulin G serum levels were determined by a commercially available heterogeneous solid phase enzyme immunoassay using microtiter plates (Pharmacia & Upjohn Diagnostics, Freiburg i. Br., Germany). The assay was performed according to the instruction of the manufacturer. Serum levels >10 U/ml were considered as H. pylori seropositive.

Statistical Analysis

The Statistical Package for the Social Science (SPSS for Windows 7.5) was employed for statistical analyses. Differences between subgroups were tested by non-parametric Mann-Whitney U test for independent samples Multiple logistic regression analysis was performed in order to evaluate the independent effect of parameters investigated with respect to H. pylori seropositivity. All analyses performed were two-sided and p values <0.05 were considered as statistically significant.

Results

H. pylori age-adjusted overall seroprevalence was significantly different between Germans (13.1%) and Turkish subgroups, with 30.4% seropositive individuals in Germany and 44.5% in Turkey ($p<0.001$). Strafication by age group (Fig. 1) showed the initial disapperance of maternal H. pylori specific immunoglobulin G within the first year in all subgroups. In the age group from newborn to 12 month the average age of Turkish children living in Germany tended to be lower compared to the corresponding subgroups. Thus, maternal antibodies more likely contributed to serum levels. Consequently, the prevalence of seropositive children was biased to higher levels in this subgroup.

Differences between the H. pylori immunoglobulin positivity rates of the subgroups constantly increased with increasing age. German children remained at a low prevalence level. Peak levels were reached in the 10 to 15 years of age subgroup, with 20% seropositive German children. In contrast, Turkish children showed an earlier and evidently more pronounced increase of H. pylori seropositivity, with a plateau after the age of 15 years. While adolescent and adult Turkish individuals living in Germany exhibited seroprevalences of more than 40%, the corresponding subgroups in Turkey showed more than 80% seropositvitiy.

Considering the relation between age and H. pylori seropositivity, we further evaluated the correlation between age of parents at delivery, the number of siblings and the rank of children among their siblings (Table I). No differences were evident regarding seropositivity related to age of parents or rank within siblings. Average family size was larger in Turkish individuals, in particular in Turkey, and paralleled the differences in H. pylori seroprevalence between subgroups. Mean number of siblings tended to be higher in seropositive individuals in all subgroups. However, statistical significance was reached only in Turks living in Germany. Figure 2 depicts a steady increase of H. pylori seroprevalence with the number of siblings in Germans and Turkish offspring in Germany. In contrast, no linear association was seen in individuals living in Turkey. Logistic regression analysis was performed in order to assess the impact of demographic factors, ethnicity, and family structure on H. pylori seropositivity (Table II). Univariate analysis revealed the highest odds ratio for the place of residence (e.g. Germany or Turkey), followed by ethnicity and number of children. Age and rank within children had only a minor but significant effect on H. pylori seropositivity. In order to exclude biases, in particular those caused by age-dependent variables such as number of children, a multivariate logistic regression analysis was performed. Using this approach only age and ethnicity remained statistically significant. Ethnicity was the main predictor for H. pylori seropositivity with an odds ratio of 2.5 (1.3-5.0), followed by age as a minor but still significant explanatory variable. Number of children and place of residence tended to contribute to H. pylori seropositivity, but

Table I. Influence of Sociodemographic Factors on H. pylori Seropositivity

	Turks				Germans	
	in Germany		in Turkey			
	Negative n=181	Positive n=79	Negative n=54	Positive n=94	Negative n=591	Positive n=84
Age of mother at birth (5.7)	25.2 (6.3)	28.2 (7.0)	28.6 (11.5)	27.6 (8.6)	26.9 (4.9)	2 7 . 4
Age of father at birth (5.3)	28.1 (6.2)	30.9 (7.3)	30.8 (8.3)	29.9 (10.0)	30.4 (6.2)	2 9 . 7
Number of children	1.7[a] (2.0)	2.6[a] (2.0)	3.3 (2.3)	3.5 (2.5)	1.1 (1.0)	1.2 (1.0)
Rank within siblings	2.2 (1.6)	2.8 (1.7)	2.5 (1.1)	3.2 (1.9)	1.8 (1.0)	1.8 (0.9)

