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Prevalence and Predictors of Pancreatic Exocrine Insufficiency Among Adults Under 60 Years Presenting with Dyspepsia in Primary Care: A Cross-Sectional Study

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Abstract

Aim: Dyspepsia is one of the most common reasons for consultation in primary care, yet underlying pancreatic exocrine insufficiency (PEI) may remain unrecognized. This study aimed to determine the prevalence of PEI among adults under 60 years presenting with dyspeptic symptoms in primary care and to identify associated sociodemographic, clinical, and symptom-related predictors.

Methods: This cross-sectional study was conducted in the Family Medicine Clinic of a tertiary training and research hospital. A total of 375 adults aged 18–60 years presenting with dyspepsia were included. Data were collected through a structured case report form and the Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q), consisting of A, B, and C subcomponents. PEI positivity was defined according to the questionnaire scoring system. Logistic regression analysis was used to identify independent predictors of PEI positivity. Receiver operating characteristic (ROC) analyses were performed to evaluate the discriminative performance of PEI-Q scores for dyspeptic symptoms.

Results: A total of 375 participants were included in the analysis, with a mean age of 42.85 ± 11.91 years; 67.7% were female. Based on the Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q), 120 participants (32.0%) were classified as PEI-positive. Participants in the PEI-positive group were significantly younger and had a higher body mass index compared with PEI-negative participants. Nausea/vomiting, epigastric pain, and loss of appetite were significantly more frequent among PEI-positive individuals (all $p < 0.001$), whereas bloating was highly prevalent but not independently associated with PEI positivity. In multivariate logistic regression analysis, younger age (OR = 0.964), higher body mass index (OR = 1.074), nausea/vomiting (OR = 2.760), epigastric pain (OR = 4.630), and loss of appetite (OR = 4.168) were independently associated with PEI positivity. Receiver operating characteristic analyses demonstrated moderate discriminative ability of the PEI-Q AB score for nausea/vomiting (AUC = 0.745), epigastric pain (AUC = 0.748), and loss of appetite (AUC = 0.757).

Conclusions: Nearly one-third of adults under 60 years presenting with dyspepsia in primary care were classified as PEI-positive. Specific dyspeptic symptoms, particularly nausea/vomiting, epigastric pain, and loss of appetite, were strongly associated with PEI. The PEI-Q appears to be a practical screening tool for identifying patients at risk of PEI in primary care settings and may contribute to more targeted diagnostic evaluation and management.

Keywords: Dyspepsia; pancreatic exocrine insufficiency; primary care; screening; functional dyspepsia

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Introduction

Dyspepsia is a highly prevalent gastrointestinal complaint characterized by upper abdominal discomfort, postprandial fullness, early satiety, epigastric pain, or burning [1,2]. It represents a substantial burden on primary care services worldwide, accounting for a significant proportion of outpatient consultations [3]. Although most patients are ultimately diagnosed with functional dyspepsia, a considerable heterogeneity exists in symptom presentation, pathophysiology, and treatment response [4].

Current diagnostic frameworks emphasize the exclusion of structural or metabolic causes; however, subtle or subclinical organic contributors may remain undetected [5]. In recent years, growing attention has been directed toward pancreatic exocrine insufficiency (PEI) as a potential but frequently overlooked contributor to dyspeptic symptoms [6]. PEI results from inadequate secretion or activity of pancreatic digestive enzymes, leading to impaired nutrient digestion and a spectrum of gastrointestinal manifestations ranging from steatorrhea and weight loss to nonspecific symptoms such as bloating, nausea, and epigastric discomfort [7].

Mild or early-stage PEI may present without classical signs of malabsorption and can therefore be easily misclassified as functional dyspepsia, particularly in primary care settings [8]. Although PEI is well recognized in conditions such as chronic pancreatitis, pancreatic cancer, and cystic fibrosis, its prevalence among patients presenting solely with dyspeptic symptoms remains insufficiently explored [6,9]. Emerging evidence suggests that pancreatic enzyme abnormalities and early pancreatic dysfunction may be present in a subset of patients previously labeled as having functional dyspepsia [10].

