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• *BRIEF REPORTS* •

Helicobacter pylori serology in a birth cohort of New Zealanders from age 11 to 26

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Abstract

AIM: To determine seroprevalence of *Helicobacter pylori (H pylori)* in the Dunedin Multidisciplinary Health and Development Study (DMHDS) at age 26 in order to investigate seroconversion and seroreversion from age 11 to 26 and the association of seropositivity with risk factors for *H pylori* infection.

METHODS: Participants in the DMHDS at age 26 and retrospectively at age 21 were tested for *H pylori* antibodies using two commercially available ELISA kits. Gender, socioeconomic status (SES), smoking, educational attainment and employment at age 26 were tested for association with *H pylori* seropositivity.

RESULTS: At ages 21 and 26, seroprevalence of *H pylori* using one or other kit was 4.2% (n = 795) and 6.3% (n = 871) respectively. Seroreversion rate was lower than seroconversion rate (0.11% *vs* 0.53% per person-year) in contrast to the period from age 11 to 21 when seroreversion rate exceeded seroconversion rate (0.35% *vs* 0.11% per person-year). Serology in those tested at ages 11, 21, and 26 remained unchanged in 93.6% of the sample. Seroprevalence at age 26 was lower among those with a secondary school qualification (P = 0.042) but was not associated with gender, SES, smoking or employment status.

CONCLUSION: *H pylori* seroprevalence in a New Zealand birth cohort remains low between ages 11 and 26. *H pylori* infection remains stable from childhood to adulthood although seroreversion seems to be more common in the adolescent years than in young adults.

Key words: *H pylori*; Seroprevalence; Cohort

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INTRODUCTION

Helicobacter pylori (*H pylori*) is one of the most common bacterial infections in the world[1] and is now recognized as the main acquired factor in the pathogenesis of duodenal ulcer disease[2]. *H pylori* acquisition (i.e., seroconversion) occurs at any age but chiefly during childhood[3]. Infection in adulthood appears to be stable and is unlikely to be resolved unless suitable antimicrobial treatment is sought[4,5]. Thus, although age is a risk factor for *H pylori* infection[6], the apparent increase in seroprevalence in a given population mainly arises from a cohort effect (increasing risk of exposure associated with earlier year of birth)[5,7]. *H pylori* infection appears to be declining in developed countries probably due to a decreasing rate of childhood infections associated with improved hygiene and socioeconomic circumstances.

Of the many factors that have been investigated for their possible association with *H pylori* infection, age, lower socioeconomic status (SES), and possibly ethnicity are important, but gender, alcohol, and cigarette use are of less significance[2]. The natural history of *H pylori* infection remains poorly characterized particularly in relation to the question of spontaneous seroreversion. In our study of the DMHDS birth cohort, seroprevalence of *H pylori* antibodies was low, decreasing from 6.6% at age 11 to 4.1% at age 21[8,9]. We were interested to determine if this decline in seroprevalence continued on into early adulthood and accordingly studied *H pylori* seroprevalence as the birth cohort turned 26 in 1998-1999.

MATERIALS AND METHODS

Participants

The Dunedin Multidisciplinary Health and Development Study (DMHDS) was established in 1975-1976 when the families of 1 037 children born at Queen Mary Hospital, Dunedin in 1972-1973 agreed to participate[10]. Cohort families represented the full range of SES in the general population of New Zealand's South Island and were predominantly Caucasians. The cohort has been studied every 2 years from age 3 to 15 and again at ages 18, 21, and 26 but blood collection was only carried out at ages 11, 21, and 26. Of

the total sample remaining at age 26 (n = 1 019; 525 males, 494 females), 980 study members (499 males, 481 females) were seen around the time of their 26th birthday. Approval to collect blood was obtained from 882 of these study members (452 males, 430 females), a consent rate of 90%. The study was approved by the Ethics Committee of the Otago District Health Board, and each study member gave informed consent for the donation of a blood sample.

H pylori testing

Serum was collected and stored at -80 ℃ until tested for anti-*H pylori* IgG antibodies using two commercial ELISA kits: the Cobas® Core Anti-*H pylori* EIA (Roche SA, Basel, Switzerland)[11] and the *H pylori* DTect ELISA (Diagnostic Technology, Australia)[12]. The Cobas kit was used in our previous studies[8,9] and has been validated in New Zealand against the urea breath test in 123 subjects with dyspepsia (sensitivity 100%, specificity 87%)[13]. The *pylori* DTect kit has been validated in Australia against *H pylori* status as defined by biopsy in 209 patients with dyspepsia and reflux symptoms (sensitivity 96%, specificity 94%)[12]. Serum samples for testing with the Cobas and *pylori* DTect kits were available for 854 and 870 study members respectively. Stored serum samples collected at age 21 (previously tested with the Cobas kit in 1994) were available for retrospective testing with the *pylori* DTect kit for 764 study members (402 males, 362 females). A total of 755 study members (401 males, 362 females) had serology at ages 21 and 26, and 452 (256 males, 196 females) had serology at ages 11, 21, and 26.

