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Original Paper

INVESTIGATING THE PREVALENCE OF UPPER GASTROINTESTINAL SYMPTOMS AND RELATED FACTORS USING THE GASTROPARESIS CARDINAL SYMPTOM INDEX IN AN ENDOSCOPY COHORT IN LATVIA

Kristīne Ričarda Muceniece[1,2,4], Danute Ražuka-Ebela[1,2,3,#], Linda Grantiņa[1], Dace Dosone[1], Inguna Ebela[3], Ivars Tolmanis[1,4], and Mārcis Leja[1,2,3]

[1] Centre for Digestive Diseases GASTRO, 1 Gaiļezera Str., LV-1079, Rīga, LATVIA

[2] Institute of Clinical and Preventive Medicine, University of Latvia, 1 Gaiļezera Str., LV-1079, Rīga, LATVIA

[3] Faculty of Medical and Life Sciences, University of Latvia, 3 Jelgavas Str., LV-1004, Rīga, LATVIA

[4] Rīga Stradiņš University, 16 Dzirciema Str., LV-1007, Rīga, LATVIA

[#] Corresponding author: danute.razuka-ebela@lu.lv

Contributred by Mārcis Leja

Symptoms of gastroparesis (GP) and functional dyspepsia often overlap, and it is unclear whether Helicobacter pylori (H. pylori) *infection or other common clinical factors are linked to specific symptom profiles. We therefore aimed to assess whether* H. pylori*, demographic factors and diabetes are associated with dyspepsia and dysmotility-type symptom scores. In this retrospective cross-sectional study of 951 adults undergoing upper endoscopy, participants completed the American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index-Daily Diary (ANMS GCSI-DD), and composite scores were created for D-PDS (dyspepsia — postprandial distress syndrome), D-EPS (dyspepsia — epigastric pain syndrome), and GP-like (nausea/vomiting) symptoms. By using multivariable analysis, we examined associations between these symptom scores and* H. pylori *infection, age, sex, body mass index, diabetes, erosive reflux esophagitis, and hiatal hernia. Female sex and younger age were associated with higher symptom severity across all domains, while diabetes was selectively associated with higher dysmotility-type scores (GP-like and D-PDS) and moderate-to-severe overall symptom burden, but not D-EPS. After adjustment for other factors,* H. pylori*, erosive reflux esophagitis and hiatal hernia were not associated with higher symptom scores, suggesting that upper gastrointestinal symptom severity in this cohort was driven primarily by female sex, younger age, and diabetes rather than by* H. pylori *infection or endoscopically detected disease.*

Keywords: *dyspepsia, gastroparesis,* Helicobacter pylori*, diabetes mellitus, motility.*

INTRODUCTION

Symptoms related to gastroparesis (GP) are rarely observed in the general population with an estimated prevalence of just 0.9% (Huang *et al*., 2022), while functional dyspepsia (FD) as defined by Rome criteria (I–IV) is a common health problem with a global estimated prevalence of 6.8% to 11.9% (Lee *et al*., 2024).

However, there is a significant overlap of symptoms between both conditions, which increases the chances of missing a diagnosis of GP (Cangemi *et al*., 2023). Both GP and

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FD often share overlapping symptoms such as nausea, vomiting, early satiety, postprandial fullness, and epigastric discomfort. In patients with GP, nausea is reported in up to 96% and vomiting in up to 88%, whereas postprandial fullness and bloating are also common (68% and 52%, respectively) (Anaparthy *et al*., 2009). In FD, the predominant symptoms include postprandial fullness (86%), bloating (84%), and epigastric pain (74%) (Tack *et al*., 2004). Epidemiological data indicate that approximately two-thirds of functional dyspepsia patients fall under the postprandial distress syndrome (PDS) subtype, while around 15% present with the epigastric pain syndrome (EPS) subtype, and about 18% have overlapping features of both (Tack *et al*., 2004).

Recent literature has increasingly challenged the rigid separation of FD and GP, which are often indistinguishable in clinical practice (Sato and Grover, 2023). Instead, many experts now propose that FD and GP "represent two ends of the same disease spectrum in a major subgroup" (Egboh *et al*., 2025). This spectrum model proposes a continuum of gastroduodenal neuromuscular disorders, with shared pathophysiological mechanisms such as impaired accommodation, visceral hypersensitivity, and gut-brain axis dysregulation (Sato and Grover, 2023).