Primary care physicians are uniquely positioned to identify such patients; however, routine diagnostic testing for PEI is rarely feasible at this level due to cost, accessibility, and limited sensitivity of available tests for mild disease [11]. In this context, symptom-based screening tools may provide a practical approach for early risk stratification [6]. The Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q) has been developed as a simple and rapid assessment tool suitable for primary care use, yet data on its performance among dyspeptic populations are limited [12].

Therefore, the present study aimed to determine the prevalence of PEI among adults under 60 years presenting with dyspepsia in a primary care setting and to identify clinical and symptom-related factors associated with PEI positivity. Additionally, we evaluated the discriminative performance of PEI-Q scores for common dyspeptic symptoms to assess its potential utility as a screening tool in routine primary care practice.

Methods

Study Design and Setting

This cross-sectional descriptive study was conducted in the Kestel No. 5 Vani Mehmet Neighborhood Family Health Center, a primary care setting located in Bursa, Türkiye. The Family Health Center provides first-level healthcare services and serves an adult population registered within its catchment area. The study aimed to evaluate the prevalence of pancreatic exocrine insufficiency (PEI) among adults under 60 years presenting with dyspeptic symptoms in a primary care setting and to identify associated clinical and demographic factors.

Participants

Adults aged 18–60 years presenting to the Kestel No. 5 Vani Mehmet Neighborhood Family Health Center with dyspeptic symptoms during the study period were consecutively assessed and invited to participate. Dyspepsia was defined as one or more upper gastrointestinal symptoms, including bloating, epigastric pain, nausea/vomiting, early satiety, or loss of appetite.

Inclusion criteria were age 18–60 years, dyspeptic symptoms, and written informed consent. Exclusion criteria included age ≥60 years, pregnancy, known malignancy, severe organ failure, acute surgical abdomen or infection, severe cognitive impairment, dyspepsia due to an identified organic cause, or incomplete data.

A total of 375 participants were included in the final analysis.

Data Collection

Data were collected through face-to-face interviews conducted by a family physician using a structured case report form. Sociodemographic variables (age, sex, education level, marital status, income level), lifestyle factors (smoking, alcohol use), anthropometric measurements (height, weight, body mass index), comorbid conditions, medication use, and dyspeptic symptoms were recorded.

Assessment of Pancreatic Exocrine Insufficiency

Pancreatic exocrine insufficiency was assessed using the PEI-Q, a screening tool designed for rapid evaluation in primary care settings [1]. The questionnaire consists of three subcomponents: Component A: clinician-assessed clinical findings, Component B: patient-reported gastrointestinal symptoms, and Component C: clinician's overall clinical judgment and risk assessment [12].

The questionnaire was administered in two stages: clinician-completed items were recorded during the interview, followed by patient self-completion of the symptom-based section. PEI positivity was determined according to the predefined scoring criteria of the PEI-Q. Higher scores indicated greater severity of pancreatic enzyme insufficiency–related symptoms [12].

The Turkish version of the PEI-Q has demonstrated acceptable internal consistency and diagnostic performance in previous validation studies, supporting its use as a reliable screening instrument in clinical practice [13].

No biochemical or functional pancreatic tests, such as fecal elastase measurement, were performed as part of the study.

Statistical Analysis

Descriptive statistics were used to summarize participant characteristics and clinical variables. Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages.

Comparisons between participants classified as pancreatic exocrine insufficiency (PEI)–positive and PEI-negative were performed using the independent samples t-test for normally distributed continuous variables. Categorical variables were compared using the chi-square test, as appropriate.

To identify factors independently associated with PEI positivity, a binary logistic regression analysis was conducted. Age, body mass index (BMI), sex, smoking status, hypertension, diabetes mellitus, and dyspeptic symptoms (bloating, nausea/vomiting, epigastric pain, bitter or sour taste in the mouth, constipation, and loss of appetite) were entered into the multivariate model. Regression coefficients (B), standard errors (SE), Wald statistics, odds ratios (ORs), and 95% confidence intervals (CIs) were calculated. Model fit was assessed using the likelihood ratio chi-square test and Nagelkerke's R^2.

