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Association of Reflux Characteristics on 24-Hour pH-Impedance Monitoring with Clinical Manifestations of Laryngopharyngeal Reflux: A Cross-sectional Study

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ABSTRACT: Laryngopharyngeal reflux (LPR) is characterized by the retrograde movement of gastric contents into the laryngopharynx. The clinical relevance of specific reflux characteristics detected by 24-hour pH-multichannel intraluminal impedance (pH-MII) monitoring remains incompletely understood. This study evaluated the association between reflux acidity and physical composition with clinical manifestations of LPR. This cross-sectional observational study included 40 patients with LPR at two tertiary hospitals in Makassar, Indonesia. Clinical manifestations were assessed using the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS). Reflux episodes were characterized according to acidity (acid, weakly acid, and non-acid) and physical composition (liquid, gas, and mixed) using 24-hour pH-MII monitoring. Associations were analyzed using the Kruskal–Wallis test. Weakly acid reflux was the predominant reflux type, accounting for 2,825 episodes, whereas mixed reflux was the most frequent physical composition, with 1,650 episodes. The mean RSI and RFS scores were 16.23 ± 2.74 and 10.38 ± 2.98, respectively. Reflux acidity was not significantly associated with any RSI or RFS component ($P > 0.05$). In contrast, reflux composition was significantly associated with heartburn/regurgitation ($P = 0.018$), with the highest mean score observed in the mixed-reflux group (3.38 ± 1.43). No other RSI or RFS component differed significantly according to reflux composition. In conclusion, reflux acidity was not associated with LPR symptoms or laryngoscopic findings, whereas reflux composition was associated with heartburn/regurgitation. Further prospective studies with larger and more balanced cohorts are warranted to clarify the clinical significance of distinct reflux phenotypes.

1. INTRODUCTION

Laryngopharyngeal reflux (LPR) is a condition characterized by the retrograde movement of gastric or gastroduodenal contents into the upper aerodigestive tract, where exposure to refluxate may induce mucosal irritation, inflammation, and functional disturbances of the larynx and pharynx. Unlike classic gastroesophageal reflux disease, LPR frequently presents without typical heartburn or regurgitation and is instead associated with a broad spectrum of nonspecific manifestations, including globus sensation, throat clearing, hoarseness, chronic cough, excessive throat mucus, and dysphagia (1,2). The nonspecific nature of these symptoms and laryngoscopic findings poses a diagnostic challenge because similar manifestations may occur in allergic, inflammatory, infectious, functional, and other upper airway disorders. Although the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) are widely used to characterize the symptom burden and laryngoscopic findings of suspected LPR, neither instrument is sufficiently specific to establish reflux as the underlying cause (2,3).

Objective reflux monitoring is therefore increasingly important in the evaluation of patients with suspected LPR. Twenty-four-hour pH monitoring combined with multichannel intraluminal impedance (pH-MII) provides information beyond acid exposure by detecting reflux episodes irrespective of their acidity and by characterizing the physical composition of the refluxate. In particular, impedance monitoring can identify acid, weakly acid, and non-acid reflux and distinguish liquid, gas, and mixed reflux events, thereby providing a more comprehensive assessment of reflux physiology than conventional pH monitoring alone (1,2). This distinction is clinically relevant because reflux-related laryngopharyngeal injury may occur in the presence of weakly acidic or non-acidic material, and persistent symptoms may occur despite acid-suppressive therapy. Contemporary consensus recommendations have consequently emphasized objective reflux monitoring, particularly hypopharyngeal-esophageal impedance-pH assessment, as an important component of the diagnostic evaluation and individualized management of LPR (4).

Despite advances in objective reflux monitoring, the clinical significance of individual reflux characteristics remains incompletely established. The presence or number of reflux episodes does not necessarily correspond directly to symptom severity or laryngoscopic abnormalities, reflecting the complex and multifactorial pathophysiology of LPR. Mucosal susceptibility, impaired epithelial defense, exposure to pepsin and other reflux components, proximal extent of refluxate, and individual sensory responses may all influence the development and severity of clinical manifestations (2). Furthermore, systematic evidence has demonstrated considerable limitations in the validity and reliability of clinical instruments used to assess LPR, while the absence of a universally accepted diagnostic gold standard continues to complicate the interpretation of associations between objective reflux testing and clinical findings (1,3). Accordingly, examining the relationship between specific reflux characteristics identified by pH-MII and clinically relevant measures such as RSI and RFS may provide additional insight into the pathophysiological relevance of different reflux phenotypes.

