Precancerous gastric conditions in high *Helicobacter pylori* prevalence areas: comparison between Eastern European (Lithuanian, Latvian) and Asian (Taiwanese) patients

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Key words: *Helicobacter pylori; gastritis; atrophy; intestinal metaplasia.*

Summary. *The aim of the study was to compare the prevalence and severity of precancerous condition – gastric atrophy and intestinal metaplasia (IM) between Eastern European (Lithuania and Latvia) and Asian (Taiwan) countries in population older than 55 years.*

Methods. Patients aged 55 years and older, referred for upper endoscopy due to dyspeptic symptoms, were included in the study. Gastric biopsies were histological investigated according modified Sydney classification. Helicobacter pylori (H. pylori) was detected if any two of three methods (urease test, histology, and serology) were positive.

Results. Overall 322 patients included: 52 from Taiwan (TW), 171 from Latvia (LV) and 99 from Lithuania (LT). There were 227 (70%) females and 95 (30%) males. The mean age of TW patients was significantly lower (61.0±5.8 years), than of LV (68.1±7.3 years) and LT (66.5±7.5 years) patients. H. pylori was established in 224 (69.6%) patients. H. pylori positivity was established in 43 (82.7%) TW patients, in 112 (65.5%) LV patients, and in 69 (69.7%) LT patients (P>0.05). In H. pylori-infected patients, any atrophy either in the corpus or in the antrum of the stomach was detected in 26 (60.5%) TW patients, in 40 (35.7%) LV patients, and in 36 (52.2%) LT patients (between TW and LV patients P<0.005). Severe atrophy (grade 2 or 3) detected in 8 (18.6%) TW patients, in 17 (15.2%) LV patients, and in 18 (26.1%) LT patients (P>0.05). Intestinal metaplasia was detected in 22 (51.2%) TW patients, in 37 (33.0%) LV patients and in 31 (44.9%) LT patients among countries (P>0.05). There were no significant differences in proportions of different degrees of both atrophy and intestinal metaplasia among countries. Intestinal metaplasia was found in 79 (77.5%) of 102 patients with any degree of atrophy and in 11 (9.0%) of 122 patients without atrophy (P<0.0001). We found strong statistically significant correlations between atrophy and intestinal metaplasia in antrum (r=0.89), P<0.01, and corpus (r= 0.73), P<0.01.

Conclusions. The prevalence of H. pylori in the elderly population is still high in LT, LV, and TW. There are no significant differences in prevalence of gastric atrophy and intestinal metaplasia among TW, LT, and LV. There is a strong correlation between gastric atrophy and intestinal metaplasia.

Introduction

The role of *Helicobacter pylori* infection in the pathogenesis of gastric cancer is well established (1–4). The Correa cascade can explain the sequence from *H. pylori* gastritis through precancerous conditions to gastric cancer (5, 6). Gastric atrophy and intestinal metaplasia (IM) are recognized as precancerous conditions (7). The prevalence of atrophy and IM is higher in the areas with a high incidence of gastric cancer. It remains unclear whether or not the atrophy is reversible and where the point-of-no-return could be established. Gastric cancer is more prevalent in elderly population indicating that atrophy and intestinal metaplasia could also be related to age, probably due to long standing *H. pylori* gastritis. Up till there are no data on the prevalence of gastric atrophy and IM in the elderly population. Little data on the atrophy and IM are available in the Eastern European countries, where the prevalence of gastric cancer is still high as well as in Baltic States and TW (8, 9).

Therefore, we conducted the study in which the population aged 55 years and more from TW, LT and

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LV were investigated for the prevalence of precancerous condition such as gastric atrophy and IM.

Methods

Patients aged 55 years and older, referred for upper endoscopy due to dyspeptic symptoms, were included in the study. Patients with known history of former *H. pylori* eradication, with history of peptic ulcer disease and gastric cancer, with recent use of proton pump inhibitors, antibiotics or bismuth compounds could not be included in the study as well as users of NSAIDs.

During upper gastrointestinal endoscopy, six biopsy specimens from stomach were obtained: two for urease test, two from antrum 2–3 cm from the pylorus (1 from lesser and 1 from greater curvature), and 2 from corpus (1 from lesser and 1 from greater curvature) for histological examinations.

