EUROPEAN JOURNAL OF CANCER 47 (2011) 1211–1218

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The prevalence of premalignant gastric lesions in asymptomatic patients: Predicting the future incidence of gastric cancer

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ARTICLE INFO

Article history:
Received 16 September 2010
Received in revised form 3 December 2010
Accepted 14 December 2010
Available online 14 January 2011

Keywords:
H. pylori gastritis
Atrophic gastritis
Intestinal metaplasia
Risk factors
Gastric cancer
Screening

ABSTRACT

Background: *Helicobacter pylori* is the main risk-factor for gastric cancer through a cascade from gastritis through atrophic gastritis (AG), intestinal metaplasia (IM), dysplasia (DYS) to malignancy. The presence of these lesions in the general population predicts the gastric cancer incidence in the coming decades. Prevalence data are mostly obtained from serological studies and endoscopy data in symptomatic patients.

Aim: To investigate the prevalence of *H. pylori* infection and its related gastric changes in asymptomatic subjects.

Methods: 383 Patients undergoing routine colonoscopy were included. All subjects underwent upper GI endoscopy and completed the Gastrointestinal Symptom Rating Scale (GSRS). Biopsies were taken from antrum and corpus.

Results: *H. pylori* infection was present in 22%. Non-Caucasian subjects had a significantly higher *H. pylori* prevalence ($p < 0.001$). AG, IM and DYS were together found in 9.3% of subjects. Subjects with AG, IM or DYS were significantly older ($p < 0.001$). No differences were found with respect to gender, presence of GI symptoms as scored by GSRS, lifestyle and medication use.

Conclusions: The prevalence of premalignant gastric lesions is considerable in general Western population with increasing age as the main risk factor. One time screening for premalignant lesions at the age of 60 years is a reasonable strategy since the numbers found imply that gastric cancer will remain a prevalent disease.

1. Introduction

Gastric cancer represents the fourth most common malignancy and second leading cause of cancer-related mortality worldwide. Its worldwide incidence is increasing due to expansion and ageing of the world population.[1–3] In The Netherlands as in many Western countries, the incidence of gastric cancer is relatively low with approximately 6.9 cases/

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0959-8049/$ - see front matter
doi:10.1016/j.ejca.2010.12.012

100,000/year (WSR).[4] Colonisation with *Helicobacter pylori* is the main risk factor for gastric cancer. It is one of the most common infections in humans with a prevalence in many developing countries arising to more than 90% in young adults, and a prevalence in the developed world varying between 30% and 50%.[5,6] *H. pylori* causes gastritis in virtually all infected patients, which can lead to atrophic gastritis (AG), intestinal metaplasia (IM), dysplasia (DYS) and eventually invasive cancer.[7,8] The identification of these precursor lesions may assist in timely diagnosis of gastric carcinoma and consequently a better prognosis. A previous study showed that around 7000 patients in The Netherlands are diagnosed with one of these gastric precursor lesions every year.[9]

These data are relevant for the determination of future developments in the incidence of gastric cancer and the potential impact of screening. However, they are based on symptomatic patients referred for upper gastrointestinal endoscopy. Since most patients with *H. pylori* infection and premalignant gastric lesions are asymptomatic, one may assume that a large proportion of these lesions remain undetected. Data on the epidemiology of premalignant gastric lesions in the general population are thus scarce, especially in populations with an overall low incidence of gastric cancer.[9–11] Available data are either based on serology testing or on used information obtained from patients with an indication for upper gastrointestinal endoscopy.[12,13] A recent population-based study from Germany reported a prevalence of serologically diagnosed atrophic gastritis of 5% in the age group from 50 to 54 years, increasing to 9% in the age group of 70–74 years.[14] This may have been an underestimate, as serological assessment of atrophic gastritis has suboptimal predictive values for mild to moderate degrees of atrophy, even more so in populations with lower prevalence of the condition.[15]

The prevalences of *H. pylori* gastritis and its sequelae amongst asymptomatic subjects are not clear. Studies that use random samples of the general population and histology to diagnose premalignant lesions mostly contain small numbers of patients and are rarely conducted in low incidence populations.[16,17] Adequate data are required for public health discussions on the potential benefits of screening and treatment for *H. pylori* infection.

The objective of this study, therefore, was to obtain histological assessed data on the age-related prevalence of *H. pylori* infection and its related macroscopic and pathologic gastric changes in subjects without an indication for upper gastrointestinal endoscopy.