Therefore, this study aimed to evaluate the association between reflux characteristics detected by 24-hour pH-MII monitoring and the clinical manifestations of LPR, as assessed by RSI and RFS. Specifically, the study examined the relationship of reflux acidity (acid, weakly acid, and non-acid reflux) and physical composition (liquid, gas, and mixed reflux) with symptom burden and laryngoscopic findings. By integrating objective reflux characterization with standardized clinical assessment, this study seeks to clarify whether specific reflux patterns are associated with the clinical expression of LPR and to contribute to a more objective and individualized approach to the evaluation of patients with suspected LPR.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This observational cross-sectional study was conducted at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Teaching Hospital, Makassar, Indonesia. Patient recruitment was conducted from December 2025 to June 2026.

2.2 Study Population and Participants

The study population consisted of patients with suspected LPR who presented to the participating hospitals. Participants were selected using purposive sampling, whereby eligible patients were consecutively considered for enrollment until the predetermined sample size was reached.

The required sample size was determined using the sample size estimation approach described by Hulley et al. (5–8), assuming an expected correlation coefficient of 0.60, a two-sided α of 0.05, and 80% statistical power. The calculation yielded a minimum sample size of 20 participants. To increase the number of observations available for analysis, 40 eligible patients were ultimately enrolled in the study.

Participants were eligible if they were 18–65 years of age; had clinical findings suggestive of LPR based on medical history, physical examination, fiberoptic laryngoscopy (FOL), a RSI score ≥13, and a RFS score ≥ ≥7; and demonstrated abnormal proximal reflux exposure during impedance monitoring (defined as at least one proximal reflux episode reaching the hypopharynx). Furthermore, participants were required to be able to understand Indonesian, cooperate during the examination, and have discontinued proton pump inhibitor (PPI) therapy and other antacids for at least 7 days before assessment. Patients were excluded if they had a history of laryngeal surgery or trauma, intralaryngeal abnormalities such as a mass, Alzheimer disease, Parkinson disease, chronic obstructive pulmonary disease, rheumatoid arthritis, or third-trimester pregnancy.

2.3 Ethical Considerations

All participants received an explanation of the study objectives, procedures, potential benefits, and possible discomfort associated with the examinations before enrollment. Written informed consent was obtained from all participants. Fiberoptic laryngoscopy and 24-hour pH-MII monitoring were performed by otorhinolaryngology specialists or appropriately trained medical personnel according to the applicable institutional standard operating procedures. The study was approved by the Biomedical Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (No. 1200/UN4.6.4.5.31/PP36/2025).

2.4 Clinical Assessment

Clinical manifestations of LPR were assessed using the RSI and RFS. The RSI is a nine-item patient-reported instrument assessing the severity of LPR-related symptoms, including hoarseness, throat clearing, excess throat mucus or postnasal drainage, difficulty swallowing, coughing after meals or when lying down, breathing difficulties or choking, troublesome cough, globus sensation, and heartburn or regurgitation (9). Each item is scored from 0 to 5, yielding a total score ranging from 0 to 45, with higher scores indicating greater symptom severity.

The RFS was used to assess objective laryngeal findings on fiberoptic laryngoscopy. The RFS evaluates eight laryngeal abnormalities: subglottic edema or pseudosulcus vocalis, ventricular obliteration, erythema or hyperemia, vocal fold edema, diffuse laryngeal edema, posterior commissure hypertrophy, granuloma or granulation tissue, and thick endolaryngeal mucus (10). The total score ranges from 0 to 26, with an RFS ≥7 considered supportive of LPR in this study.

2.5 24-Hour pH-MII Monitoring

Objective reflux characteristics were assessed using 24-hour pH-MII monitoring with a dual-probe catheter measuring 2.3 mm in diameter (UNISENSOR AG, Attikon, Switzerland). Prior to intubation, the pH electrodes were calibrated using standard buffer solutions (pH 4.0 and 7.0). The catheter incorporated six impedance channels and two pH electrodes. The distal pH electrode was positioned approximately 5 cm above the lower esophageal sphincter, whereas the proximal electrode was positioned in the laryngopharyngeal region approximately 1–2 cm above the upper esophageal sphincter. The six impedance channels (Z1–Z6) were positioned at 17, 15, 9, 7, 5, and 3 cm above the lower esophageal sphincter.