Biopsy materials were fixed in 10% formalin and then embedded in paraffin, cut in sequential sections and stained hematoxylin-eosin. Histological evaluation was performed and read by single pathologist, which was blinded to any clinical or demographic data. Scoring of atrophy and IM was done according modified Sydney classification by 3 point scale: 0 – no atrophy or intestinal metaplasia, 1 – mild feature, 2 – moderate feature, 3 – severe feature (10). *H. pylori was* detected by three methods: urease test, histological and serologically (testing of IgG *H. pylori* antibodies). Presence of *H. pylori* confirmed if the results of any two of these tests were positive.

Calculation was performed using SPSS for Windows. One-way ANOVA testing with post hoc multiple comparisons, chi-square statistics and Pearson's correlation coefficient were used for statistical analysis. Significance level was set at $P<0.05$.

The study was approved by the Ethic Committees of the university hospitals in TW, LT, and LV.

Results

Overall, 322 patients were included in the study: 52 from TW, 171 from LV, and 99 from LT. Mean age – 66.4±7.5 years. There were 227 (70%) female and 95 (30%) male. Among TW patients there were 24 (46%) female and 28 (54%) male, among LV – 130 (76%) female and 41 (24%) male, among LT – 73 (74%) female and 26 (26%) male. Statistically significantly more female in LV and LT groups. Mean age of TW patients was 61.0±5.8 years, of LV patients – 66.9±6.9 years, of LT – 66.5±7.5 years. Mean age of TW patients was significantly lower than of LV and LT patients.

H. pylori was established in 224 (69.6%) patients. *H. pylori* was established in 43 (82.7%) TW patients, in 112 (65.5%) LV patients and 69 (69.7%) LT patients, $p<0.062$ between LV and TW.

Mean age of *H. pylori* infected TW patients was 60.3±5.1 years, of HP positive LV patients – 66.9±6.8 years, of *H. pylori* infected LT – 66.3±7.0 years. Mean age of TW patients was significantly lower than of LV and LT patients.

Further analysis only of *H. pylori* infected patients will be provided.

Scores of atrophy and IM of *H. pylori* positive patients are presented in Table 1. There are no differences among countries in the intensity of IM both in the antrum and the corpus, and no difference in the score of the atrophy in the corpus of the stomach. Statistically significantly lower mean score in the antrum was found in the LV patients comparing to TW patients.

Out of *H. pylori* infected patients any atrophy either in the corpus or in the antrum of the stomach was detected in 102 (45.5%) patients. Any atrophy either in the corpus or in the antrum of the stomach was detected in 26 (60.5%) TW patients, in 50 (44.6%) LV patients and in 36 (52.2%) LT patients, $P>0.05$

Table 1. **Scores of atrophy and intestinal metaplasia of *Helicobacter pylori* positive patients**

Finding	Taiwan (TW) N=43		Latvia (LV) N=112		Lithuania (LT) N=69		*P* value
	score	SD	score	SD	score	SD	
Antrum							
Atrophy	0.58	0.73	0.36	0.70	0.41	0.71	NS
Intestinal metaplasia	0.60	0.72	0.38	0.74	0.54	0.72	NS
Corpus							
Atrophy	0.35	0.65	0.40	0.80	0.57	0.79	NS
Intestinal metaplasia	0.14	0.35	0.21	0.58	0.20	0.47	NS

NS – non significant, SD – standard deviation.

among countries.

To avoid possible investigator bias, as significant and severe atrophy we accepted the atrophy score 2 and 3 either in corpus or in the antrum of the stomach. It was detected in 43 (19.2%) patients. The atrophy with grade 2 or 3 was detected in 8 (18.6%) TW patients, in 17 (15.2%) LV patients and in 18 (26.1%) LT patients, no statistical difference among countries.

In *H. pylori* infected persons, IM was found in 90 (40.2%). IM was detected in 22 (51.2%) TW patients, in 37 (33.0%) LV patients, and in 31 (44.9%) LT patients, P>0.05 among countries.

Distribution of the degrees of atrophy and IM in the upper and lower parts of the stomach is presented in the Figure 1 and Figure 2 there are no significant differences among countries.