Statistical analysis

Data were analyzed using Stata 7.0 (Stata Corporation, College Station, TX, USA) and differences evaluated by Student's t-test or Pearson's χ^2-test. Seroprevalence at ages 21 and 26 was defined as the number of persons who were seropositive by one or both tests in recognition of the fact that no single antigen is recognized by sera from all subjects in a given population[14]. Level of agreement between tests was indicated by the κ statistics, where $\kappa = 0$ reflects agreement at chance level and $\kappa = 1$ reflects perfect agreement. Confidence intervals (95%CI) of prevalence estimates were based on the binomial distribution. SES was based on the Elley-Irving category of the father when sample members were aged 5 (low, unemployed and categories 5 and 6; medium/high, categories 1-4)[15]. Employment status was based on employment at the time of interview at age 26. Smoking status was based on the number who had smoked daily for at least 1 mo in the previous year. Educational attainment was based on the number with a secondary school qualification.

RESULTS

The number of seropositive and seronegative males and females and the seroprevalences determined by the two kits at ages 21 and 26 are shown in Table 1. At age 26, a total of 55 study members was seropositive by one or both kits, a seroprevalence of 6.3% (95%CI 4.7-7.9). The two kits had 34 seropositivities in common, suggesting good agreement between tests (κ = 0.75, 95%CI 0.68-0.82). At age 21, a total of 33 study members was seropositive by one or both kits, a seroprevalence of 4.2% (95%CI 2.8-5.5). The two kits had 19 seropositivities in common, again suggesting good agreement (κ = 0.74, 95%CI 0.67-0.81). Seroprevalence of *H pylori* using the Cobas kit was higher than that using the *pylori* DTect kit at both ages, but increase in seroprevalence from age 21 to 26 was slightly greater for the DTect kit (2.2%) than for the Cobas kit (1.4%).

Seroprevalence at age 26 in relation to risk factors is given in Table 2. Seroprevalence was higher in males, daily smokers and those in employment but the differences were not significant. Seroprevalence was not associated with SES but was significantly lower in those with a secondary school qualification than those without the qualification (P = 0.042).

The distributions of DMHDS members (total, male and female) among the four categories of serology (stable positivities, stable negativities, seroconverters, and seroreverters) at ages 21 and 26 (n = 755) and among the eight categories of serology

Table 2 Seropositivity of *H pylori* infection in the DMHDS at age 26 in relation to risk factors

	n	Number of seropositivities (%)	Significance by χ^2-test
Gender			
Male	451	35 (7.8)	0.069
Female	420	20 (4.8)	
SES at age 5			
High	580	37 (6.4)	NS
Low	237	15 (6.3)	
Daily smokers			
Yes	343	26 (7.6)	NS
No	528	29 (5.5)	
Secondary school qualifications			
Yes	704	42 (5.6)	0.042
No	112	13 (10.4)	
Employment			
Yes	654	44 (6.7)	NS
No	217	11 (5.1)	

Table 1 *H pylori* serology (as determined with Cobas® and *pylori* DTect ELISA kits), gender, and seroprevalence in the DMHDS at ages 21 and 26

Test	Age (yr)	n	Seropositivity		Seronegativity		Seroprevalence (95%CI)
			Males	Females	Males	Females	
Cobas	21	785	24	8	389	364	4.1 (2.7-5.5)
DTect	21	764	15	5	387	357	2.6 (1.5-3.7)
Both tests	21	795	24	9	394	368	4.2 (2.8-5.5)
Cobas	26	854	32	15	412	395	5.5 (4.0-7.0)
DTect	26	870	28	14	422	406	4.8 (3.4-6.2)
Both tests	26	871	35	20	416	400	6.3 (4.7-7.9)

at ages 11, 21, and 26 (n = 452) are presented in Table 3. Seroconversion and seroreversion rates from age 21 to 26 were 0.53% and 0.11% per person-year respectively. In those tested at ages 11, 21, and 26, corresponding rates were 0.44% and 0.04% per person-year respectively. From age 11 to 21, seroconversion and seroreversion rates in this subset were 0.11% and 0.35% per person-year respectively.

