Symptom Correlation in Patients Undergoing Ambulatory 24-hour pH Study

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ABSTRACT

Background: There is scarce data from India on symptom correlation in patients undergoing ambulatory 24-hour pH monitoring. **Aim:** Retrospective analysis of symptom correlation in patients undergoing ambulatory 24-hour pH study at our center. **Material and methods:** The study included patients who had 24-hour pH testing from 2015 to 2017 for typical or extra-esophageal symptoms of gastroesophageal reflux disease (GERD). Patient information included age, gender and indications for the pH study. Collected data included reflux details in upright and recumbent position, correlation with meals, duration and number of reflux events, Johnson/DeMeester score, symptom index (SI) and symptom sensitivity index (SSI). Descriptive analysis was carried out by median and range for quantitative variables, and frequency and proportion for categorical variables. Chi-square tests and Mann-Whitney U test were used. P value <0.05 was considered statistically significant. **Results:** Thirty-six of the 66 patients had Johnson/DeMeester score >14.7 (Group 1). Heartburn, regurgitation and extra-esophageal symptoms were significantly more common in Group 1. These patients also had significantly more reflux in both upright and supine position, with significant reflux episodes in both positions. They also had more reflux episodes lasting for more than 5 minutes. Post meal reflux episodes were common. SI was significantly high in Group 1. The positive symptom correlation, as assessed by SI >50% and SSI >10%, was higher for heartburn, regurgitation compared to chest pain and extra-esophageal symptoms, although not statistically significant. **Conclusion:** About 45% of patients undergoing pH study had no pathological reflux. 24-hour pH study is useful to identify pathological acid exposure with good symptom correlation for typical as well as extra-esophageal symptoms.

Keywords: Reflux, symptom, severity, esophagus

Newer techniques for esophageal functional testing, such as impedance testing and wireless pH capsule monitoring, are currently available in most centers in the West. With impedance testing, movements of liquid and air within the esophageal lumen, either in an antegrade or retrograde direction, can be monitored and reflux can be detected independently of the acid in the refluxate.[1] Combined pH impedance monitoring can identify the causative agent for extra-esophageal symptoms of reflux.[2] Wireless pH capsule is well-tolerated by most patients and improves symptom assessment in those with atypical reflux symptoms in comparison to 24-hour pH monitoring.[3,4]

In India, ambulatory 24-hour esophageal pH monitoring is most popular and widely used. It provides quantitative information on esophageal acid exposure and symptom correlation with acid exposure events. Indications for 24-hour pH testing in our setting include testing prior to fundoplication, evaluation of nonerosive reflux disease, extra-esophageal symptoms of gastroesophageal reflux disease (GERD) and poor response to medical management. Symptom correlation in these patients may guide us to appropriate management.

The present study is a retrospective analysis of symptom correlation in patients undergoing ambulatory 24-hour pH study at GI Motility Unit, Institute of GI and HPB Sciences, Gleneagles Global Health City, Chennai, Tamil Nadu, India. A Johnson/DeMeester score of >14.7 pH was considered as significant for acid reflux in patients with typical and extra-esophageal symptoms of GERD.[5]

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MATERIAL AND METHODS

The study was retrospective and included patients who had 24-hour pH testing from 2015 to 2017 for typical or extra-esophageal symptoms of GERD. Patient information included age, gender and indications for the pH study. Gastroesophageal reflux (GER) symptoms were categorized as: typical GER symptoms (heartburn, regurgitation, dysphagia or combination), noncardiac chest pain and extra-esophageal symptoms that included hoarseness of voice, chronic cough, otalgia, wheeze and constant throat clearance.

The procedure was done using single sensor pH probe using standard protocol. The localization of the lower esophageal sphincter (LES) was determined by high resolution esophageal manometry (HREM). The pH probe was then passed into the stomach and using pull-through technique was placed 5 cm above the LES. Patients were asked to note a symptom directed documentation in relation to meal and posture (upright or supine). In addition, they were asked to identify three predominant symptoms that they associated with GERD and accordingly to tap the code on the pH recorder when these occurred. The data was stored via an interface on a compatible computer. Analysis was performed using computerized software and was also reviewed manually.
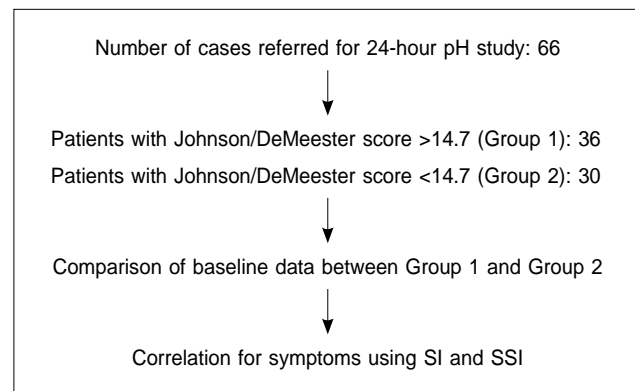
Data obtained included reflux details in upright and recumbent position, correlation with meals, duration and number of reflux events. Johnson/DeMeester score was available in the final computerized analysis.