2. Methods

Participants for this study were recruited from the list of patients planned for routine, non-urgent colonoscopy in the Erasmus Medical Center in Rotterdam, The Netherlands. At least 2 weeks prior to endoscopy, all candidates were sent a reply-card letter explaining the aim, background and methods of the study. The patients were asked to return the reply-card if they were willing to be enrolled in the study or wished to receive further information. The patient's referring physicians also received a letter. Only the patients who returned the reply-card were then contacted by the investigators by phone. After informed consent, they were prepared for upper gastrointestinal endoscopy to take place under midazolam sedation prior to the colonoscopy in the same session.

All patients entering the study were asked to complete the Gastrointestinal Symptom Rating Scale (GSRS) prior to the endoscopic examination. The GSRS measures 15 specific gastrointestinal symptoms, using a Likert scale graded from 1 = no discomfort to 7 = very severe discomfort, and depicts five symptom dimensions (*reflux*, *indigestion*, *constipation*, *diarrhoea* and abdominal pain). Progressive scores indicate increasing symptom levels. The GSRS is well documented with regard to reliability and validity in adults with dyspepsia.[18]

For each subject demographical and lifestyle characteristics were collected together with information about medication use. Exclusion criteria were a previous or present history of oesophageal or gastric carcinoma, previous surgery to the upper gastrointestinal tract as well as an upper gastrointestinal endoscopy in the 6 months prior to the colonoscopy. The study was reviewed and approved by the Erasmus MC institutional review board.

2.1. Endoscopy

Upper gastrointestinal endoscopy and biopsy sampling were performed with an Olympus GIF-XP160 endoscope prior to colonoscopy. Before the start of the procedure local anaesthetic spray was applied orally (Xylocaine 10%) and sedation with 5–7.5 mg midazolam was given intravenously. Macroscopic appearance of the stomach was assessed. Routine endoscopic images were made of antrum, corpus and cardia, any abnormalities and visible lesions were additionally photographed. Biopsy specimens were obtained for histology according to the updated Sydney classification from the antrum ($n = 2$) and corpus ($n = 2$). In addition biopsies were taken of any visible abnormality or lesion.

2.2. Histology

Biopsy specimens were fixed in 4% formalin, embedded in paraffin wax, sectioned (5 μm) on two levels, stained with haematoxylin–eosin and mounted on glass slides. Sections were independently reviewed by two expert pathologists, who were unaware of the endoscopic and clinical findings. For each section, the presence and severity of gastritis and the degree of neutrophilic infiltration, lamina propria mononuclear infiltration and glandular atrophy were graded on the Sydney scales from 0 to 3. Intestinal metaplasia was scored as either absent or present and confirmed in all cases by evaluation of PAS staining. The presence of dysplasia was determined using the standardised definition also used in Barrett's oesophagus and classified with the use of the standardised classification as defined by the Vienna classification.[19–21]

2.3. Statistical analysis

Categorical data analysis was conducted using the chi-square or Fisher exact test performed with Statistical Package for the Social Sciences (SPSS) 15.0. Continuous data were analysed

using the student *t*-test. To test for the potential relationship between medication use and lifestyle characteristics and gastritis, logistic regression analysis was performed with SPSS. The level of significance was set at 0.05. All tests were two-tailed.

3. Results

3.1. Baseline characteristics

A total of 383 patients were included in the study, with a male to female ratio of 191/192 and a mean age of 53.1 years (range 17–86 years). Their baseline characteristics are described in Table 1. Most patients were referred to our outpatient clinic for a colonoscopy because of changes in defecation pattern (25%), abdominal pain (12%), or suspicion of inflammatory bowel disease (20%). The majority of the patients were of Caucasian descent (90%). Forty-three percent of the patients were current or former smokers, and 63% regularly consumed alcohol with an average intake of two consumptions daily (range 1–10). Complaints of dyspepsia as scored in the GSRS scale were found in 35% of the patients. Protonpump inhibitors were currently used by 20% of the total patient group.

Table 1 – Baseline characteristics of subjects (N = 383).