Multicollinearity among independent variables was evaluated using tolerance and variance inflation factor (VIF) values, with tolerance >0.20 and VIF <5 considered acceptable.

The discriminative performance of the Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q) AB score for dyspepsia-related symptoms was assessed using receiver operating characteristic (ROC) curve analysis. Area under the curve (AUC) values with 95% confidence intervals were calculated for each symptom. Optimal cut-off points were determined using the Youden index, and corresponding sensitivity and specificity values were reported.

All statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA). A two-sided p value <0.05 was considered statistically significant.

Results

Participant Characteristics

A total of 375 participants were included in the analysis. The mean age was 42.85 ± 11.91 years, and the mean body mass index (BMI) was 27.99 ± 5.02 kg/m^2. Of the participants, 254 (67.7%) were female. Most participants had primary school education or below (55.2%) and were married (88.0%). Smoking was reported by 31.2% of participants, while alcohol consumption was reported by 1.6%. Baseline demographic and clinical characteristics are summarized in Table 1.

Hypertension was the most common comorbidity (23.5%), followed by diabetes mellitus (12.3%) and hypothyroidism (2.9%). Nonsteroidal anti-inflammatory drug (NSAID) use was reported by 38.7% of participants.

Table 1. Demographic and clinical characteristics of the participants (n = 375)

Variables	Value
Age, years	42.85 ± 11.91
BMI (kg/m²)	27.99 ± 5.02
Sex, n (%)	
Female	254 (67.7)
Male	121 (32.3)
Education level, n (%)	
Primary education or less	207 (55.2)
Secondary education	92 (24.5)
Higher education	76 (20.3)
Marital status, n (%)	
Single	45 (12.0)
Married	330 (88.0)
Income level, n (%)	
Low	91 (24.3)
Middle	273 (72.8)
High	11 (2.9)
Smoking status, n (%)	
Smoker	117 (31.2)
Non-smoker	258 (68.8)
Alcohol consumption, n (%)	
Yes	6 (1.6)
No	369 (98.4)

Note: Continuous variables are presented as mean ± standard deviation (SD); categorical variables are presented as number (percentage).

Dyspeptic Symptoms

The most frequently reported dyspeptic symptom was bloating, present in 96.3% of participants. Other common symptoms included epigastric pain (40.3%), nausea/vomiting (33.3%), and loss of appetite (24.8%). Less frequent symptoms were bitter or sour taste in the mouth (5.3%) and constipation (3.5%). The distribution of dyspeptic symptoms among participants is summarized in Table 2.

Table 2. Distribution of dyspeptic symptoms among participants

Dyspeptic symptom	n (%)
Bloating	361 (96.3)
Epigastric pain	151 (40.3)
Nausea/Vomiting	125 (33.3)
Loss of appetite	93 (24.8)
Bitter or sour taste	20 (5.3)
Constipation	13 (3.5)

Categorical variables are expressed as n (%).

Prevalence of Pancreatic Exocrine Insufficiency

Based on the Pancreatic Exocrine Insufficiency Questionnaire (PEI-Q), 120 participants (32.0%) were classified as PEI-positive, while 255 (68.0%) were classified as PEI-negative.

Median scores for PEI-Q subcomponents were 4.00 (interquartile range [IQR]: 3.00–8.00) for component A, 0.00 (IQR: 0.00–2.00) for component B, and 0.00 (IQR: 0.00–1.00) for component C. The median AB score was 0.38 (IQR: 0.21–0.73), and the median ABC score was 0.25 (IQR: 0.14–0.57).

Comparison of PEI-Positive and PEI-Negative Groups

Participants in the PEI-positive group were significantly younger than those in the PEI-negative group (40.51 ± 11.75 vs. 43.96 ± 11.85 years, p = 0.009). Female sex was more common among PEI-positive participants (75.8% vs. 63.9%, p = 0.021), and alcohol consumption was also more frequent in this group (p = 0.014).