Helicobacter pylori (*H. pylori*) infection remains a major contributor to dyspeptic symptoms worldwide (Mazzoleni *et al*., 2011; Lee *et al*., 2024), yet its role in generating or exacerbating GP-like or dysmotility-type symptoms remains uncertain. While some studies suggest that *H. pylori* eradication improves upper gastrointestinal symptoms in subsets of dyspeptic patients, the benefit appears to vary according to symptom pattern, with greater improvement reported in EPS forms and minimal benefit in PDS or GP-like presentations (Lan et al., 2011; Mazzoleni et al., 2011; Xu *et al*., 2013). This variability suggests that *H. pylori* may not contribute uniformly across different symptom subgroups.

The American Neurogastroenterology and Motility Society (ANMS) and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) developed the Gastroparesis Cardinal Symptom Index–Daily Diary (GCSI-DD), a validated tool designed to quantify daily symptom burden in patients with suspected or confirmed GP (Food and Drug Administration, 2018; Chen *et al*., 2025). Although originally developed for GP, several studies have noted that its symptom scores (e.g., nausea/vomiting, fullness/early satiety, bloating) overlap substantially with those observed in FD, and although it has not been designed as a tool to differentiate FD and GP, it allows exploratory comparisons between GP-like and FD symptom patterns (Revicki *et al*., 2012; Lacy *et al*., 2019; Lee, 2019).

In this study, we aimed to explore whether *H. pylori* infection and other clinical factors (age, sex, body mass index (BMI), and endoscopic findings such as hiatal hernia or erosive reflux esophagitis) differ across specific GCSI-DD symptom subgroups, and particularly, whether *H. pylori* shows a distinct association with GP-like symptoms compared with dyspeptic profiles.

MATERIALS AND METHODS

Study population. This was a retrospective, cross sectional study including adult patients who underwent a diagnostic upper endoscopy and subsequently completed the American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index–Daily Diary (ANMS GCSI-DD) (Food and Drug Administration, 2018) at the tertiary referral Centre for Digestive Diseases "GASTRO" in Latvia between October 2023 and April 2025. The questionnaire was offered to all patients who underwent gastroscopy at the clinic.

Data on additional variables were collected from patient files, including age, sex, BMI, and presence of diabetes mellitus. Endoscopy reports were reviewed for erosive reflux esophagitis, hiatal hernia, as well as other substantial findings (peptic ulcer disease, cancer). The presence of *H. pylori* infection was determined either by rapid urease test or histology.

Patients who had incomplete questionnaires were not tested for *H. pylori*, or who had a history of gastric surgery were excluded.

Symptom assessment. Upper gastrointestinal symptoms were assessed using the ANMS GCSI-DD questionnaire (Food and Drug Administration, 2018). Patients were asked in the questionnaire to rate the severity of each symptom on an average day during the past week. The following symptoms were each rated on a five-point Likert scale (0 = none, 4 = very severe): bloating, nausea, early satiety, postprandial fullness, and upper abdominal pain. Patients were also asked to report the number of episodes of vomiting per day, scored on a 0–4 scale (0 = none, 1 = 1 episode, 2 = 2 episodes, 3 = 3 episodes, 4 = ≥ 4 episodes). The total GCSI-DD score was calculated as the mean of the severity of the five symptoms (nausea, early satiety, postprandial fullness, upper abdominal pain and vomiting), resulting in a range of 0–4, with higher scores indicating greater overall symptom burden.

Participants with a GCSI-DD total score of ≥ 2 were considered to have moderate-to-severe gastroparesis symptoms (Food and Drug Administration, 2018).

In addition to the total GCSI-DD score, we investigated both individual symptoms and combinations thereof (symptom composite scores). The original Gastroparesis Cardinal Symptom Index GCSI was developed with three symptom subscales (postprandial fullness/early satiety, nausea/vomiting and bloating) (Revicki *et al*., 2004), with the ANMS GCSI-DD generating both individual item scores and a total symptom score. Based on this structure and by referring to the Rome classification of FD into PDS and EPS syndromes, we constructed three exploratory composite variables: 1) dyspepsia — postprandial distress syndrome (D-PDS), derived by calculating the mean of early satiety, postprandial fullness and bloating scores, 2) dyspepsia — epigastric pain syndrome (D-EPS), equal to the upper abdomi-

nal pain score, and 3) GP-like, derived by calculating the mean of nausea and vomiting scores.

Statistical analysis. Data was compiled using MS Excel, and analysis was performed using IBM SPSS Statistics version 29 (IBM Corp., Armonk, NY). Continuous variables are presented as means with standard deviations (SD) for normally distributed variables and medians with interquartile ranges (IQR) for variables without a normal distribution. Categorical variables are presented as counts (% of total).