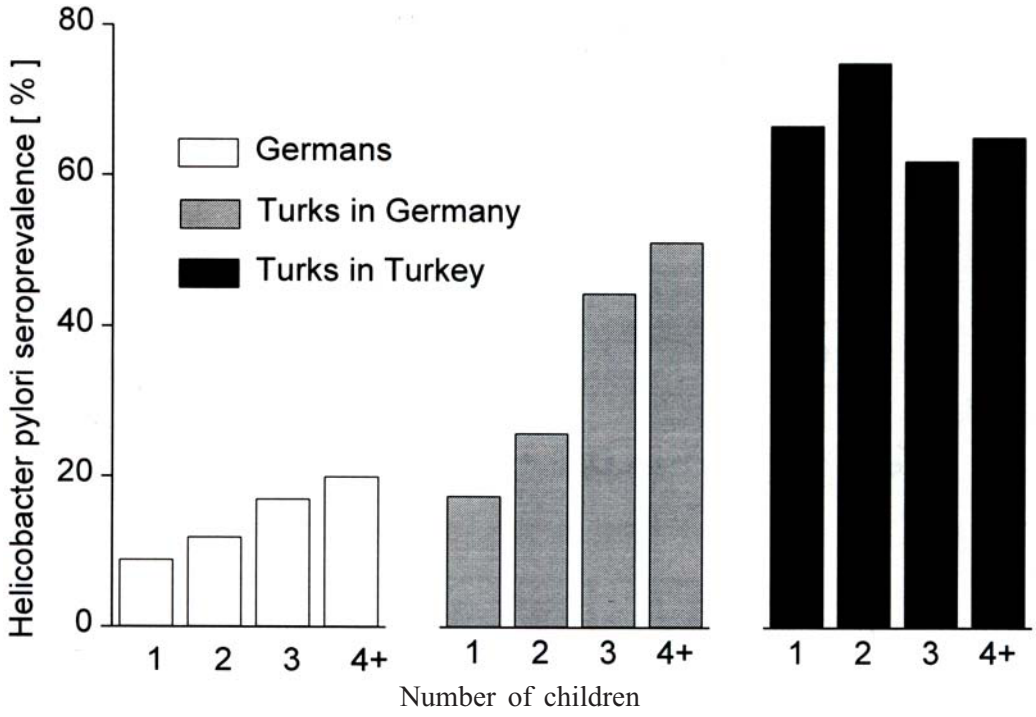

Fig. 2. Influence of number of children on H. pylori seroprevalence.

Table II. Logistic Regression Analysis Testing the Relationship Between Sociodemographic Factors, Ethnicity, and Helicobacter pylori Seropositivity.

	Unadjusted		Adjusted[a]	
Variable	OR (95% CI)	p value	OR (95% CI)	p value
Age of proband	1.082 (1.064-1.101)	>0.001	1.059 (1.005-1.116)	0.032
Ethnicity	5.031 (3.767-6.720)	>0.001	2.516 (1.265-5.003)	0.008
Place of residence	7.776 (4.880-12.390)	>0.001	2.371 (0.849-6.618)	0.099
Age of mother at birth	1.024 (0.984-1.067)	0.246	1.036 (0.963-1.115)	0.341
Age of father at birth	1.000 (0.964-1.038)	0.993	0.975 (0.911-1.044)	0.467
Number of children	1.676 (1.331-2.110)	>0.001	1.495 (0.968-2.311)	0.070
Rank within siblings	1.321 (1.116-1.564)	0.001	0.866 (0.631-1.190)	0.376

[a] Variables were adjusted for all remaining parameters listed in the table.

without statistical significance (p=0.07 and 0.1, respectively).

Discussion

Several seroepidemiological studies in developing countries have shown a high H. pylori infection rate in childhood[9,10]. In contrast, reports from developed countries indicate a significantly lower prevalence of H. pylori, suggesting that infection may be related in part to socioeconomic status and living conditions. Additionally, there are indications that genetic factors may be important in this context, explaining the ethnic tropism of H. pylori[11]. Turkish people have been reported as a high-risk population[6,7]. Due to the high migration rate to more industrialized countries over the past 40 years, the Turkish population is ideal for assessing the impact of different environmental settings regarding H. pylori infection. We therefore compared serological data of German children and adolescents with Turkish people born and raised in Turkey and Germany.