Intestinal metaplasia in atrophic gastritis

IM was found in 79 (77.5%) of 102 patients with any degree of atrophy and in 11 (9.0%) of 122 patients without atrophy (P<0.0001).

IM was found in 39 (90.7%) of 40 patients with severe atrophy and in 51 (28.2%) of 181 patients without severe atrophy (P<0.0001).

Relationship between atrophy and IM in *H. pylori*-positive patients in different countries is presented in Table 2. There was not significant difference in mean age between patients with atrophy or without atrophy and between patients with IM or without IM.

We found a strong statistically significant correlations between the following parameters in *H. pylori* positive subjects: between antrum atrophy and antrum IM r=0.89, P<0.01; corpus atrophy and corpus IM r=0.73, P<0.01. There were no strong correlations between age and atrophy or age and IM in our series.

Discussion

H. pylori is well recognized as a causative agent of chronic gastritis (1, 7) and as a gastric cancer risk factor (2–4). Since the incidence and prevalence of gastric cancer remains different in separate geographic areas the studies of the type and features of *H. pylori* associated gastritis are going on. It is established that the prevalence of *H. pylori* and gastric cancer is higher in the countries with lower socioeconomic status. It still remains not fully understood, if the prevalence of *H. pylori* itself or other factors (as the properties of the pathogen, the type or extent of gastritis, gastric atrophy and intestinal metaplasia) are more important in the pathogenesis of gastric cancer. There is high incidence and prevalence of gastric cancer in the Far East countries *i.e.* TW, China and others (9). Therefore, the comparison of the clinicopathological features of the patients from latter regions with the European countries seems to be challenging. In the recent study (11) there were compared Chinese and Dutch patients: prevalence of atrophy and IM were higher in Chinese patients, also atrophy and IM occurred earlier and were more severe in Chinese patients. Another recent publication (12) presented the comparison of *H. pylori* gastritis in China, Thailand, Japan, Portugal, The Netherlands, Finland, and Germany. The highest scores of antrum atrophy were found in Japanese and Chinese patients (countries with high incidence of gastric cancer) and lowest scores in European countries. The scores of IM were low in all countries, probably due to young population studied (mean age of 48.9±14 years). The prevalence of antrum atrophy correlated significantly with gastric cancer incidence.

In our study, we compared the precancerous conditions of the patients from TW, LT, and LV. Peculiarity of our study is that only elderly patients (mean age 66.4±7.5 years) were included. Our data revealed that the prevalence of *H. pylori* is high in all investigated countries, although tends to be higher in TW. We previously reported some data on the prevalence of *H. pylori* in LT: the seroprevalence among 50–60 years old blood donors – 80 % (13), the prevalence of *H. pylori* among dyspeptics (mean age – 40 years) – 78.9%. Therefore, it seems that the prevalence of *H. pylori* in LT did not change much in the elderly population and probably it will decrease with a new generation.

The prevalence of *H. pylori* in LV was studied only

Table 2. **Intestinal metaplasia among *Helicobacter pylori*-positive patients with and without atrophy**

Category of patients	Taiwan	Latvia	Lithuania	*P* value
Patients with intestinal metaplasia among patients with any atrophy	21 (80.8%)	32 (80%)	26 (72.2%)	NS
Patients with intestinal metaplasia among patients with severe atrophy	7 (87.7%)	16 (94%)	16 (88.9%)	NS
Patients with intestinal metaplasia among patients without atrophy	1 (5.9%)	5 (6.9%)	5 (15.2%)	NS

NS – non significant.