Hypertension was significantly less prevalent in the PEI-positive group compared with the PEI-negative group (16.7% vs. 26.7%, p = 0.033), whereas hypothyroidism was more frequent among PEI-positive participants (5.8% vs. 1.6%, p = 0.042). No significant differences were observed between groups with regard to diabetes mellitus, smoking status, or medication use (p > 0.05 for all).

Association Between Dyspeptic Symptoms and PEI

Nausea/vomiting, epigastric pain, and loss of appetite were significantly more frequent among PEI-positive participants compared with PEI-negative participants (all p < 0.001). In contrast, no significant differences were observed for bloating, bitter or sour taste in the mouth, or constipation.

Predictors of PEI Positivity

In binary logistic regression analysis (Table 3), younger age (OR = 0.964, p = 0.013), higher body mass index (OR = 1.074, p = 0.017), nausea/vomiting (OR = 2.760, p < 0.001), epigastric pain (OR = 4.630, p < 0.001), and loss of appetite (OR = 4.168, p < 0.001) were independently associated with PEI positivity.

Sex, smoking status, hypertension, diabetes mellitus, bloating, bitter or sour taste in the mouth, and constipation were not independently associated with PEI positivity in the multivariate model. The model explained 39.4% of the variance in PEI positivity (Nagelkerke R^2 = 0.394) and demonstrated acceptable goodness of fit.

Table 3. Factors associated with Pancreatic Exocrine Insufficiency (PEI) positivity

Variables	B	SE	Wald	df	p-value	OR	95% CI (LL–UL)
Age	-0.037	0.015	6.161	1	0.013	0.964	0.937–0.992
BMI	0.071	0.030	5.735	1	0.017	1.074	1.013–1.138
Sex (Female)	-0.021	0.330	0.004	1	0.950	0.979	0.513–1.870
Smoking (Yes)	0.414	0.311	1.776	1	0.183	1.513	0.823–2.781
Hypertension (Yes)	-0.475	0.387	1.502	1	0.220	0.622	0.291–1.329
Diabetes (Yes)	0.567	0.453	1.566	1	0.211	1.762	0.725–4.281
Bloating (Yes)	0.969	0.458	4.484	1	0.035	2.634	1.066–6.503
Nausea/Vomiting (Yes)	1.015	0.289	12.321	1	<0.001	2.760	1.566–4.867
Epigastric pain (Yes)	1.533	0.280	30.066	1	<0.001	4.630	2.677–8.008
Bitter/Sour taste in mouth (Yes)	0.328	0.589	0.310	1	0.577	1.388	0.438–4.399
Constipation (Yes)	-0.225	0.781	0.083	1	0.773	0.799	0.173–3.961
Loss of appetite (Yes)	1.428	0.311	21.085	1	<0.001	4.168	2.266–7.666

LL = Lower Limit, UL = Upper Limit, CI = Confidence Interval, SE = Standard Error. Binary logistic regression analysis: χ^2 = 124.044, p < 0.001; Nagelkerke R^2 = 0.394. No multicollinearity was detected among independent variables (Tolerance > 0.20, VIF < 5 for all variables).

ROC Curve Analysis

Receiver operating characteristic (ROC) analyses demonstrated that the PEI-Q AB score had moderate discriminative ability for selected dyspeptic symptoms. The area under the curve (AUC) was 0.745 (95% CI: 0.695–0.795) for nausea/vomiting, 0.748 (95% CI: 0.695–0.796) for epigastric pain, and 0.757 (95% CI: 0.697–0.809) for loss of appetite (Figure 1). The discriminative performance of the AB score for other symptoms was limited.