In addition to analysing symptom scores as continuous variables, we dichotomised the derived D-PDS, D-EPS, and GP-like composite scores according to symptom score severity using a cut-off of at least 2 to reflect moderate-to-severe symptoms. This cut-off was chosen, as a score of 2 or more on the original 0–4 GCSI-DD scale corresponds to at least moderate symptom severity, and therefore, indicates substantial symptom burden.

To compare differences between groups, Mann–Whitney U or chi-square (χ^2) tests were used. Spearman rank correlations (ρ) were used to evaluate associations between continuous predictors (age, BMI) and symptom scores. Multiple linear regressions were used to determine whether factors such as *H. pylori* infection, sex, age, BMI, diabetes, reflux esophagitis, and hiatal hernia were associated with total GCSI-DD, D-PDS, D-EPS, and GP-like scores. For dichotomised outcomes (GCSI-DD-total ≥ 2, D-PDS ≥ 2, D-EPS ≥ 2, GP-like ≥ 2), multivariable logistic regression models were constructed including the same covariates (*H. pylori* status, sex, age, BMI, diabetes, erosive reflux esophagitis, and hiatal hernia). Results of logistic regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs). A $p < 0.05$ was considered statistically significant.

RESULTS

Main characteristics. A total of 1143 patients undergoing upper endoscopy filled out ANMS GCSI-DD questionnaires. Of these, 37 were missing symptom data and 155 were not tested for *H. pylori* and so were excluded from analysis. A total of 951 individuals were included in the final analysis. The average age was 53.2 ± SD 14.3 years, 724 (76.1%) were female, and the median BMI was 26.0 IQR 6.7 kg/m^2. A total of 57 (6.0%) reported diabetes, 179 (18.8%) had erosive reflux esophagitis and 58 (6.1%) hiatal hernia upon endoscopy, and 238 (25.0%) were infected with *H. pylori*.

Prevalence of symptoms. Overall, 305 patients (32.1%) reported none of the upper gastrointestinal symptoms covered in GCSI-DD, while the remaining two-thirds reported at least one upper gastrointestinal symptom. The distribution of individual ANMS GCSI-DD symptom prevalence is summarised in Table 1. Bloating was the most frequently reported symptom, followed by postprandial fullness and upper abdominal pain.

Composite symptom scores. When symptoms were grouped into predefined composite symptom scores, D-PDS symptoms were present in 147 patients (15.5%), of which 78 (8.2%) reported moderate-to-severe symptoms (≥2). D-EPS symptoms were present in 443 patients (46.6%), and 222 (23.3%) had moderate-to-severe symptoms. GP-like symptoms were identified in 36 patients (3.8%), of whom 14 (1.5%) reported moderate-to-severe severity. In addition, GCSI-DD-total ≥ 2 was observed in 24 patients (2.5%), indicating a high overall symptom burden in only a small subset of the cohort. Median values of the composite symptom scores further reflected a generally low symptom burden in the cohort.

Comparison of symptom prevalence and scores for factors investigated. Inverse associations were found for age and all GCSI-DD composite symptom scores, indicating higher symptom burden in younger patients (Table 2). Similar associations were observed between age and single symptoms. Higher BMI was associated with slightly lower symptom scores, with statistically significant inverse associations for bloating and D-PDS.

Significant differences in symptom severity were observed for women and patients with diabetes. Female participants consistently reported higher symptom severity than males across all composite GCSI-DD symptom scores and for all single symptom scores, including bloating, nausea, early satiety, postprandial fullness, upper abdominal pain and vomiting (all $p < 0.01$, Table 2). In agreement with these findings, moderate-to-severe symptom burden (score ≥ 2) was more prevalent among women for GCSI-DD-total, D-PDS, and D-EPS, and only women had GP-like scores ≥ 2 (Table 3).