	Total	N	%
Male/female	383	191/192	50/50
Age (average)	383	53 (17–86)	
Ethnicity	373		
Caucasian		336	90
Negroid		21	5.5
Asian		4	1
Other		12	3.4
BMI	368		
<20		28	7.6
20–25		171	47
25–30		122	33
30–35		31	8.4
35–40		15	4.1
>40		1	0.3
Smoking	367		
None		188	51
Current		91	25
Former		88	24
Alcohol	369		
None		143	39
0–2 units/day		176	48
3–5 units/day		41	11
>5 units/day		9	2.4
NSAIDS	371		
None		322	87
Sometimes		24	6.5
Often		25	6.7
Aspirin	371		
No		330	89
80 mg daily		38	10
38 mg daily		3	0.9
PPI	371		
No		293	79
Yes		78	21
GSRS score:	383		
Dyspepsia score > 2.5		135	35
Indigestion score > 2.5		87	23
IBS score > 2.5		206	54

3.2. Endoscopic findings

One-hundred twenty-three (32%; 95% CI [27–37%]) subjects demonstrated macroscopic evidence of gastric pathology. Twenty-five percent (n = 95; 95% CI [21–29%]) showed evidence of gastritis. Erosions were seen in 5% (n = 20; 95% CI [2.8–7.2%]) of the subjects. The erosions were all located in the antrum. Two (0.5%; 95% CI [0–1.2%]) subjects had an ulcer, one in the lesser curvature and one on the angulus. Macroscopic evidence of atrophy was seen in 1.6% (95% CI [0.3–2.8%]). The prevalence of gastritis and erosions in subjects undergoing a colonoscopy because of IBD was equal to the subjects referred for other causes. In the subjects referred for suspected IBD, 20% (95% CI [16–24%]) showed evidence for gastritis and 4% (95% CI [2.0–5.9%]) for antrum erosions, respectively.

3.3. Histopathological findings

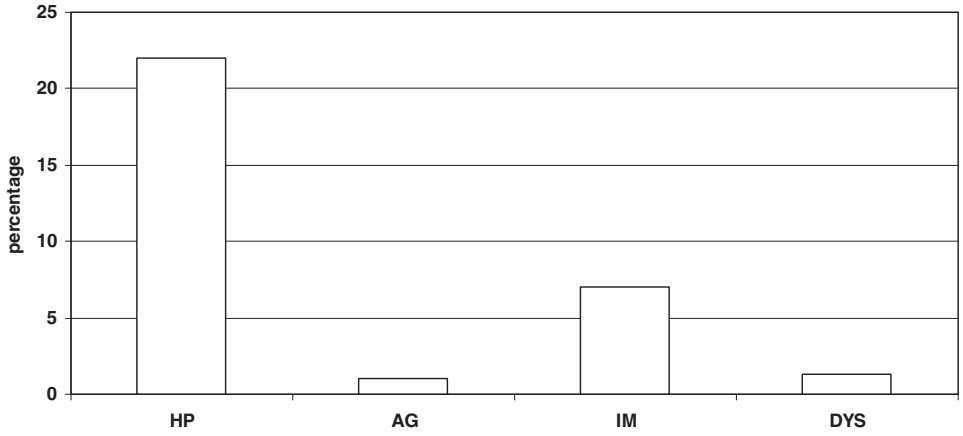
H. pylori infection was demonstrated in 22% (95% CI [18–26%]) of subjects (Fig. 1). Subjects with *H. pylori* gastritis were significantly older than subjects with normal gastric mucosa (mean age 56.1 versus 51.9; 95% CI [0.5–7.3], p 0.03). The prevalence of *H. pylori* gastritis increased with age. Eleven percent of subjects under 40 years of age were colonised with *H. pylori*. This prevalence rose to a maximum of 33% in subjects 50–60 years of age (Fig. 2). In the non-Caucasian subjects the prevalence of *H. pylori* was 44% overall, ranging from 33% (95% CI [28–38%]) in the subjects under 40 years of age to 57% (95% CI [54–60%]) in those above 50 years (Table 2).

In 11% of the subjects with histopathologically diagnosed gastritis, no signs of *H. pylori* were identified, this percentage decreased to 9.5% when excluding subjects referred for IBD. Most subjects with *H. pylori*-negative gastritis demonstrated signs of foveolar hyperplasia, suggestive for chemical gastritis.