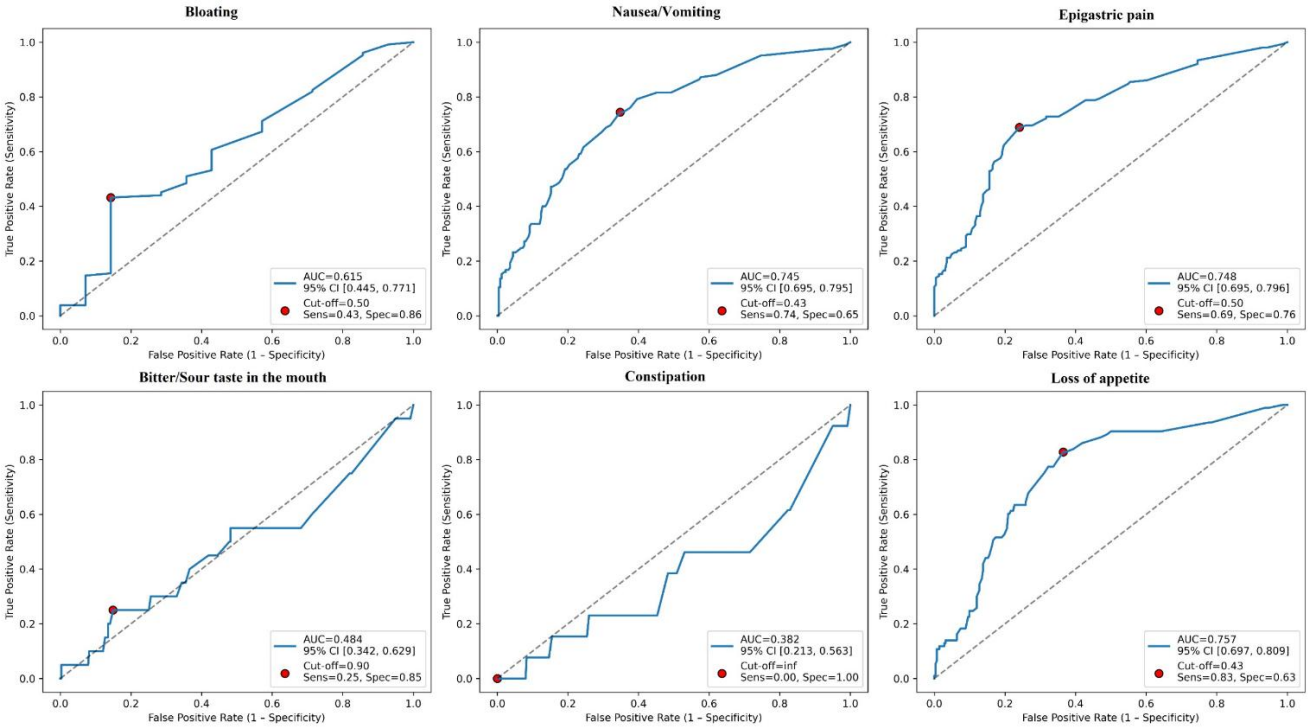

Figure 1. Receiver operating characteristic (ROC) curves of the PEI Questionnaire total score for dyspepsia-related symptoms: Bloating, Nausea/vomiting, Epigastric pain, Bitter/sour taste in the mouth, Constipation, and Loss of appetite. AUC values with 95% confidence intervals, optimal cut-off points, sensitivity, and specificity are shown for each symptom.

Discussion

This cross-sectional study demonstrated that nearly one-third of adults under 60 years presenting with dyspepsia in a primary care setting were classified as pancreatic exocrine insufficiency (PEI)–positive using the PEI-Q. This finding highlights that PEI may represent a substantially underrecognized contributor to dyspeptic symptoms in routine primary care practice, particularly among patients who might otherwise be labeled as having functional dyspepsia [1,5,7,8,10,12,14].

The observed PEI positivity rate of 32% is higher than traditionally expected in a relatively young and ambulatory dyspeptic population. Prior literature has predominantly examined PEI within the context of chronic pancreatitis, pancreatic malignancy, or advanced metabolic disease [6,7,9,11,15,16], whereas milder or subclinical forms have received less attention. Our findings align with evidence indicating that pancreatic dysfunction exists along a clinical continuum and may initially present with nonspecific upper gastrointestinal symptoms rather than overt malabsorption [7,8,10,14,16,17].