When comparing single symptoms, diabetics reported more pronounced nausea and early satiety as well as more frequent vomiting episodes, while the prevalence of bloating, postprandial fullness and upper abdominal pain were similar

Table 1. Prevalence of symptoms from most to least common

Symptom, n (%)	Any (at least mild)	None	Mild	Moderate	Severe	Very severe
Bloating	621 (65.3%)	330 (34.7%)	262 (27.5%)	256 (26.9%)	67 (7.0%)	36 (3.8%)
Postprandial fullness	467 (49.1%)	484 (50.9%)	268 (28.2%)	145 (15.2%)	40 (4.2%)	14 (1.5%)
Upper abdominal pain	443 (46.6%)	508 (53.4%)	221 (23.2%)	163 (17.1%)	43 (4.5%)	16 (1.7%)
Nausea	269 (28.3%)	682 (71.7%)	165 (17.4%)	80 (8.4%)	20 (2.1%)	4 (0.4%)
Early satiety	195 (20.5%)	756 (79.5%)	108 (11.4%)	69 (7.3%)	15 (1.6%)	3 (0.3%)
Vomiting	54 (5.7%)	897 (94.3%)	33 (3.5%)	14 (1.5%)	4 (0.4%)	3 (0.3%)

Table 2. Comparing differences in ANMS GCSI-DD composite scores and single symptom scores between subgroups of investigated factors

Symptom / Composite symptom score	Age (years) Spearman's ρ, *p*-value	BMI (kg/m²) Spearman's ρ, *p*-value	*H. pylori* (positive / negative) median (IQR), *p*-value	Sex (female / male) median (IQR), *p*-value	Diabetes (yes / no) median (IQR), *p*-value
GCSI-DD-total, median (IQR)	ρ = –0.20 $p < 0.01$	ρ = –0.08 $p = 0.01$	0.20 (0.80) / 0.40 (0.80) $p = 0.17$	0.40 (0.80) / 0.20 (0.40) $p < 0.01$	0.40 (1.00) / 0.40 (0.80) $p = 0.07$
D-PDS, median (IQR)	ρ = –0.23 $p < 0.01$	ρ = –0.10 v 0.01	0.66 (1.00) / 0.66 (1.00) $p = 0.10$	0.67 (1.00) / 0.33 (0.66) $p < 0.01$	0.67 (1.33) / 0.67 (1.00) $p = 0.54$
D-EPS, median (IQR)	ρ = –0.14 $p < 0.01$	ρ = –0.06 $p = 0.06$	0.00 (1.00) / 0.00 (1.00) $p = 0.11$	1.00 (2.00) / 0.00 (1.00) $p < 0.01$	0.00 (2.00) / 0.00 (1.00) $p = 0.55$
GP-like, median (IQR)	ρ = –0.12 $p < 0.01$	ρ = –0.02 $p = 0.63$	0.00 (0.50) / 0.00 (0.50) $p = 0.92$	0.00 (0.50) / 0.00 (0.00) $p < 0.01$	0.00 (0.80) / 0.00 (0.50) $p = 0.01$
Bloating, median (IQR)	ρ = –0.19 $p < 0.01$	ρ = –0.07 v = 0.03	1.00 (2.00) / 1.00 (2.00) $p = 0.05$	1.00 (2.00) / 0.00 (1.00) $p < 0.01$	1.00 (2.00) / 1.00 (2.00) $p = 0.85$
Nausea, median (IQR)	ρ = –0.12 $p < 0.01$	ρ = –0.01 $p = 0.87$	0.00 (1.00) / 0.00 (1.00) p = 0.77	0.00 (1.00) / 0.00 (0.00) $p < 0.01$	0.00 (1.00) / 0.00 (1.00) $p = 0.01$
Early satiety, median (IQR)	ρ = –0.14 $p < 0.01$	ρ = –0.06 $p = 0.05$	0.00 (0.00) / 0.00 (0.00) $p = 0.46$	0.00 (0.00) / 0.00 (0.00) $p < 0.01$	0.00 (1.00) / 0.00 (0.00) $p = 0.02$
Fullness, median (IQR)	ρ = –0.18 $p < 0.01$	ρ = –0.05 $p = 0.11$	0.00 (1.00) / 0.00 (1.00) $p = 0.68$	1.00 (1.00) / 0.00 (1.00) $p < 0.01$	1.00 (1.00) / 0.00 (1.00) $p = 0.26$
Abdominal pain, median (IQR)	ρ = –0.14 $p < 0.01$	ρ = –0.06 $p = 0.06$	0.00 (1.00) / 0.00 (1.00) $p = 0.11$	1.00 (2.00) / 0.00 (1.00) $p < 0.01$	0.00 (2.00) / 0.00 (1.00) $p = 0.55$
Vomiting episodes, median (IQR)	ρ = –0.08 $p = 0.01$	ρ = 0.01 $p = 0.81$	0.00 (0.00) / 0.00 (0.00) $p = 0.24$	0.00 (0.00) / 0.00 (0.00) $p = 0.01$	0.00 (0.00) / 0.00 (0.00) $p = 0.01$