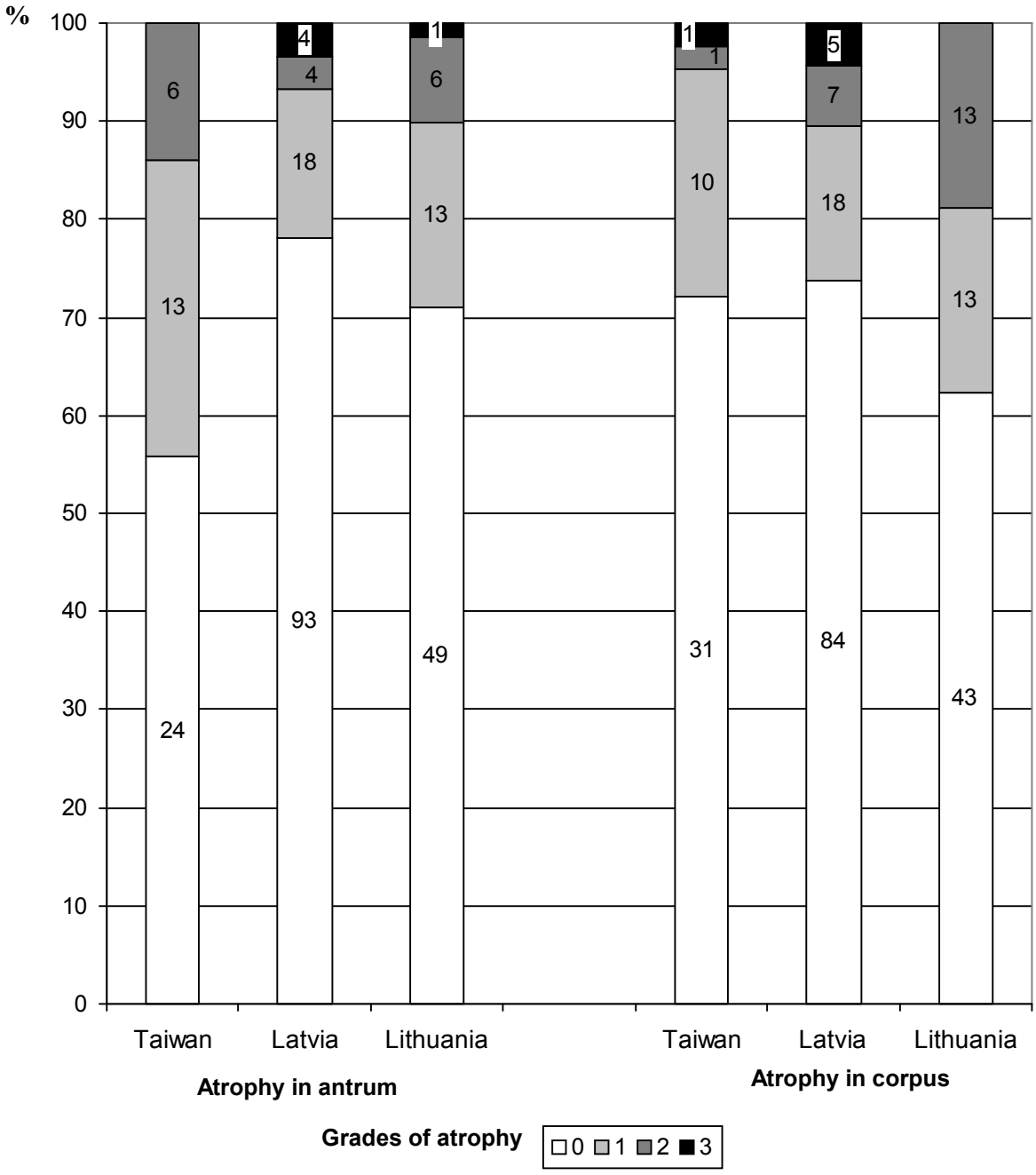

Fig. 1. **Distribution of different degrees of atrophy**

in pediatric population, so we are no able to make any comparisons, but we think the situation must be close to LT population, while these neighboring countries have a lot of common in their history and are similar socioeconomically (14).

Recently published data from TW indicate that the prevalence of *H. pylori* among dyspeptic patients (mean age of 51.0 years) is 72.6% (15). Our data corresponds to that and confirms the high prevalence of *H. pylori* in TW in adult population.

Fifteen years ago Lin et al. reported the *H. pylori* seroprevalence of 62.0% among TW healthy volunteers, so it seems that situation is about the same now (16).