Among the dyspeptic symptoms evaluated, nausea/vomiting, epigastric pain, and loss of appetite showed strong and independent associations with PEI positivity. These symptoms substantially overlap with functional dyspepsia and may therefore contribute to diagnostic overshadowing in daily practice [1,2,5,10]. The strong association with epigastric pain is clinically relevant, as pancreatic-origin pain may be misattributed to gastroduodenal causes in the absence of established pancreatic disease [4,6,10,16]. Likewise, loss of appetite may reflect subtle digestive inefficiency and early satiety related to impaired enzymatic activity [7,8,14,17].

Although bloating was highly prevalent, it did not independently predict PEI positivity. This suggests that bloating, while common in dyspepsia, lacks specificity for pancreatic dysfunction and should be interpreted cautiously when isolated [1,3-5,7,8]. In contrast, symptom clusters characterized by nausea, epigastric pain, and appetite loss appear more informative for PEI risk stratification in primary care [7,8,10,12,14].

Younger age and higher body mass index were independently associated with PEI positivity. The inverse association with age contrasts with the traditional view of PEI as a condition primarily affecting older patients with long-standing pancreatic disease [6,11,18]. This may indicate earlier-stage

pancreatic dysfunction or metabolic influences preceding overt disease. The association with higher BMI is consistent with growing evidence linking metabolic dysregulation and insulin resistance to pancreatic exocrine dysfunction, even in the absence of established diabetes mellitus [9,15,19].

Receiver operating characteristic analyses showed that the PEI-Q AB score had moderate discriminative ability for clinically relevant dyspeptic symptoms, with AUC values approaching 0.75 for nausea/vomiting, epigastric pain, and loss of appetite. While insufficient as a stand-alone diagnostic test, these findings support the PEI-Q as a pragmatic screening tool to identify patients who may benefit from further evaluation or therapeutic trials of pancreatic enzyme replacement therapy (PERT) [8,12,14,20]. From a clinical perspective, the moderate AUC values observed for nausea/vomiting, epigastric pain, and loss of appetite suggest that the PEI-Q AB score may be useful for risk stratification rather than definitive diagnosis. In routine primary care, where access to pancreatic function testing is often limited, such symptom-based discrimination may help clinicians identify patients who warrant further evaluation, referral to secondary care, or consideration of empiric pancreatic enzyme replacement therapy. Thus, the PEI-Q may function as a decision-support tool that complements clinical judgment, rather than replacing objective diagnostic testing.

From a primary care perspective, these results have important implications. Objective diagnostic tests for PEI—such as fecal elastase—are limited by availability and reduced sensitivity in mild disease [17,21]. In contrast, symptom-based tools are easily implementable and may facilitate targeted referral, diagnostic work-up, or empiric PERT in selected patients [7,8,12,22]. Early recognition of PEI may improve symptom control, reduce unnecessary investigations, and prevent prolonged misclassification as purely functional disorders [6–8,10,23].

Several limitations warrant consideration. The cross-sectional design precludes causal inference. PEI classification relied on a validated questionnaire rather than direct pancreatic function testing, which may have resulted in misclassification, particularly in borderline cases. However, this approach reflects real-world primary care constraints, where advanced diagnostic modalities are often unavailable. The single-center design may also limit generalizability.

Despite these limitations, strengths include the relatively large sample size, standardized data collection, and focus on a primary care population that is underrepresented in PEI research. The incorporation of ROC analyses further strengthens the assessment of PEI-Q performance in relation to clinically relevant dyspeptic symptoms.

In conclusion, PEI appears to be a common and underdiagnosed condition among adults under 60 years presenting with dyspepsia in primary care. Symptom patterns—particularly nausea/vomiting, epigastric pain, and loss of appetite—are key indicators of PEI risk. Integrating symptom-based screening tools such as the PEI-Q into primary care practice may enhance early detection and support more individualized and effective management strategies.

Ethical Considerations

The study was approved by the Clinical Research Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital (Approval No: 2011-KAEK-25 2023/04-01, Date: 20/04/2023). All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion.

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Conflict of Interest

The authors declare no conflicts of interest related to this study.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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