Differences compared between groups by using Mann–Whitney U test with values shown as medians with interquartile range (IQR), except for factors age and BMI, where analysis was conducted using Spearman's rank correlation. Negative coefficients (Spearman's ń) indicate higher symptom scores in younger or leaner patients. BMI – body mass index, GCSI-DD – Gastroparesis Cardinal Symptom Index-Daily Diary, PDS – postprandial distress syndrome, EPS – epigastric pain syndrome, GP-like – gastroparesis-like symptoms.

between those with and without diabetes (Table 2). Patients with diabetes also reported a greater symptom burden with higher prevalence of GP-like symptoms and were more likely to have a GCSI-DD-total score of ≥ 2, D-PDS ≥ 2 and GP-like ≥ 2 when compared to non-diabetic patients (Table 3). The prevalence of D-EPS ≥ 2 did not differ by the presence of diabetes.

Presence of *H. pylori* infection, erosive reflux esophagitis and hiatal hernia were not found to be significantly associated with single and composite symptom scores.

Additional sensitivity analysis was performed after excluding patients with diabetes with still no significant differences found for single symptoms and composite symptom scores between *H. pylori* positive and negative individuals.

Multivariable analysis. To determine independent predictors of symptom severity, multivariable linear regression models were constructed for each symptom score and adjusted for age, sex, BMI, *H. pylori* infection, diabetes, erosive reflux esophagitis, and hiatal hernia (Table 4). Across all four composite symptom scores — GCSI-DD-total, D-PDS, D-EPS, and GP-like — female sex and younger age remained strong and consistent predictors of higher symptom scores (all $p < 0.01$). The magnitude of these effects was clinically relevant, with standardised coefficients demonstrating that sex and age accounted for the largest proportion of explained variance across models.

Diabetes mellitus was an additional predictor of symptom burden. After adjustment, diabetes was associated with significantly higher GCSI-DD-total, D-PDS, and GP-like symptom scores (all $p < 0.01$), whereas its association with D-EPS did not reach significance ($p = 0.21$). These findings align with the results of multivariable analysis for moderate-to-severe symptoms (composite symptom score ≥ 2, Table 5).

Although no associations were identified for BMI and GCSI-DD-total, D-PDS, or D-EPS, a statistically significant association with a small effect size was observed between higher BMI and GP-like symptoms (B = 0.006 ± 0.003, β = 0.068, $p = 0.04$).

Table 3. Comparing prevalence of moderate-to-severe symptom burden (score ≥ 2) in subgroups of investigated factors

Factor	GCSI-DD-total ≥ 2	D-PDS ≥ 2	D-EPS ≥ 2	GP-like ≥ 2
Sex	24 (3.3%)	70 (9.7%)	192 (26.5%)	14 (1.9%)
(female vs. male)	0 (0.0%)	8 (3.5%)	30 (13.2%)	0 (0.0%)
	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p = 0.04$
H. pylori (positive vs. negative)	8 (3.4%)	19 (8.0%)	45 (18.9%)	4 (1.7%)
	16 (2.2%)	59 (8.3%)	177 (24.8%)	10 (1.4%)
	$p = 0.34$	$p = 0.89$	$p = 0.06$	$p = 0.76$
Diabetes (yes vs. no)	5 (8.8%)	11 (19.3%)	18 (31.6%)	5 (8.8%)
	19 (2.1%)	67 (7.5%)	204 (22.8%)	9 (1.0%)
	$p < 0.01$	$p < 0.01$	$p = 0.13$	$p < 0.01$

Comparisons between subgroups were performed using the χ^2 test (or Fisher's exact test when expected cell counts were < 5). BMI – body mass index, GCSI-DD – Gastroparesis Cardinal Symptom Index-Daily Diary, D – dyspepsia, PDS – postprandial distress syndrome, EPS – epigastric pain syndrome, GP-like – gastroparesis-like symptoms.