The catheter was connected to an external electronic recorder for continuous monitoring over 24 hours. Participants were instructed to maintain their routine daily activities, consume their normal diet, and precisely record meal times, changes in body position, medication use, and the occurrence of symptoms during the monitoring period. Data recorded during meal periods were excluded from the final reflux analysis to prevent artifacts.

2.6 Definition and Classification of Reflux Characteristics

The primary exposure variables were the acidity and physical composition of reflux episodes detected during 24-hour pH-MII monitoring. According to reflux acidity, episodes were classified as acid reflux when the pH was <4, weakly acid reflux when the pH was ≥4 and <7, and non-acid reflux when the pH was ≥7. The number of episodes in each category was recorded throughout the 24-hour monitoring period.

According to physical composition, reflux episodes were classified as liquid, gas, or mixed reflux based on standard impedance characteristics. Specifically, liquid reflux was defined as a retrograde drop in impedance of ≥50% from baseline occurring sequentially in at least two distal impedance channels. Gas reflux was defined as a rapid, simultaneous increase in impedance (>3,000 Ohms) occurring in at least two consecutive channels. Mixed reflux was defined as a combination of both gas and liquid characteristics during a single episode. The total number of episodes in each category was recorded during the 24-hour monitoring period.

2.7 Statistical Analysis

All analyses were performed using IBM SPSS Statistics version 23.0. Normality was assessed using the Shapiro–Wilk test. Because RSI and RFS scores were non-normally distributed, the Kruskal–Wallis test was used to compare clinical manifestations across reflux-acidity (acid, weakly acid, and non-acid) and reflux-composition (gas, liquid, and mixed) groups. For variables that demonstrated a statistically significant difference in the overall Kruskal-Wallis test ($P < 0.05$), post-hoc pairwise comparisons were conducted using Dunn's test with a Bonferroni correction for multiple comparisons to identify specific inter-group differences. A two-sided $P < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Study Population

A total of 40 patients with LPR fulfilled the predefined eligibility criteria and were included in the final analysis. The majority of participants were 25–44 years old (55.0%), followed by those aged 45–59 years (32.5%). Women accounted for 72.5% of the study population. Most participants had a university-level education (75.0%), and 60.0% were employed in the private sector (Table 1).

Table 1. Characteristics of the study population

Characteristic	n (%)
Age group, years	
15–24	3 (7.5)
25–44	22 (55.0)
45–59	13 (32.5)
60–74	2 (5.0)
Sex	
Female	29 (72.5)
Male	11 (27.5)
Education	
University	30 (75.0)
High school	10 (25.0)
Occupation	
Government sector	16 (40.0)
Private sector	24 (60.0)

3.2 Reflux Characteristics on 24-Hour pH-MII Monitoring

The 24-hour pH-MII recordings demonstrated variation in both reflux acidity and physical composition (Table 2). Weakly acid reflux was the predominant reflux type, with a total of 2,825 episodes and a mean of 70.63 ± 58.24 episodes per participant (range, 1–273). Acid reflux accounted for 938 episodes, with a mean of 23.45 ± 22.27 episodes per participant (range, 0–104), whereas non-acid reflux was least frequent, with 231 episodes and a mean of 5.78 ± 12.67 episodes per participant (range, 0–57).

Regarding physical composition, mixed reflux was the most frequent pattern, accounting for 1,650 episodes, followed by gas reflux with 1,379 episodes and liquid reflux with 938 episodes. The corresponding mean numbers of episodes per participant were 41.25 ± 42.31, 34.48 ± 32.16, and 23.45 ± 24.59, respectively (Table 2).

Table 2. Reflux characteristics detected by 24-hour pH-MII monitoring

Reflux characteristic	Total episodes	Mean ± SD per participant	Range
Acidity			
Acid	938	23.45 ± 22.27	0–104
Weakly acid	2,825	70.63 ± 58.24	1–273
Non-acid	231	5.78 ± 12.67	0–57
Physical composition			
Liquid	938	23.45 ± 24.59	0–109
Gas	1,379	34.48 ± 32.16	2–126
Mixed	1,650	41.25 ± 42.31	2–189

Note: Data represent the total number of reflux episodes recorded during 24-hour pH-MII monitoring and the corresponding mean number of episodes per participant.