Correlation of symptoms with pH was done by calculating symptom index (SI) for all the symptoms mentioned by the patient using the computerized software and values >50% were taken as positive. Symptom sensitivity index (SSI) was calculated for all the cases manually and values >10% were considered positive.[6,7] Both SI and SSI provide data on the strength of the association between symptoms and severity of reflux. The SI does not incorporate the total number of reflux episodes into account. Likewise, SSI does not take into account the total number of symptom episodes.

The flow chart of the study is shown in Figure 1.

Statistical Analysis

The data was entered in Microsoft Excel sheet. Descriptive analysis was carried out by median and range for quantitative variables, and frequency and proportion for categorical variables. Chi-square tests and Mann-Whitney U test were used to assess

Number of cases referred for 24-hour pH study: 66

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Patients with Johnson/DeMeester score >14.7 (Group 1): 36
Patients with Johnson/DeMeester score <14.7 (Group 2): 30

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Comparison of baseline data between Group 1 and Group 2

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Correlation for symptoms using SI and SSI

Figure 1. Flowchart of the study.

statistical significance. A p value <0.05 was considered statistically significant.

RESULTS

Sixty-six patients underwent upper endoscopy and ambulatory 24-hour pH monitoring during the study period. Endoscopy was normal in 52 (78.8%) and 13 of the remaining 14 had Los Angeles (LA) Grade A esophagitis. One patient had LA Grade B esophagitis. Thirty-six of the 66 patients had Johnson/DeMeester score >14.7 (Group 1).

Between Group 1 and Group 2, there was no difference in age and gender distribution (Table 1). Heartburn, regurgitation and extra-esophageal symptoms were significantly more common in Group 1. These patients also had significantly more reflux in both upright and supine position, with significant higher number of reflux episodes in both positions. They also had more reflux episodes lasting for more than 5 minutes. Post meal reflux episodes were common. SI was significantly high in Group 1.

Symptom Correlation as Noted by SI and SSI in Group 1

The positive symptom correlation, as assessed by SI >50%, was highest in patients with typical symptoms and least for those with extra-esophageal symptoms, but not statistically significant (p = 0.483) (Table 2). Similarly, the SSI was greater for heartburn, regurgitation compared to chest pain and extra-esophageal symptoms, although not statistically significant (Table 2).

DISCUSSION

The study highlights that 45% of patients undergoing pH study had no pathological reflux. Patients with pathological reflux presented with heartburn, regurgitation and extra-esophageal symptoms in both

Table 1. Comparison of Group 1 and Group 2

Parameter	Group 1 DM score >14.7 (n = 36)	Group 2 DM score <14.7 (n = 30)	P value
Age in years (median)	48 (25-72)	45 (24-69)	0.34
Sex (M:F)	22:14	24:6	0.09
Symptoms present in one or more combinations			
Heartburn	32 (88.8%)	14 (46.7%)	<0.0001
Regurgitation	28 (77.7%)	14 (46.7%)	0.002
Chest pain	7 (19.4%)	02 (6.6%)	0.08
Extra-esophageal symptoms	19 (52.7%)	06 (20%)	0.001
Upright pH <4 for >6.3% of time	18 (50%)	0 (0%)	<0.0001
Recumbent pH <4 for >1.2% of time	26 (72.2%)	6 (16.6%)	<0.0001
Median no. of reflux episodes in upright posture	63 (1-268)	23 (0-74)	<0.0001
Median no. of reflux episodes in recumbent position	18 (0-260)	3 (0-34)	0.002
Median no. of episodes >5 min	3 (0-23)	0 (0-1)	<0.0001
Median duration of longest episode of reflux in minutes	9 (0-781)	3 (0-17)	<0.0001
Median symptom index with meals	55.07% (0-100%)	21.2% (0-100%)	<0.0001
SI >50% (for all symptoms)	73/86 (84.8%)	18/36 (50%)	0.0001

DM: Johnson/DeMeester score.