One potential limitation of the study was the lack of information about the area of Turkey from which Turkish people in Germany migrated. This information might have been of interest, since there are also geographical differences of H. pylori seroprevalence in Turkey with the Diyarbakır region having a high positivity rate. Nevertheless, our results were in accordance with previous studies that separately investigated these subgroups in preschool children[7,12]. Additionally, we extended the age range up to 30 years. Turkish children and adolescents living in Germany showed a significantly lower H. pylori seroprevalence than those in Turkey, but still more than two-fold higher than German individuals. The difference in prevalence was most pronounced in the age groups older than 10 years irrespective of country. German children showed a delayed and less obvious increase at the age of 10 to 15 years.

These data suggest that the acquisition of infection may depend on distinct or differently pronounced genetic and/or peristaltic factors. According to proposed transmission routes, transmission within the family is of central importance. Goodman et al.[13] found a strong association between birth order, birth space, and infection status of siblings in Andean children younger than 10 years. These factors were enhanced by the number of older siblings. In our population, there was a tendency to larger family size in seropositive children in all subsets, but only in Turkish children living in Germany was statistical significance reached. The rank within siblings tended to be higher in H. pylori infected Turkish individuals, while no association was seen in German subjects. In accordance with these data, univariate logistic regression analysis of sociodemographic parameters revealed that number of children and rank within siblings predicted seropositivity. However, after including all sociodemographic variables in a multiple logistic regression analysis, only ethnicity and age of children remained significant predictors. Place of residence had only an insignificant impact. These data implicate that the high seroprevalence in Turkish individuals depends no specific ethnic factors. Turkish people have a 2.5-fold increased risk of H. pylori infection even after adjustment for other risk factors. Increased seropositivity in a population sharing the same environmental setting with subjects showing consistently lower H. pylori prevalence rates points to an ethnic cohort phenomenon as already reported for other ethnic groups[14]. Environmental factors within an ethnic group and/or sociocultural practices peculiar to a racial group may perpetuate and encourage the spread of infection within the group. Since H. pylori infection is not highly contagious and requires close proximity, as within a family or a community, it is conceivable that the reservoir of infection is grandparents or even young parents starting at the age of 20 years[15,16]. Consistent with this hypothesis, Turkish people in Germany still remain fairly separated from the German population within large clans, resembling living conditions in Turkey. However, sanitation is improved and standards of living are increased in comparison with Turkey. Another underlying factor may be the tradition that almost all Turkish families living in Germany visit their homeland at least once a year and generally spend one month in Turkey. A more hypothetical mechanism that might contribute to higher H. pylori susceptibility, which has not been investigated in a Turkish population, emerges from the observation that alcoholic beverages have antimicrobial effects against H. pylori

in vitro[17]. The high seroprevalence is further maintained by a marked reinfection rate among Turkish people after eradication therapy[6].

Prevention of H. pylori infection could be optimized by discovery of the source of predilection for certain ethnic groups. This would then enable a cost-effective approach to lower the direct and indirect economic impact of gastritis and duodenal ulcer disease[18], and last but not least cancer. Furthermore, it is controversial as to whether or not H. pylori is a pathogenic factor involved in atherogenesis[19]. There is also evidence that H. pylori infection might be one of the environmental factors causing constitutional delay of growth and puberty[20].

The insignificant impact of living in an industrialized country for two or three generations implies that according to the cohort theory, prevalence rates mainly depend on the reservoir of infection among Turkish parents. Even though we did not investigate intra-familial clustering, there is strong evidence from other studies that H. pylori is transmitted from parent to child[15]. We also did not investigate socioeconomic status, which is one of the major risk factors for the acquisition of H. pylori. Our study, which compared for the first time these three populations over a relatively wide age range, encourages conduction of surveys that elucidate in detail the differences between these populations with regard to socioeconomic factors contributing to H. pylori infection. Such an effort might be helpful to distinguish between risk influenced by socioeconomic status and that by specific traditions of the different ethnicities.

Thus, we conclude that eradication of H. pylori in parents is mandatory to achieve a long-lasting decrease in H. pylori infections in high-risk populations. Study of the Turkish cohort in Germany offers opportunities to further elucidate the mode of H. pylori transmission and prevalence rates after improvement of living conditions.

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