There was no correlation between the presence of *H. pylori* gastritis and dyspeptic symptoms. In fact, the Gastrointestinal Symptom Rating Scale (GSRS) showed an equal proportion of subjects with dyspeptic symptoms among the gastritis-negative subjects and the *H. pylori*-positive subjects (36%; 95% CI [31–40%]) versus (41%; 95% CI [36–46%], p 0.44). No differences were found with respect to smoking behaviour, BMI and medication use between *H. pylori*-positive and -negative subjects (Table 2). However, both groups differed with respect to alcohol use (*H. pylori*-positive versus -negative 47%; 95% CI [42–52%] versus 67%; 95% CI [63–72%], p 0.02). Furthermore, we found a significantly higher percentage of non-Caucasian subjects in the *H. pylori*-positive group compared to the group of subjects who were *H. pylori* negative (24%; 95% CI [20–28%] versus 5.5%; 95% CI [3.2–7.8%], $p < 0.01$).

3.4. Premalignant gastric lesions

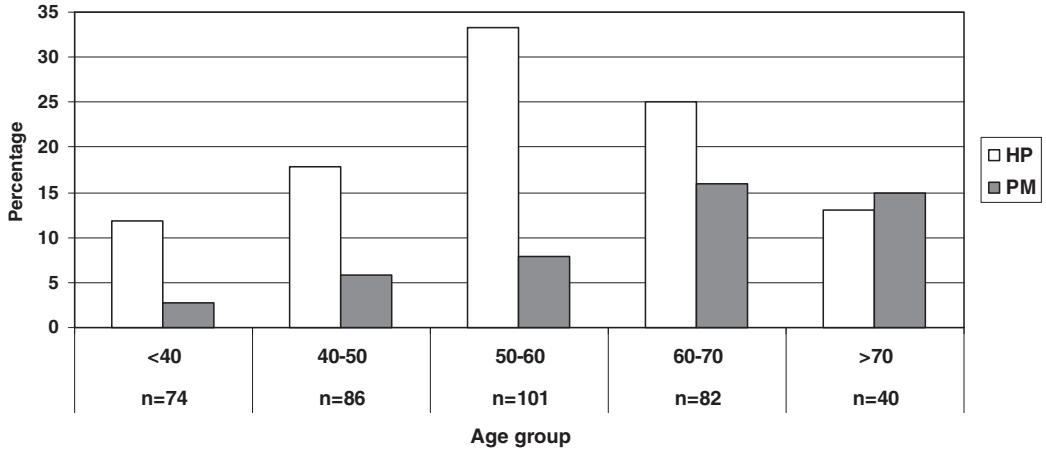
In total, 9.3% (95% CI [6.4–12%]) of subjects had signs of premalignant gastric lesions; 0.8% had the most severe diagnosis



Legend : *H. pylori* infection (HP), Atrophic Gastritis (AG), Intestinal Metaplasia (IM)

Dysplasia (DYS)

Fig. 1 – Prevalence of *H. pylori* colonization and histopathologic findings.



Legend: *H. pylori* infection (HP), premalignant gastric lesions (PM)

Fig. 2 – The prevalence of *H. pylori* infection and premalignant gastric lesions per age.

of atrophic gastritis (AG), 7.1% in addition to AG had intestinal metaplasia (IM) and 1.4% in addition had signs of gastric dysplasia (DYS).

Subjects with pre-malignant gastric lesions were significantly older than subjects with either normal gastric mucosa or non-atrophic gastritis (mean age 60.0 versus 52.5 years; 95% CI [3.7–11.5], $p < 0.01$). Premalignant gastric lesions occurred mostly in the subjects over 60. Intestinal metaplasia and dysplasia were highly prevalent in the higher age groups. IM was present in 2.3% of the 30–40 years old subjects, increasing to 13.4% in the age group 60–70 years (Fig. 2). Comparing subjects with and without histopathological evidence of premalignant gastric lesions, no differences were identified with respect to sex, lifestyle and medication use. Use of protonpump inhibitors tended to be lower in the group with premalignant gastric lesions, (67%, 95% CI [62–72%] versus 78%, 95% CI [74–82%]), this difference was, however, not significant (p 0.07). The GSRS scores did not have a predictive value for the presence of premalignant gastric lesions p 0.17 (95% CI [0.7–3.5]) for positive GSRS score indicating dyspepsia, p 0.35 (95% CI [0.7–3.3]) for positive GSRS score indicating indigestion (Table 2). An association between ethnicity and the occurrence of premalignant gastric lesions was not demonstrated (95% CI [0.57–1.58]; p 0.07) (Table 2).