The prevalence of atrophic gastritis of any degree and the more severe atrophy was not different among patients from different countries in our study. Contrarily to (11, 12) data, which have showed higher frequency of atrophy in patients from Asian countries in comparison to patients from Western Europe, we have found similar prevalence of this precancerous condition in *H. pylori* positive patients from Baltic countries

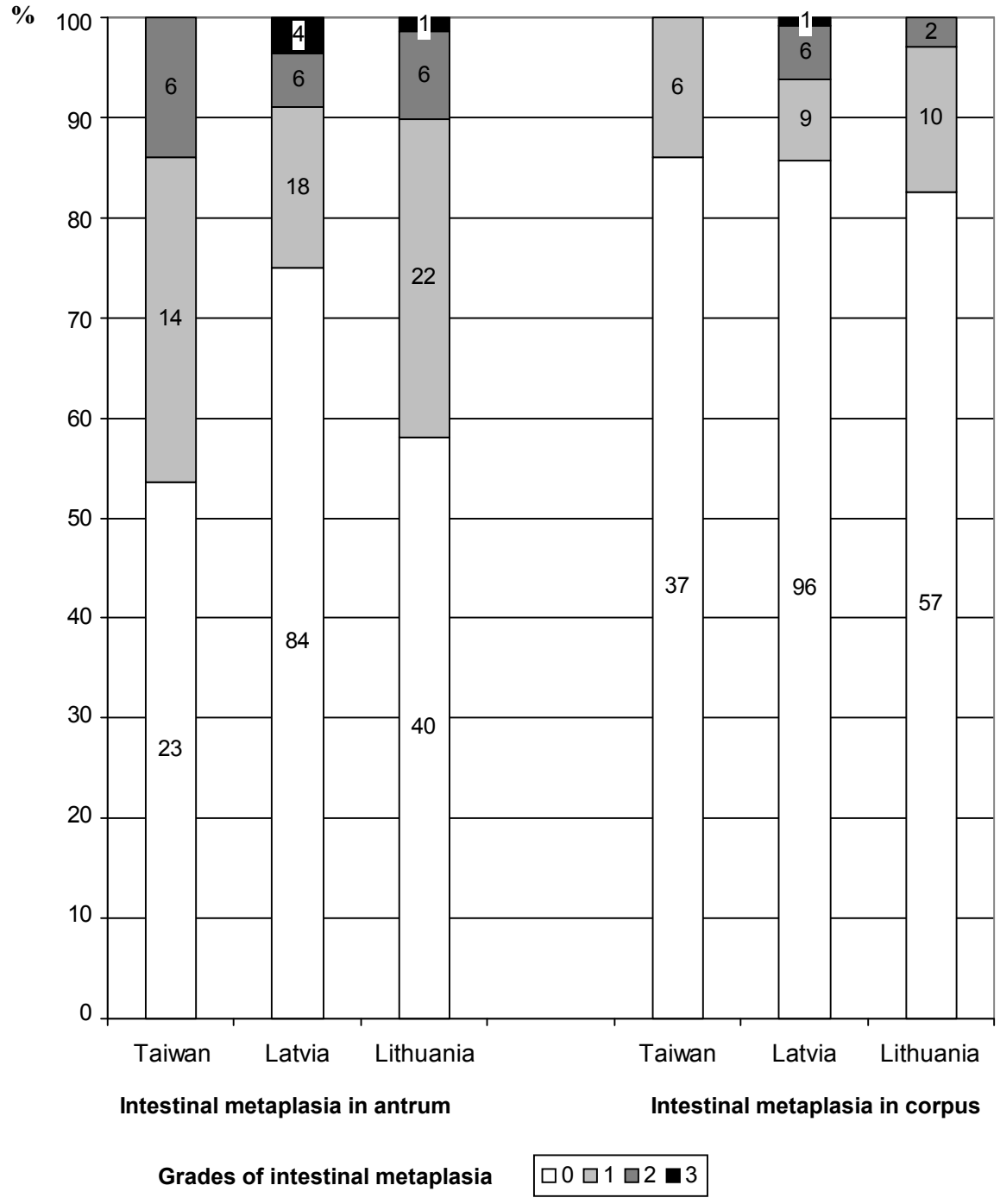

Fig. 2. **Distribution of different degrees of intestinal metaplasia**

and TW. Cited authors (11) have also found a significant correlation between prevalence of atrophy and incidence of gastric cancer in different countries. Our findings are not unexpected because incidence of gastric cancer in TW is one of the lowest in Asia (17.7/100 000 in males, 9.3/100 000 in females (9), and even lower than in Baltic States (correspondingly 27.6 and 13.9 for LV and 28.1 and 12.9 for LT (8).

