Helicobacter pylori infection: an added stressor on iron status of women in the community

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Abstract

Objective: To explore a possible association between *Helicobacter pylori* infection and iron status.

Design: Cross-sectional study.

Setting: Ballarat (a major regional city in Victoria), population 78 000, October – November 1997.

Participants: 160 women and 152 men, a subsample of participants in a cardiovascular disease risk factor prevalence survey for whom frozen plasma was available.

Main outcome measures: *H. pylori* IgG antibody status by enzyme immunoassay; iron intake; plasma iron, transferrin and ferritin concentrations.

Results: 28% of women and 33% of men were infected with *H. pylori*. The mean (SEM) plasma ferritin concentration of infected women (59.3 [7.6] µg/L) was significantly lower than for non-infected women (88.8 [7.9] µg/L; $P=0.002$), after adjusting for age. Mean daily dietary iron intakes were similar in infected and non-infected women.

Conclusions: *H. pylori* infection appears to be an additional stressor on women's iron status, but the mechanism remains to be determined.

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A recent study estimated that 31% of adults in an Australian regional city were infected with *Helicobacter pylori*.[1] Studies in other developed and developing countries have estimated the prevalence of *H. pylori* infection to be even higher.[2] The infection usually persists indefinitely and is implicated in the development of gastric atrophy, peptic ulcer and gastric cancer.[3] Several recent studies reported that *H. pylori* infection presented as iron deficiency.[4-6] We have explored whether there is an association between *H. pylori* infection and iron status.

Methods

Setting and population

Our study was conducted in October and November 1997. The sample comprised 312 subjects for whom frozen plasma was available. The sample was drawn from the 338 participants (out of 501 adults randomly selected from the electoral roll) in a cardiovascular disease risk factor prevalence survey in Ballarat in 1992.

The study was approved by the Ballarat Base Hospital Ethics Committee.

Questionnaire data

During the cardiovascular survey, data were collected on potential confounders between *H. pylori* infection and iron status, namely age, education, smoking, alcohol consumption, diet, and socioeconomic status.[2,7] Data were also collected on menstruation, pregnancy and the use of non-steroidal anti-inflammatory drugs, all of which might cause iron deficiency.[7]

A random subsample of 239 participants in the cardiovascular survey completed a food frequency questionnaire, from which daily nutrient intakes, including iron, were derived using NUTTAB, a computerised database of the nutrient composition of foods.[8,9] Iron intakes were available for 218 of the 312 subjects in this study. In these 218 subjects confounding factors, iron status and causes of iron deficiency were similar to those of the whole sample.

The derivation of the study sample is summarised in the Figure.

Laboratory investigations

In 1994–1995 plasma samples of subjects in the cardiovascular survey had been tested for *H. pylori* IgG antibodies during a prevalence study of *H. pylori* infection.[1] Antibody titres were available for all 312 subjects. A cutoff titre of 500 was used to classify them as positive or negative (sensitivity, 92.5%; specificity, 84.3%).[10] An uninfected man with a peptic ulcer was excluded from the analysis.

Frozen plasma samples were retrieved and thawed. The concentrations of transferrin and ferritin were measured by an immunoturbidimetric assay and that of iron by a colorimetric method (Boehringer Mannheim Corporation, Indianapolis, Ind, USA). Iron deficiency was defined as a plasma ferritin concentration below the normal range (men, <20 µg/L; women, <15 µg/L), with a plasma transferrin level above normal (>33 µmol/L) (Dorevitch Pathology Pty Ltd, Melbourne, Vic., laboratory definition).