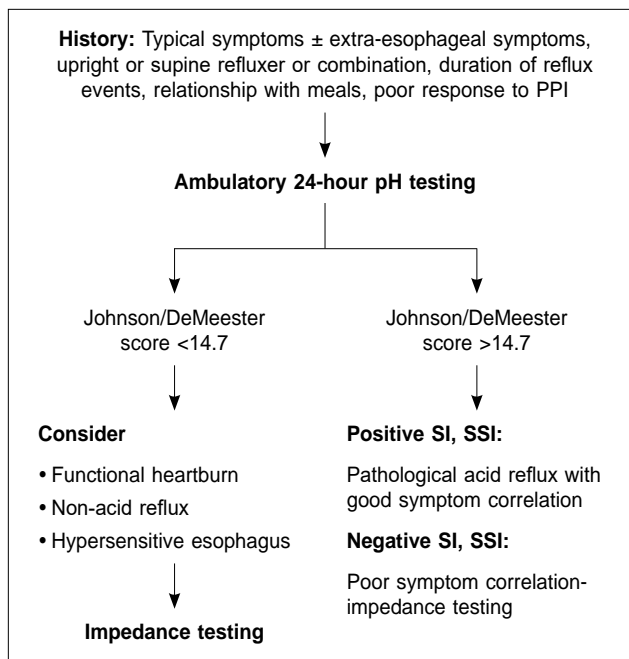**Table 2.** Correlation of SI and SSI with Symptoms

	Heartburn (n = 32)	Regurgitation (n = 28)	Chest pain (n = 7)	Atypical features (n = 19)	P value
Correlation of symptoms with SI					
Positive (>50%)	28 (87.5%)	25 (89.3%)	6 (85.7%)	14 (73.7%)	0.483
Negative <50%	4 (12.5%)	3 (10.7%)	1 (14.3%)	5 (26.3%)	
Correlation of symptoms with SSI					
Positive (>10%)	24 (67%)	22 (61%)	3 (43%)	9 (47.3%)	0.43
Negative (<10%)	12 (33%)	14 (39%)	4 (57%)	10 (52.7%)	

upright and supine position, with more frequent reflux episodes in either position lasting more than 5 minutes compared to those with a normal pH, with longer duration of reflux episodes with symptoms after a meal. Symptom correlation in those with pathological reflux was higher for typical GERD symptoms like regurgitation and heartburn.

Functional heartburn is characterized by the presence of symptoms of heartburn with physiological acid exposure while hypersensitive esophagus is characterized by normal acid exposure but positive correlation between symptoms and acid reflux events.[8] In our cohort of patients, 15 patients in Group 2 had normal acid exposure but an SI >50% and represent the hypersensitive esophagus subset. Addition of impedance monitoring to pH monitoring is likely to yield higher symptom correlation using various scoring systems.[9,10]

Ambulatory 24-hour esophageal pH monitoring has the ability to correlate symptoms with acid exposure events. SI and SSI are simple indices that assist in predicting response to proton pump inhibitors.[11] Despite these advantages, ambulatory pH monitoring has a few shortcomings too. It does not take into account the day-to-day variation in acid exposure[12] and the recommended

History: Typical symptoms ± extra-esophageal symptoms, upright or supine refluxer or combination, duration of reflux events, relationship with meals, poor response to PPI

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Ambulatory 24-hour pH testing

Johnson/DeMeester score <14.7

Johnson/DeMeester score >14.7

Consider
- Functional heartburn
- Non-acid reflux
- Hypersensitive esophagus

Impedance testing

Positive SI, SSI:

Pathological acid reflux with good symptom correlation

Negative SI, SSI:

Poor symptom correlation-impedance testing

Figure 2. Interpretation of 24-hour ambulatory pH study.

cut-offs to distinguish pathological from physiological reflux differ considerably in various studies.[5,13,14] Furthermore, the available symptom indices rely on patient's recording of events. For example, frequent tappings or inappropriate pressing of position/symptom codes may lead to errors in analysis.

Earlier studies have highlighted a good correlation between pathological acid exposure time and symptoms like heartburn and regurgitation.[15] However, temporal relation of symptoms like globus sensation, hoarseness, chronic cough[9] and chest pain[10,16] with acid reflux is less clear. Furthermore, functional heartburn and hypersensitive esophagus can also coexist and interfere with symptom correlation.

Based on our preliminary observations and review of literature, we recommend an algorithmic approach for Indian patients undergoing ambulatory pH testing (Fig. 2).

To conclude, 24-hour pH study is useful to identify pathological acid exposure with good symptom correlation for typical as well as extra-esophageal symptoms. However, in those with physiological acid exposure with persistent symptoms and poor symptom correlation, impedance testing has an important role.

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IJCP SUTRA 182: Hypothyroidism is linked to weight gain. Thus, a person with this condition can find it difficult to lose weight.

233