3.3 Distribution of RSI and RFS

The mean total RSI score was 16.23 ± 2.74, with a median of 16 and a range of 13–24. The mean RFS was 10.38 ± 2.98, with a median of 9 and a range of 7–16 (Table 3). Both RSI and RFS demonstrated non-normal distributions according to the Shapiro–Wilk test (RSI, $P = 0.003$; RFS, $P < 0.001$).

Among the individual RSI symptoms, globus sensation had the highest mean score (3.08 ± 1.33), followed by heartburn/regurgitation (2.87 ± 1.49), throat clearing (2.70 ± 1.04), and excess throat mucus/postnasal drip (2.58 ± 1.26). Difficulty breathing had the lowest mean score (0.63 ± 0.98) (Table 3).

Table 3. Distribution of RSI and RFS scores

Clinical assessment	Mean ± SD	Median	Range
RSI total score	16.23 ± 2.74	16	13–24
RFS total score	10.38 ± 2.98	9	7–16
RSI component	Mean ± SD		
Hoarseness	1.35 ± 1.44		
Throat clearing	2.70 ± 1.04		
Excess throat mucus/postnasal drip	2.58 ± 1.26		
Dysphagia	1.22 ± 1.33		
Cough after meals/lying down	1.08 ± 1.25		
Difficulty breathing	0.63 ± 0.98		
Troublesome cough	0.75 ± 0.95		

Clinical assessment	Mean ± SD	Median	Range
RSI total score	16.23 ± 2.74	16	13–24
RFS total score	10.38 ± 2.98	9	7–16
RSI component	Mean ± SD		
Globus sensation	3.08 ± 1.33		
Heartburn/regurgitation	2.87 ± 1.49		

Note: *RSI and RFS were non-normally distributed according to the Shapiro–Wilk test (RSI, P = 0.003; RFS, P < 0.001).*

3.4 Association Between Reflux Acidity and Clinical Manifestations

The association between reflux acidity and clinical manifestations was evaluated using the Kruskal–Wallis test because the RSI and RFS data were not normally distributed. Patients were categorized according to acid, weakly acid, or non-acid reflux.

No significant differences were observed in any of the assessed RSI components across the three reflux-acidity groups. The P values ranged from 0.258 to 0.994, including hoarseness (P = 0.698), throat clearing (P = 0.847), excess throat mucus (P = 0.994), dysphagia (P = 0.971), cough after meals or when lying down (P = 0.258), difficulty breathing (P = 0.538), troublesome cough (P = 0.544), globus sensation (P = 0.536), and heartburn/regurgitation (P = 0.773) (Table 4; Supplementary Table S1).

Likewise, none of the RFS components differed significantly according to reflux acidity. The P values ranged from 0.348 to 1.000. Erythema/hyperemia was the most prominent laryngoscopic finding across all three groups and was present in all participants in the acid, weakly acid, and non-acid groups (Table 4; Supplementary Table S1).

Table 4. Association between reflux acidity and clinical manifestations

Clinical outcome	Overall finding	p-value
RSI components	No significant differences across acid, weakly acid, and non-acid reflux groups	>0.05
Hoarseness	No significant difference	0.698
Throat clearing	No significant difference	0.847
Excess throat mucus	No significant difference	0.994
Dysphagia	No significant difference	0.971
Cough after meals/lying down	No significant difference	0.258
Difficulty breathing	No significant difference	0.538
Troublesome cough	No significant difference	0.544
Globus sensation	No significant difference	0.536
Heartburn/regurgitation	No significant difference	0.773
RFS components	No significant differences across groups	>0.05

Note: p-values were calculated using the Kruskal–Wallis test. Detailed RFS component-level results are provided in Supplementary Table S1.

3.5 Association Between Reflux Composition and Clinical Manifestations

The relationship between reflux physical composition and clinical manifestations was assessed across gas, liquid, and mixed reflux groups. Most RSI components did not differ significantly between the three groups (Table 5).