Table 4. Multivariable analysis for composite symptom scores

Factor, B ± SE (β), *p*-value	GCSI-DD-total	D-PDS	D-EPS	GP-like
H. pylori infection	–0.016 ± 0.038 (–0.013), $p = 0.68$	–0.053 ± 0.052 (–0.032), $p = 0.30$	–0.129 ± 0.073 (–0.056), $p = 0.08$	0.026 ± 0.035 (0.023), $p = 0.46$
Female sex	0.296 ± 0.039 (0.234), $p < 0.01$	0.406 ± 0.053 (0.237), $p < 0.01$	0.397 ± 0.075 (0.170), $p < 0.01$	0.235 ± 0.036 (0.205), $p < 0.01$
Age (per year)	–0.010 ± 0.001 (–0.275), $p < 0.01$	–0.015 ± 0.002 (–0.284), $p < 0.01$	–0.013 ± 0.002 (–0.180), $p < 0.01$	–0.007 ± 0.001 (–0.219), $p < 0.01$
BMI (kg/m²)	0.002 ± 0.003 (0.023), $p = 0.48$	0.001 ± 0.005 (0.010), $p = 0.75$	–0.001 ± 0.006 (–0.004), $p = 0.91$	0.006 ± 0.003 (0.068), $p = 0.04$
Diabetes	0.279 ± 0.071 (0.123), $p < 0.01$	0.268 ± 0.097 (0.087), $p < 0.01$	0.171 ± 0.136 (0.041), $p = 0.21$	0.315 ± 0.066 (0.153), $p < 0.01$

Multivariable linear regression adjusted for listed covariates, as well as erosive reflux esophagitis and hiatal hernia (insignificant). Unstandardised regression coefficients (B ± SE) and standardised regression coefficient (β) shown, $p < 0.05$ considered statistically significant.
Abbreviations: SE – standard error; BMI – body mass index; GCSI-DD – Gastroparesis Cardinal Symptom Index-Daily Diary. D – dyspepsia, PDS – postprandial distress syndrome, EPS – epigastric pain syndrome, GP-like – gastroparesis-like symptoms.

Table 5. Multivariable analysis for moderate-to-severe symptom burden

Factor	GCSI-DD-total ≥ 2 OR (95% CI)	D-PDS ≥ 2 OR (95% CI)	D-EPS ≥ 2 OR (95% CI)	GP-like ≥ 2 OR (95% CI)
H. pylori infection	1.57 (0.64–3.87) $p = 0.33$	0.98 (0.56–1.71) $p = 0.94$	0.72 (0.49–1.04) $p = 0.08$	1.11 (0.32–3.91) $p = 0.87$
Female sex	— (unreliable*)	3.48 (1.61–7.52) $p < 0.01$	2.59 (1.68–3.98) $p < 0.01$	— (unreliable*)
Age (per year)	0.94 (0.90–0.97) $p < 0.01$	0.95 (0.93–0.97) $p < 0.01$	0.98 (0.97–0.99) $p < 0.01$	0.92 (0.87–0.96) $p < 0.01$
BMI (kg/m²)	1.07 (1.00–1.15) $p = 0.06$	1.01 (0.97–1.06) $p = 0.59$	1.01 (0.98–1.04) $p = 0.51$	1.10 (1.01–1.20) $P = 0.03$
Diabetes	6.22 (1.86–20.72) $p < 0.01$	4.80 (2.17–10.59) $p < 0.01$	1.73 (0.94–3.19) $p = 0.08$	15.74 (3.62–68.47) $p < 0.01$

*Unreliable estimates due to complete separation (zero cases in reference category).
Models adjusted for: *H. pylori* status, sex, age, BMI, diabetes, erosive reflux esophagitis, and hiatal hernia. BMI – body mass index, GCSI-DD – Gastroparesis Cardinal Symptom Index-Daily Diary, D – dyspepsia, PDS – postprandial distress syndrome, EPS – epigastric pain syndrome, GP-like – gastroparesis-like symptoms.

Other clinical factors, including *H. pylori* infection, erosive reflux esophagitis, and hiatal hernia, were not significantly associated with symptom severity.

DISCUSSION

The results of the analysis suggest that in a general population referred for endoscopy, factors such as sex, age, and presence of diabetes are more likely to affect upper gastrointestinal symptoms as assessed by the ANMS GCSI-DD than the presence of *H. pylori* infection and common endoscopic findings such as erosive reflux esophagitis and hiatal hernia.

***Helicobacter pylori*, dyspeptic and gastroparesis-like symptoms.** Initially, the main aim of the study was to ex-

plore whether *H. pylori* infection, a known contributor to dyspeptic symptoms, was associated with upper gastrointestinal symptom patterns. The literature suggests varying benefit of *H. pylori* eradication, reporting greater improvement in EPS presentations and smaller benefit in PDS or gastroparesis-like syndromes (Lan *et al*., 2011; Mazzoleni *et al*., 2011; Xu *et al*., 2013).