Statistical analyses

SPSS was used to analyse the data.[11] Analyses of variance were used to compare the mean plasma iron, transferrin

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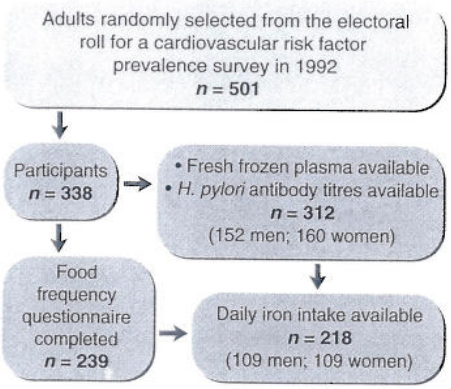

Derivation of the sample and data available to study the association between Helicobacter pylori *infection and iron status*

and ferritin concentrations of infected and non-infected subjects, adjusting for confounding factors. *H. pylori* status, potential confounding factors for iron deficiency and other causes of iron deficiency were tested for their association with plasma ferritin level by backward multiple linear regression.

Results

Twenty-eight per cent of the women (44/160) and 33% of the men (50/152) were infected with *H. pylori*. The association between *H. pylori* infection and frequency of iron deficiency, mean (SEM) plasma iron, transferrin and ferritin concentrations and mean (SEM) daily dietary iron intake is shown in the Table.

Women (but not men) infected with *H. pylori* had a significantly lower average plasma ferritin concentration than their non-infected counterparts after adjusting for age. Age was the only potential confounding factor which differed significantly between infected (53.9 [SEM, 2.4] years) and non-infected women (44.9 [SEM, 1.5] years) (t test; $P = 0.002$; df = 158). There was no significant difference in the average daily iron intake of infected and non-infected women.

Only seven women had laboratory-defined iron deficiency (plasma ferritin level, < 15 µg/L; plasma transferrin level, > 33 µmol/L). After excluding these seven women, the mean (SEM) plasma ferritin concentration of infected women (61.8 [7.7] µg/L) was still significantly lower than that of non-infected women (92.4 [8.1] µg/L) (analysis of variance, $P = 0.003$).

The multiple linear regression analysis, with inclusion of all the potential confounding factors and other variables which might affect plasma ferritin level, still showed an association between infection with *H. pylori* and a lower plasma ferritin concentration in women (coefficient (B) = −42.1 [SE, 13.6]; $P = 0.002$; standardised coefficient (β) = −0.24).

Discussion

An association between *H. pylori* infection and iron status found among Alaskan Yupik Eskimos was attributed to erosive haemorrhagic gastritis,[12] but this condition is believed to be rare in most populations.[13] This, then, is the first report to our knowledge of *H. pylori* infection being associated with lower plasma ferritin concentrations in a community in which erosive haemorrhagic gastritis is believed to be rare.[13] We did find one study of elderly people where infected subjects had much lower mean ferritin concentrations than non-infected subjects, but the differences were not statistically significant and the authors did not comment upon them.[14]

The direction of the association between *H. pylori* infection and lower plasma ferritin concentrations cannot be determined from this cross-sectional study. However, the fact that we found the association only among women favours *H. pylori* causing a lower plasma ferritin concentration, rather than the reverse. Women of reproductive age have a higher prevalence of iron-deficiency anaemia;[7] if *H. pylori* is an additional stressor on the body's iron status, the association would be more likely to be found in women than in men. If a lower plasma ferritin concentration predisposes to *H. pylori* infection, the association would be expected in both sexes. The hypothesis that *H. pylori* infection causes a lower plasma ferritin concentration is also supported by a patient with superficial gastritis caused by *H. pylori* in which anaemia was reversed and serum ferritin concentration improved after eradication therapy.[6]

H. pylori infection might theoretically reduce plasma ferritin concentration by several means: by a change in diet and iron intake; by its association with haemorrhagic peptic ulcers or erosive haemorrhagic gastritis, atrophic gastritis, hypochlorhydria and impaired iron absorption; or by the scavenging of iron in the stomach.

H. pylori infection was not associated with a reduction in iron intake. Furthermore, none of our subjects had a haemorrhagic peptic ulcer, and atrophic gastritis is probably uncommon in the general population. Iron on the gastric mucosal surface is sequestered by lactoferrin. *H. pylori* must acquire iron from its environment to survive and its membrane contains a receptor which can specifically bind lactoferrin.[15] However, evidence linking the scavenging of lactoferrin-bound iron to reduced iron status would be needed for this explanation to be considered.