However, heartburn/regurgitation was significantly associated with reflux composition (P = 0.018). The mean score was highest in the mixed-reflux group (3.38 ± 1.43), followed by the gas-reflux group (2.64 ± 1.34), and lowest in the liquid-reflux group (1.40 ± 1.14) (Table 5). The remaining RSI components showed no statistically significant differences, including hoarseness (P = 0.611), throat clearing (P = 0.692), excess throat mucus (P = 0.166), dysphagia (P = 0.711), cough after meals or when lying down (P = 0.424), difficulty breathing (P = 0.649), troublesome cough (P = 0.998), and globus sensation (P = 0.172) (Supplementary Table S1).

No RFS component demonstrated a statistically significant difference across the gas, liquid, and mixed reflux groups (Table 5). Erythema/hyperemia remained the most prominent laryngoscopic finding, with mean scores of 2.71 ± 0.99 in the gas group, 2.80 ± 1.10 in the liquid group, and 2.95 ± 1.02 in the mixed group. The corresponding p-value was 0.783 (Supplementary Table S1).

Table 5. Association between reflux composition and clinical manifestations

Clinical outcome	Gas (n=14)	Liquid (n=5)	Mixed (n=21)	p-value
Heartburn/regurgitation (mean ± SD)	2.64 ± 1.34	1.40 ± 1.14	3.38 ± 1.43	0.018
Other RSI components	NS	NS	NS	>0.05
RFS components	NS	NS	NS	>0.05

Note: p-values were calculated using the Kruskal–Wallis test. Detailed component-level results are provided in Supplementary Table S1.

3.4 Discussion

The main finding of this study was that reflux acidity was not significantly associated with any assessed symptom or laryngoscopic manifestation of LPR, whereas reflux physical composition was significantly associated with heartburn/regurgitation. Specifically, acid, weakly acid, and non-acid reflux did not differ significantly in any RSI or RFS component, while mixed reflux was associated with a higher heartburn/regurgitation score than liquid or gas reflux (P = 0.018). Weakly acid reflux was the predominant acidity pattern, whereas mixed reflux was the most frequent physical composition. These findings suggest that the clinical expression of LPR may not be adequately explained by reflux acidity alone and that the physical characteristics of refluxate may have a more selective relationship with individual symptoms.

The predominance of weakly acid reflux in this study is consistent with the increasingly recognized heterogeneity of reflux events in patients with LPR. In contrast to conventional gastroesophageal reflux disease, in which acid exposure is often emphasized, LPR may involve acid, weakly acid, and non-acid refluxate reaching the proximal esophagus or hypopharynx. Previous studies using impedance-pH monitoring have demonstrated that non-acid and weakly acid events constitute an important proportion of reflux episodes in patients with LPR. In a large cohort of 344 patients, non-acid reflux represented 74.1% of detected laryngopharyngeal reflux events (11). Similarly, weakly acidic pharyngeal reflux has been reported to occur more frequently than acidic or weakly alkaline events (12). Our finding that weakly acid reflux predominated therefore supports the concept that LPR cannot be considered exclusively an acid-mediated disorder. The clinical relevance of weakly acid reflux may also reflect the presence of other potentially injurious constituents, including pepsin and bile components, rather than pH alone (2).

The absence of a significant association between reflux acidity and RSI symptoms is also consistent with previous evidence demonstrating a relatively weak relationship between objective reflux parameters and subjective LPR symptoms. In a prospective study of 45 patients, most parameters obtained from 24-hour MII-pH monitoring showed weak or no correlations with RSI and quality-of-life measures; only non-acid and total reflux events reaching the larynx and pharynx demonstrated significant associations with heartburn (13). Similarly, Salgado et al. reported that symptoms classically attributed to LPR did not correlate significantly with proximal esophageal or pharyngeal reflux events (14). These observations support the interpretation that symptom generation in LPR is multifactorial and may depend not only on acidity but also on the frequency and duration of exposure, proximal extent of reflux, mucosal susceptibility, and individual sensory responses. In the present study, the lack of significant differences across acid, weakly acid, and non-acid groups for all RSI components further supports the limited ability of reflux acidity alone to explain the heterogeneous symptom profile of LPR.

The absence of significant differences in RFS findings according to reflux acidity provides a complementary finding. None of the eight laryngoscopic components differed significantly among acid, weakly acid, and non-acid reflux groups, despite erythema/hyperemia being the most prominent finding across the groups. This observation is clinically relevant because laryngoscopic findings traditionally attributed to reflux are not specific for acid exposure. Current literature emphasizes that the diagnosis of LPR should not rely solely on symptoms or laryngoscopic appearance because these findings may overlap with other inflammatory or functional disorders (2). Objective impedance-pH monitoring provides additional information by identifying reflux events according to both acidity and physical composition, although interpretation remains challenging because normative thresholds and optimal diagnostic criteria are still evolving (2–4). The recent European consensus further emphasizes hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring as an important objective approach for identifying reflux phenotypes and guiding individualized management (4).