In multivariable analysis, *H. pylori* infection was not associated with either D-PDS score ($p = 0.30$) or GP-like score ($p = 0.46$). This aligns with a substantial body of evidence suggesting that *H. pylori* is not a primary driver of dysmotility-type symptoms and is considered a minor, rather than major, cause in the complex pathophysiology of FD (Lee, 2021). The lack of a significant association with the D-EPS domain ($p = 0.08$), where an association might have been anticipated, must be interpreted carefully, as there are some limitations that could affect the interpretation of findings in relation to *H. pylori*. First of all, the prevalence of *H. pylori* of 25% is lower than expected, as a prevalence as high as 50% is reported in other studies (Razuka-Ebela *et al*., 2020). In a subset of patients, *H. pylori* status was determined using a rapid urease test. However, rapid urease testing can have reduced sensitivity compared with histology and ^{13}C-urea breath testing, particularly in settings with low bacterial density or upper gastrointestinal bleeding and may therefore be more prone to false-negative results (Uotani and Graham, 2015; Abd Rahim *et al*., 2018). The analysis also did not account for possible concomitant use of proton pump inhibitors, which would both increase the chances of false negative rapid urease tests as well as alter or "mask" symptoms and their severity.

Symptom burden among women. Female sex was consistently and independently associated with higher symptom scores across every domain analysed. This observation is highly consistent with extensive epidemiological data that showed a higher prevalence of FD and GP in women (Kim *et al*., 2018; Sato and Grover, 2023; Guo *et al*., 2025).

Our findings, however, contribute to a growing body of evidence suggesting this disparity is not merely in prevalence but is rooted in distinct pathophysiological mechanisms. Recent reviews highlight that women with FD often report lower quality of life than men and that pathophysiology likely varies by gender. This has led to the exploration of the "microgenderome", defined as the bidirectional interaction between the gut microbiota and sex hormones (Kim and Kim, 2020). Sex hormones are known to shape gut microbiome composition, which in turn can influence visceral sensitivity, gut motility, and gut-brain axis signalling (Khalil *et al*., 2024). The fact that our data show a uniformly strong association of female sex with all symptom types — D-EPS, D-PDS, and GP-like —underscores the gravity of a potentially sex-based disparity, reinforcing the need for investigating whether tailoring approaches based on sex could increase the efficacy of treatment.

Age paradox: younger age associated with high symptom severity. An unexpected finding of this study was the strong inverse association between age and symptom severity. Across all domains, younger age was predictive of a higher symptom burden (all $p < 0.001$). This finding appears to contradict several systematic reviews that have associated older age (e.g., ≥ 64 years) with a high prevalence of FD (Arnaout *et al*., 2023; Guo *et al*., 2025). However, other recent studies have also identified younger age as an independent risk factor for FD (Park *et al*., 2025). One review noted that the prevalence of FD tends to peak in the 20s and 30s and subsequently decrease with age (Sato and Grover, 2023).

Referral patterns and age-related tendencies may have contributed to referral bias. Younger patients with functional symptoms may be referred for endoscopy earlier, whereas in older patients similar complaints may be attributed to comorbidities or polypharmacy. Moreover, some participants in the colorectal cancer screening programme (≥50 years) may undergo upper endoscopy solely due to a positive faecal immunochemical test, with little or no upper gastrointestinal symptoms. A more precise assessment of referral bias would require detailed analysis of the indications and reasons for referral, which are not consistently or clearly reflected in the recorded referral diagnosis.

It must also be considered that dyspepsia may have different pathophysiology when comparing younger to older individuals. For example, dyspepsia in older cohorts may be driven by other factors, such as gastric atrophy, chronic medication use, or reduced gastric accommodation (Guo *et al*., 2025). Conversely, the dyspepsia observed in our study and other studies in younger populations may be a separate phenotype driven more by visceral hypersensitivity, post infectious syndromes, or gut-brain axis dysregulation (Egboh *et al*., 2025).

Diabetes and dysmotility. After multivariable adjustment, diabetes was a powerful predictor of higher scores in dysmotility-related domains: the GP-like score (B = 0.32, $p < 0.01$) and D-PDS score (B = 0.27, $p = 0.01$). Furthermore, diabetes was the strongest predictor of a high overall symptom burden (OR 6.22 for GCSI-DD-total score ≥ 2). This association was very selective, as diabetes showed no significant relationship with D-EPS score ($p = 0.21$).

The Rome criteria separate FD into PDS and EPS (Stanghellini *et al*., 2016). Clinical reviews have hypothesised that PDS, due to its basis in motility alterations, is the subtype most likely to overlap with GP (Bonetto *et al*., 2021). Diabetes, in turn, is a well-established cause of autonomic neuropathy, which directly impairs gastric motility and emptying (Park *et al*., 2025).