If *H. pylori* infection is a stressor on iron status, it may reduce the body's

Association between iron deficiency, parameters of iron status (mean [SEM]), daily dietary iron intake (mean [SEM]) and *H. pylori* infection among Ballarat residents

	Men		Women	
	Infected	Non-infected	Infected	Non-infected
Iron deficient	4.0%	0	4.5%	4.3%
Plasma iron (µmol/L)	21.4 (0.9)	22.4 (0.6)	19.1 (0.9)	19.9 (0.6)
Plasma transferrin (µmol/L)	26.8 (0.7)	27.2 (0.4)	29.8 (0.9)	28.6 (0.5)
Plasma ferritin (µg/L)	268.5 (32.1)	282.3 (27.3)	59.3 (7.6)*	88.8 (7.9)*
Dietary iron (mg/day)	16.7 (1.1)	17.0 (0.7)	16.0 (1.0)	15.1 (0.6)
Total number of participants	50	102	44	116
Number with information about dietary iron intake	36	73	23	86

* The difference in plasma ferritin concentration between infected and non-infected women was significant ($P < 0.002$).

response to iron deficiency from other causes. Medical practitioners should consider coexisting *H. pylori* infection in iron deficiency, particularly if there is a suboptimal response to therapy.

Acknowledgements

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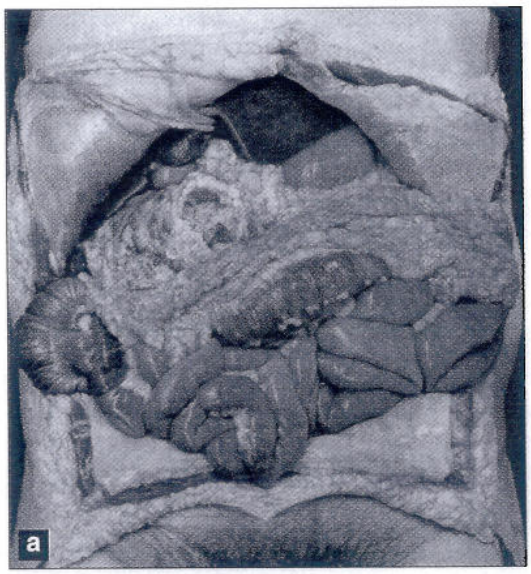
Book Review

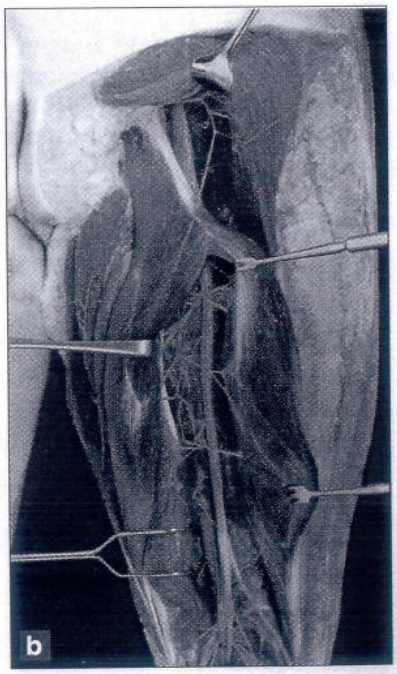
Body beautiful

Photographic Atlas of Practical Anatomy (Vol. 1). Professor Dr Walter Thiel. Graz, Austria. Springer, 1997. Blackwell Science (2 vols [vol. 1, vi + 427pp; vol.2, xii + 417pp], $573.00). ISBN: 3-540-61195-9.

An ideal text for undergraduates and postgraduate surgical candidates, this volume presents the anatomy of the abdomen and lower limb in vivid and clear detail. This clarity is the result of a new preservation technique in which the specimens retain a lifelike colour and shape, leaving the grey prosections of the past for dead! To avoid clutter the book of colour photographs has a companion volume which presents the same pictures in black-and-white, with arrows and key symbols. Stand by for the rest of the body in volume two!

Ruth Armstrong, *MJA*





a) Abdominal cavity
b) Posterior femoral region
c) Sole of the foot