3.5. *Correlation of macroscopic and histopathological findings*

Erosions and peptic ulcers were found in 9.5% (95% CI [6.6–12%]) of subjects with *H. pylori* compared to 4.7% (95% CI [2.6–6.8%]) of those without *H. pylori* infection (p 0.04). Erosions and ulcers were identified in 15% of subjects with premalignant lesions (95% CI [11–19%]) compared to 4.9% in subjects without histopathological lesions (95% CI

Table 2 – Characteristics of patients with histopathological evidence of gastritis, *H. pylori* infection and premalignant gastric lesions, compared to subjects with unaffected gastric mucosa.

	Tot (*N* = 383)	PA nl (*N* = 226)	Gastr (*N* = 95)	*p*-Value	*HP* (*N* = 84)	*p*-Value	PM (*N* = 34)	*p*-Value
Sex male	50%	51%	44%	0.24	44%	0.27	50%	1.0
female	50%	49%	56%		56%		50%	
Age (average)	53	53	55	0.12	56	<0.01	60	0.03
Smoking				0.31		0.35		0.20
Never	55%	52%	61%		61%		43%	
Current	25%	27%	21%		21%		30%	
Former	20%	21%	18%		18%		27%	
Alcohol				0.02		0.02		0.14
None	39%	34%	52%		52%		52%	
0–2	48%	51%	40%		41%		37%	
3–5	11%	13%	5.3%		4.8%		12%	
>5	2.4%	2.6%	2.2%		2.4%		0%	
Ethnicity				<0.01		<0.01		0.07
Caucasian	90%	95%	79%		76%		85%	
Negroid	5.5%	2.9%	14%		16%		12%	
Asian	1%	0.7%	1.1%		1.2%		3%	
Other	3.4%	1.8%	6.6%		7.2%		0%	
BMI > 25	46%	44%	49%	0.29	46%	1.0	46%	1.0
NSAIDS				0.64		0.35		
None	87%	88%	84%		82%		97%	0.17
Sometimes	6.5%	5.9%	6.5%		9.5%		3%	
Often	6.7%	6.3%	6.5%		8.3%			
Aspirin				0.58		0.5		0.25
None	89%	87%	90%		92%		82%	
80/100 mg	10%	10%	10%		8%		18%	
38 mg	0.9%	1.1%	0%		0%			
PPI				0.10		0.17		0.07
Yes	79%	78%	84%		84%		67%	
No	21%	22%	16%		16%		33%	
Ulcera	5.8%	4.7%	9.6%	0.06	9.5%	0.04	14.7%	0.04
GSRS score:								
Dyspepsia score > 2.5	35%	36%	40%	0.27	41%	0.44	48%	0.17
Indigestion score > 2.5	23%	62%	58%	0.24	62%	0.89	70%	0.35
IBS score > 2.5	54%	62%	51%	0.06	51%	0.11	59%	1.0

All subjects (Tot), normal gastric mucosa (PA nl), gastritis (Gast), *H. pylori* infection (*HP*), premalignant gastric lesions: atrophic gastritis, intestinal metaplasia or dysplasia (PM).

[2.7–7.1%]) (*p* 0.04). Endoscopic suspicion of atrophy was raised in six subjects, one of them had histopathological evidence of intestinal metaplasia, two were diagnosed with *H. pylori* infection, and the other three did not have histopathological evidence of gastric pathology.

4. Discussion

Our knowledge on the prevalence of *H. pylori* gastritis and its sequelae of glandular atrophy, intestinal metaplasia, dysplasia and gastric carcinoma is largely based on studies in symptomatic patients referred for upper gastrointestinal endoscopy. For example, studies from various countries[12,13,22,23] reported *H. pylori* prevalence rates of 30–41% and the presence of atrophic gastritis in 7–34%, intestinal metaplasia in approximately 20% and low grade dysplasia in 1% of patients with dyspeptic symptoms requiring upper GI endoscopy. However, the patients under study did not represent the general population, and thus the reported prevalences may have been overestimated. This was illustrated by a study from Norway which showed that symptomatic patients with an indication for upper GI endoscopy had a significantly lower prevalence of atrophic gastritis than asymptomatic subjects.[17]

Comparing our study to a previous nationwide study from our group, we observed a 9.3% (95% CI [6.4–12%]) prevalence of premalignant gastric lesions in the current study, compared to 14% in the previous study by de Vries et al.[9] This previous study included patients with an indication for upper GI endoscopy and biopsy sampling. This indicates even more that the numbers obtained from symptomatic patients are an overestimation of the true population prevalence of premalignant lesions.