We found a strong correlation between presence of atrophy and IM both in antrum and in corpus in all countries, confirming the Correa cascade (progression from chronic gastritis to gastric cancer through gastric atrophy and IM (5, 6).

In conclusion, we showed that the prevalence of *H. pylori* in the elderly population is still high in Eastern European countries and in TW. No significant differences in the prevalence of atrophy and intestinal metaplasia were found among investigated populations. In all countries, a strong positive correlation between gastric atrophy and IM has been established.

Ikivėžinių skrandžio gleivinės pokyčių paplitimas *Helicobacter pylori* sukelto lėtinio gastrito metu tarp Rytų Europos (Lietuvos, Latvijos) ir Azijos (Taivano) ligonių

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Raktažodžiai: *Helicobacter pylori*, gastritas, atrofija, žarninė metaplazija.

Santrauka. *Darbo tikslas.* Įvertinti ikivėžinių skrandžio gleivinės pokyčių – atrofijos ir žarninės metaplazijos paplitimą ir sunkumą tarp Rytų Europos (Lietuvos, Latvijos) ir Azijos (Taivano) šalių gyventojų, vyresnių nei 55 metų.

Tyrimo medžiaga ir metodai. Tirti 55 metų ir vyresni pacientai, atvykę endoskopinio tyrimo ir turintys dispepsijos simptomų. Skrandžio gleivinės uždegiminių pokyčių histologinis įvertinimas atliktas remiantis Sidnėjaus klasifikacija. *Helicobacter pylori* (*H. pylori*) nustatyta, jei bent du iš trijų naudotų tyrimo metodų (ureazės testas, histologinis tyrimas ir serologinis tyrimas) buvo teigiami.

Rezultatai. Ištirti 322 pacientai: 52 iš Taivano, 171 iš Latvijos ir 99 iš Lietuvos. Iš jų – 227 (70 proc.) moterys ir 95 (30 proc.) vyrai. Taivano pacientų amžiaus vidurkis (61,0±5,8 metų) buvo statistiškai reikšmingai mažesnis nei Latvijos (68,1±7,3 metų) ir Lietuvos (66,5±7,5 metų) pacientų. *H. pylori* buvo nustatyta 224 (69,6 proc.) pacientams. *H. pylori* nustatyta 43 (82,7 proc.) Taivano, 112 (65,5 proc.) Latvijos ir 69 (69,7 proc.) Lietuvos pacientams, $p>0,05$. Tarp *H. pylori* infekuotų pacientų skrandžio kūno ir antralinės dalies atrofija nustatyta 26 (60,5 proc.) Taivano, 40 (35,7 proc.) Latvijos ir 36 (52,2 proc.) Lietuvos pacientams. Didelio laipsnio atrofija (2–3 laipsnio) nustatyta 8 (18,6 proc.) Taivano, 17 (15,2 proc.) Latvijos ir 18 (26,1 proc.) Lietuvos pacientų, $p>0,05$. Žarninė metaplazija nustatyta 22 (51,2 proc.) Taivano, 37 (33,0 proc.) Latvijos ir 31 (44,9 proc.) Lietuvos pacientui, $p>0,05$. Nerasta statistiškai reikšmingo skirtumo tarp skirtingų atrofijos laipsnių ir žarninės metaplazijos tarp skirtingų šalių gyventojų. Žarninė metaplazija rasta 79 (77,5 proc.) iš 102 pacientų, kuriems nustatyta ir atrofija ir 11 (9,0 proc.) iš 122 pacientų, kuriems atrofijos nerasta, $p<0,0001$. Nustatyta statistiškai reikšminga koreliacija tarp atrofijos ir žarninės metaplazijos skrandžio antralinėje dalyje ($r=0,89$) ($p<0,01$) ir kūno srityje ($r=0,73$) ($p<0,01$).

Išvados. H. pylori paplitimas tarp vyresnių Lietuvos, Latvijos ir Taivano pacientų yra pakankamai didelis. Statistiškai reikšmingo skirtumo tarp atrofijos ir žarninės metaplazijos paplitimo tarp Taivano, Lietuvos ir Latvijos šalių gyventojų nerasta. Nustatyta stipri koreliacija tarp skrandžio atrofijos ir žarninės metaplazijos.

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