Table 3 Distribution of categories of *H pylori* serological status (A) in the DMHDS between ages 21 and 26 (n = 755), and (B) across ages 11, 21, and 26 (n = 452). Seropositive status is indicated by "+"; seronegative status by "-"

A. *H pylori* serological status between ages 21 and 26 (n, %)

Status at ages		Males (n = 401)	Females (n = 354)	Total (n = 755)
21	26			
+	+	20 (5.0)	8 (2.3)	28 (3.7)
+	-	4 (1.0)	0 (0)	4 (0.5)
-	+	11 (2.7)	9 (2.5)	20 (2.6)
-	-	366 (91.3)	337 (95.2)	703 (93.1)

B. *H pylori* serological status across ages 11, 21, and 26 (n, %)

Status at ages			Males (n = 256)	Females (n = 196)	Total (n = 452)
11	21	26			
+	+	+	11 (4.3)	2 (1.0)	13 (2.9)
+	+	-	0 (0)	0 (0)	0 (0)
+	-	+	0 (0)	2 (1.0)	2 (0.4)
+	-	-	6 (2.3)	8 (4.1)	14 (3.1)
-	+	+	3 (0.5)	1 (1.2)	4 (0.9)
-	+	-	1 (0.4)	0 (0)	1 (0.2)
-	-	+	4 (1.6)	4 (2.0)	8 (1.8)
-	-	-	231 (90.2)	179 (91.3)	410 (90.7)

The number of individuals who seroreverted from age 11 to 21 (16/29) was much higher than from age 21 to 26 (1/18). SES, smoking, and employment were not associated with either seroconversion or seroreversion. However, both females and those who attained secondary school qualifications were more likely to serorevert between ages 11 and 21 (gender: females [10/12, 83.3%], males [6/17, 35%], $\chi^2 = 6.6$, $\gamma = 1$, $P<0.05$; without qualification [0/4, 0%], with qualification [16/25, 64%], $\chi^2 = 5.7$, $\gamma = 1$, $P<0.05$).

DISCUSSION

This study used two commercially available ELISA kits to estimate *H pylori* seroprevalence in the DMHDS at ages 21 and 26. The manufacturers' recommended cut-off values were used to divide positive from negative results. The cut-off values are specifically chosen by the manufacturers to err on the side of sensitivity rather than specificity in order to reduce the likelihood of false negative results and enhance the detection of both previous and current infection[12,13]. Seroprevalence was higher with the Cobas kit which probably reflected the fact that, compared with other kits, Cobas has been shown to have somewhat lower specificity[16]. Despite the discrepancy between the two kits, it is clear that seroprevalence in the DMHDRU was very low at age 11 and remained low through to age 26.

In the interval from age 21 to 26, the increase in seroprevalence in the DMHDS from 4.2% to 6.3% reversed the trend downwards in seroprevalence from 6.6% to 4.2% in the interval from age 11 to 21. Whilst the decrease in seroprevalence from age 11 to 21 may reflect some process peculiar to the adolescent years, the possibility that the fluctuations simply resulted from measurement error could not be ruled out[17]. What is clear is that the vast majority of study members (93.6%) remained stable with respect to serological status from age 11 to 26 in line with the results of other studies of paired serum samples showing that serological status remains essentially constant over many years[4-7]. Seroprevalence in a given cohort is therefore mainly determined in childhood and risk of acquisition in adulthood is relatively low[6]. In general practice, this implies that patients with *H pylori* who undergo successful eradication therapy but have subsequent gastrointestinal problems are unlikely to benefit from further *H pylori* testing and eradication therapy.

Despite the fact that *H pylori* infection is generally associated with lower SES, this association was weak in the DMHDS. Thus, it was present at age 21[9] but absent at ages 11 and 26. However, seropositivity at age 26 was associated with lower educational attainment, which may be considered as a surrogate for lower SES. In contrast, the weak association with male sex found in the DMHDS is consistent with other studies. Although the number of seropositive males was higher at all ages tested, the difference was only significant at age 21. Similarly, the association with smoking was absent in the DMHDS as has been found in other recent studies[2].

The seroprevalence of *H pylori* antibodies in the DMHDS can be compared to values determined in two other studies in New Zealand, which also used the Cobas kit. In one study, a group of 11-year-old children of European ethnicity in South Auckland had a seroprevalence of 7%[13] and, in the other, a group of 18-24-year-old adults of largely European ethnicity in Christchurch had a seroprevalence of 4.2%[18]. Interestingly, the large study of active *H pylori* infection in the general population of England and Wales estimated seroprevalence in those born in the 1970s to be about 7% falling to about 4.3% in those born in the 1980s[5].

In conclusion, our study shows that *H pylori* infection remains stable from childhood into adulthood although seroreversion seems to be more common in the adolescent years than in young adults.

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