True population data on the prevalence of premalignant gastric lesions were in particular obtained from serologic studies.[24,25] For example, a recent large study by Weck demonstrated by means of measurements of IgG antibodies for *H. pylori*, in combination with pepsinogen I and II and their ratio, a 49% prevalence of *H. pylori*, and an 8.7% prevalence of chronic atrophic gastritis in 9444 asymptomatic subjects. A very recent study from Finland used the same serologic parameters and demonstrated a *H. pylori* prevalence rate of 19% and chronic atrophic gastritis in 3.5%.[30] However, these outcomes may have been an underestimate of the true population prevalence of atrophic gastritis, as serological assessment of atrophic gastritis has suboptimal predictive values for mild to moderate degrees of atrophy, even more so in populations with lower prevalence of the condition.[15] Furthermore, these studies do not clarify the true population prevalence of intestinal metaplasia and dysplasia, the further steps in the cascade.

Our results show that there is a marked prevalence of premalignant gastric conditions in subjects without an indication for upper GI endoscopy. These lesions vary from *H. pylori*-related gastritis to intestinal metaplasia and in some patients to dysplasia. In this group of subjects without indication for upper GI endoscopy, macroscopic lesions were identified in over 30%. The majority of cases had evidence of gastritis, with erosions, ulcers and atrophy following other common conditions. With respect to microscopy the most important finding however, was the considerable prevalence of premalignant gastric lesions. In 9.3% of the subjects premalignant gastric lesions were identified, varying from signs of gland loss to metaplastic replacement and dysplasia.

In the Swedish Kalixanda study, 16.9% of the subjects were diagnosed with gastric IM, a prevalence which was twice as high as in our Dutch population.[6] This was likely to be related to the lower prevalence of *H. pylori* infection in our subjects compared to the Kalixanda population. The mean age of our population and the Kalixanda population was equal (53.07 and 53.5 years) which means that age cannot have contributed to the difference in prevalence. Other endoscopy studies that included asymptomatic subjects showed even higher prevalences of *H. pylori* infection and premalignant gastric lesions.[26,27] These studies were, however, conducted either two or more decades ago or in areas with high *H. pylori* prevalences in the range of 40–75%.[26,27]

No clear risk factors were identified for the presence of the premalignant lesions in our subjects. The only factor related to the presence of premalignant gastric conditions was increasing age, a factor which has been described previously. GSRS scores, smoking, use of NSAIDs and BMI could not aid in identifying the subjects at risk.

In the most previously conducted studies no association between premalignant gastric lesions and symptoms, smoking, use of NSAIDs and other medications was identified.[18,25,28,29] Data on potential association between premalignant lesions and alcohol use are conflicting. We did not demonstrate such an association.[25,28,29] Our subjects were not selected on the basis of absence of symptoms, or other parameters such as absence of PPI use, or absence of *H. pylori* infection. They thus reflected the general population and they no one had a clinical indication for upper gastrointestinal endoscopy.

The *H. pylori* prevalence of 22% (95% CI [18–26%]) demonstrated in this study was lower than previously noted in our population. Overall *H. pylori* infection rates in The Netherlands, determined by serological tests, varied in previous studies between 35% and 44%.[30,31] In a recent survey among 800 healthy blood donors throughout the country, the prevalence of *H. pylori* IgG serum antibodies was 32%. This prevalence increased with age from 17% in donors aged 18–28 years to 49% in donors aged 59–70 years.[30,31] The lower prevalence in our study in comparison with previous data points at a further decline of *H. pylori* prevalence in The Netherlands. This decline occurs primarily in Caucasian subjects, the prevalence in non-Caucasian Dutch residents is still high (>44%). This ethnical diversity in prevalence has also been demonstrated by other studies.[31,32] The same applies to our observation of increasing prevalence with age.[6,17,25,27,33]