An important finding was the significant association between reflux composition and heartburn/regurgitation, with the highest score observed among patients with mixed reflux. In contrast, no significant association was observed between reflux composition and the other RSI components or any RFS component. This finding may indicate that the physical composition of refluxate has a more specific relationship with conventional esophageal reflux symptoms than with predominantly laryngopharyngeal symptoms. The mixed-reflux pattern, consisting of both liquid and gas components, may facilitate broader proximal distribution of refluxate and increase esophageal exposure. Nevertheless, this interpretation should remain cautious because the present study was not designed to determine the mechanisms underlying this association. Previous impedance-pH research similarly suggests that objective reflux parameters do not uniformly correspond to individual symptoms, emphasizing the complex relationship between reflux events and clinical manifestations (13,14).

The clinical implications of these findings are that LPR assessment should not be based on reflux acidity alone. The predominance of weakly acid reflux and the lack of significant associations between acidity and RSI/RFS findings suggest that acid suppression alone may not fully address the pathophysiological spectrum of LPR. Characterization of reflux composition may provide additional information, particularly in patients whose predominant complaints include heartburn or regurgitation. Previous prospective evidence has shown that impedance-pH phenotyping can distinguish acid, non-acid, and mixed LPR and may support phenotype-directed treatment strategies (15). However, because most clinical manifestations in the present study were not significantly associated with either acidity or composition, these findings should be interpreted as supporting phenotypic characterization rather than a direct causal relationship between a specific reflux pattern and LPR symptoms.

This study has several limitations. First, the sample size was relatively small (n = 40), and the reflux-acidity groups were markedly unequal, particularly the non-acid group, which contained only two participants. This substantially limits statistical power and the precision of comparisons involving non-acid reflux and increases the possibility of type II error. Second, the cross-sectional design prevents determination of temporal or causal relationships between specific reflux characteristics and clinical manifestations. Third, participants were enrolled using purposive sampling from two tertiary care centers, which introduces potential selection bias and may limit the generalizability of our findings to broader, primary care populations.

Furthermore, our analysis did not adjust for several potential confounding factors known to influence gastroesophageal reflux and symptom perception, including body mass index, dietary habits, tobacco use, and psychological comorbidities (such as anxiety or depression). Finally, while RSI and RFS are widely utilized and clinically practical tools, they remain subjective and semi-quantitative, lacking absolute specificity for LPR. Although we evaluated reflux acidity and physical composition, other relevant impedance-pH parameters such as the proximal extent of the refluxate, bolus clearance time, and the presence of pepsin were not comprehensively analyzed. Therefore, larger, multi-center, prospective studies with balanced reflux phenotypes and rigorous control of confounding variables are strongly warranted to firmly establish the clinical significance of these observed associations and to guide phenotype-directed therapeutic interventions.

4. CONCLUSION

In this study, weakly acid reflux was the predominant reflux acidity pattern, whereas mixed reflux was the most frequent physical composition detected by 24-hour pH-MII monitoring. Reflux acidity was not significantly associated with individual symptoms or laryngoscopic findings of LPR, suggesting that the clinical manifestations of LPR cannot be explained by reflux acidity alone. In contrast, reflux physical composition was significantly associated with heartburn/regurgitation, with the highest symptom scores observed among patients with mixed reflux. These findings support the importance of considering the broader reflux phenotype rather than focusing exclusively on acid exposure when evaluating patients with suspected LPR.

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AUTHOR CONTRIBUTIONS

WSW: Conceptualization, Methodology, Investigation, Data Curation, Writing—Original Draft.

MAA: Methodology, Investigation, Formal Analysis, Writing—Review & Editing.

YA: Laboratory Analysis, Data Curation, Validation, Writing—Review & Editing.

AS: Supervision, Statistical Analysis, Validation, Writing—Review & Editing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

The study was approved by the Biomedical Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (No. 1200/UN4.6.4.5.31/PP36/2025).

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author [WSW] upon reasonable request.

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