By demonstrating that a known cause of dysmotility (diabetes) selectively predicts a symptom group representing dysmotility (PDS/GP-like symptoms) but not pain (EPS), our data support the subclassification and separation of PDS and EPS into two syndromes. In patients with diabetes,

symptoms of postprandial distress may not be "functional" at all, but rather a direct clinical manifestation of underlying gastroduodenal dysmotility secondary to diabetic autonomic neuropathy (Park *et al*., 2025).

Strengths and limitations. This study possesses several notable strengths, including its large cohort and adjustments for multiple factors. The use of the validated, Food and Drug Administration qualified ANMS GCSI-DD provided a robust and standardised measure of symptom burden.

Despite these strengths, the study's findings must be interpreted in the context of several important limitations. First, there are some limitations pertaining to design aspects of the study. Its retrospective, cross-sectional design allows for the identification of associations only, causality cannot be inferred. The GCSI-DD was designed and validated as a tool to screen and monitor GP symptoms, while we also used it to assess the individual symptom scores separately. Second, there is some data which, if included in the analysis, could improve the interpretation of the results. This includes data on proton pump inhibitor use which could affect both rapid urease test results as well as the reporting and severity of upper gastrointestinal symptoms. Likewise, other medications not recorded could also play a role in aggravating symptoms.

CONCLUSIONS

In this large, cross-sectional endoscopy cohort, upper gastrointestinal symptom severity was mainly driven by host-related factors rather than by *H. pylori* infection or structural endoscopic findings. Female sex and younger age were consistent, independent predictors of higher symptom scores across all domains, and diabetes mellitus was strongly associated with greater overall symptom burden. In contrast, *H. pylori*, erosive reflux esophagitis and hiatal hernia were not significantly associated with symptom severity.

ETHICS

This study was approved by Rīga Stradiņš University Ethical Committee (approval No. 2-PĒK-4/951/2025).

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AUGŠĒJO KUŅĢA UN ZARNU TRAKTA SIMPTOMU IZPLATĪBAS UN AR TO SAISTĪTO FAKTORU IZPĒTE, IZMANTOJOT GASTROPARĒZES GALVENO SIMPTOMU INDEKSU ENDOSKOPIJAS KOHORTĀ LATVIJĀ

Gastroparēzes (GP) un funkcionālās dispepsijas simptomi bieži pārklājas, un nav skaidrs, vai *Helicobacter pylori (H. pylori)* infekcija vai citi bieži sastopami klīniskie faktori ir saistīti ar specifiskiem simptomu profiliem. Tādēļ mērķis bija izvērtēt, vai *H. pylori*, demogrāfiskie faktori un cukura diabēts ir saistīti ar dispepsijas un motilitātes traucējumu tipa simptomu izplatību un smagumu. Šajā retrospektīvajā šķērsgriezuma pētījumā 951 pieaugušais, kam veikta augšējā endoskopija, aizpildīja *Gastroparesis Cardinal Symptom Index-Daily Diary* (ANMS GCSI-DD) anketu, un tika aprēķināti simptomu izpausmju smagumi pa grupām: D-PDS (dispepsija-postprandiāls distresa sindroms), D-EPS (sāpes epigastrijā) un GP-līdzīgie (gastroparēzei līdzīgie simptomi — slikta dūša/vemšana). Tika izpētīts, vai ir saistība starp šo simptomu smagumu un *H. pylori* infekciju, vecumu, dzimumu, ķermeņa masas indekss, cukura diabētu, erozīvu ezofagītu un diafragmas barības vada atveres trūci. Sieviešu dzimums un jaunāks vecums bija saistīti ar lielāku simptomu smagumu visās simptomu grupās, savukārt cukura diabēts bija selektīvi saistīts ar izteiktākiem motilitātes traucējumu tipa simptomiem (GP-līdzīgie un D-PDS) un mērenu līdz smagu kopējo simptomu smagumu, bet ne ar D-EPS. Daudzfaktoru analīzē *H. pylori*, erozīvs ezofagīts un trūce nebija saistīti ar simptomu smagumu, kas liecina, ka augšējā gremošanas trakta simptomu smagumu šajā kohortā galvenokārt noteica sieviešu dzimums, jaunāks vecums un cukura diabēts, nevis *H. pylori* infekcija vai endoskopiski konstatējama patoloģija.