Despite our efforts to create a risk profile and develop tools for targeted screening and surveillance, no clear predictors for the presence of premalignant lesions were found, other than age and ethnicity. This is in line with previous studies.[31,32] Targeted screening should take these predictors into account. This, however, implies that a large proportion of the general population would need to be approached, preferentially with a stepwise strategy starting with serological testing followed by endoscopy with biopsy sampling in those with results beyond a set cut-off. Age is the primary determinant in such an approach, with the border set at a level above which the prevalence of premalignant lesions reaches a threshold. In our population, the prevalence of premalignant lesions was 15.9% at the age of 60. This high prevalence is associated with a rapid increase of gastric cancer incidence above 60 years. For that purpose, one time screening for premalignant lesions at the age of 60 years is in our Western population a reasonable strategy for which attendance, impact, costs and optimal approach would have to be determined. Considering ethnicity and the significantly higher prevalence of *H. pylori* infection in non-Caucasian subjects, non-Caucasian subjects should in such a programme be approached at a lower age, preferentially aiming at a similar prevalence of pre-malignant lesions as in Caucasians at the age of 60 years. In our study, this was reached at the age of 50 years in immigrants. Primary screening should consist of non-invasive serologic screening, testing for *H. pylori* antibodies (IgG) and pepsinogen I and II. Ultimately endoscopic surveillance should be offered to the individuals with premalignant lesions at high risk of progression. For the current subjects who were actually submitted to screening for premalignant lesions using upper GI endoscopy, endoscopic and histopathological findings did in some cases have implications for follow up. There are at present no clear guidelines on the management of patients with premalignant gastric lesions. Nevertheless, we previously showed in a large nationwide cohort study that this risk is substantial, in particular for patients with gastric dysplasia.[11] The risk of cancer is very similar to for instance the risk observed in patients with Barrett's oesophagus.[34] For these reasons, despite the absence of a management guideline, we offered patients with dysplasia a surveillance upper GI endoscopy within 1–2 years, and

those with extensive intestinal metaplasia according to the OLGIM classification[35] surveillance within 2–5 years.

Although we included subjects with a clinical indication for upper GI endoscopy some possible limitations of our study should be mentioned. All subjects included in this study had an indication for outpatient colonoscopy, which means that specific conditions of the GI tract were suspected or had previously been diagnosed. Special attention in this case was given to the group of subjects that had were known or suspected to have IBD as an indication for their colonoscopy, since this group of subjects could show some signs of IBD in the upper GI tract. Our findings, however, did not demonstrate differences between these subjects and the subjects with other indications. Especially we did not find a higher prevalence of ulcerations and gastritis in this group.

Furthermore, our study was conducted in a tertiary centre, which could have caused selection bias although we are not aware in which way this would have occurred. The histopathological diagnosis was based on four biopsies; which could have caused underdiagnosis. Our current biopsy protocol is more extensive, based on our recent observation that the optimal biopsy protocol should contain nine random biopsies (three antrum, one angulus, two corpus and one cardia) for optimal assessment of the condition of the gastric mucosa.[36] Finally, we based our diagnosis of *H. pylori* infection on histopathology only. Addition of other methods could have resulted in higher *H. pylori* prevalences, in particular in subjects with atrophic gastritis in 90% of whom we now found evidence of *H. pylori* colonisation.[6,37,38]

Considering histopathological diagnosis of atrophic gastritis and dysplasia it is known that diagnostic criteria may vary from country to country and inter-observer variability is common. In the case of atrophic gastritis the updated Sydney system does provide clear criteria to score atrophic gastritis and aides in solving this issue. In the case of dysplasia the diagnostic criteria used by our two expert pathologists were: low-grade dysplastic features, i.e. mild atypia with elongated nuclei, normal cellular orientation and presence of immature goblet cells; high-grade dysplasia, i.e. severe atypia with nuclear stratification, loss of cellular orientation and lack of goblet cell differentiation.

In conclusion we have demonstrated a considerable prevalence of premalignant gastric lesions, from *H. pylori* gastritis to high grade dysplasia, in subjects without specific symptoms. It is especially noteworthy that even severe premalignant lesions can be found in these asymptomatic subjects. Our findings imply that gastric cancer will remain a common disease in Western countries for the coming two decades. However, the prevalence of premalignant lesions is smaller in asymptomatic subjects than in symptomatic patients. This indicates that data from endoscopy series in symptomatic subjects do not reflect true population incidences. Finally, we show that only age and ethnicity help to predict the individual chance of premalignant gastric lesions. One time screening for premalignant lesions at the age of 60 years seems a reasonable strategy since the numbers found imply that gastric cancer will remain a prevalent disease.

Conflict of interest statement

None declared.

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