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# Central Obesity as a Risk Factor for Laryngopharyngeal Reflux

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**ABSTRACT**

Laryngopharyngeal reflux (LPR) is a common disease encountered in otolaryngology. The presentation differs from gastroesohageal reflux disease (GERD) despite sharing similar pathophysiology. There are various postulated risk factors to LPR amongst which is central obesity. The aim of this study is to establish central obesity as a risk factor in developing LPR. This is a comparative cross-sectional study in which 180 patients who were 18 years old and above regardless of obesity status without confounding factors in causing laryngeal mucosal change were enrolled. These patients were not diagnosed with LPR prior. No pH studies or empirical treatment with proton pump inhibitors were given before. Reflux symptom index (RSI) and reflux finding score (RFS) were used to screen for LPR sign and symptoms. 82 central-obese patients based on waist-to-hip ratio (0.9 and 0.85 and above for male and female respectively) and 98 non central-obese patients were in this study. There was a significant higher value of both RSI and RFS in central-obese patients with significant positive correlation between these variables. This study derived a linear correlation between central obesity and LPR based on the relatively simple and non-invasive RSI and RFS tool.



## 1. INTRODUCTION

Laryngopharyngeal reflux (LPR) also known as gastroesophagopharangeal reflux, reflux laryngitis or silent reflux is a condition believed to be caused by gastric content irritation over the larynx and pharynx [1]. Extraesophageal manisfestation of gastroesophageal reflux disorder (GERD) can cause LPR by retrograde spread of pepsin-containing gastric content capable of direct injury over laryngopharynx mucosa. Numerous

other mechanisms have been proposed including the defect in the physiological barriers of esophagus such as lower and upper esophageal sphincters and the esophageal mucosal barrier itself. There remains a lack of understanding in establishing an exact pathophysiology attributing solely to isolated LPR in the absence of GERD [2], [3]. GERD is proven to occur in obesity especially amongst patients with central obesity [4]. Central obesity is defined as an increased waist-to-hip ratio and can occur in normal or raised body mass index (BMI) population. Waist-to-hip ratio of 0.9 and 0.85 for men and women respectively indicates central obesity. The increase abdominal girth can directly cause increase in intragastric pressure and capacity, which over time causes lower esophageal sphincter dysfunction. Long-term complications of hiatal hernia, Barret's esophagus and even malignancy have been widely reported [5]. Till date, only few studies have been made to explore the association between LPR and obesity [6], [7]. Did a retrospective study in 2005 of dual-probe pH confirmed LPR among 285 patients and found obesity as not significant as a risk factor [6] In contrast, a study by derived an opposing result by a positive correlation between obesity and increased waist circumference amongst women with chronic laryngitis [8]. However, a study specifically to identify central obesity as a precursor to LPR has not been done.

Double-probe pH monitoring is currently widely accepted as a reliable diagnostic tool for LPR despite the drawbacks in terms of its invasive nature and complex technicality [9]. It measures the level of acidity in the esophagus by two probes each placed at the proximal and distal part of esophagus. The pitfall faced in terms of accessibility, patient discomfort, compliance and resources makes this test comparatively cumbersome. On related terms, the significant contribution of variation in food and beverage intake, the number of reflux event in 24 hours and the technical difficulty in probe placement only serves to further dissuade the active use of this diagnostic tool. The Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) devised by Belafsky have been included in the diagnostic armamentarium in view of its relative simplicity and acceptable sensitivity and specificity. Reported a sensitivity of 87.8% and specificity of 37.5% for RFS. In combination with RSI, the specificity increased to 68.3% [10]. This limitation may be partly due to the subjectivity of endoscopic observation by different clinician. In addition, a positive laryngeal finding may be multi- factorial that may explain the false positivity in patients without LPR symptoms [11], [12].

The RSI by is a simple and thorough questionnaire which can be used to screen LPR patients and even to assess treatment response [13]. It's a nine-item scoring system with each having a Likert scale of 0 to 5 with a compound score of more than 13 being considered abnormal [11]. A Malay version based on RSI was made available in 2015 [4]. Its a research tool which has shown good clinical validity based on statistics and also recommended as a self-assessment tool for our Malaysian population. This questionnaire is often in combination with dual-probe pH monitors, gastroesophageal endoscopy and laryngoscopy [15]. Based on extensive clinical endoscopic findings amongst LPR patients such as erythematous with edematous vocal folds, subglottic edema/pseudosulci vocalis, posterior commissure hypertrophy, granuloma, ventricular obliteration and thick endolaryngeal secretion; devised a validated and comprehensive scoring system. This reflux findings score (RFS) contains eight parameters with a total score of 26. A score more than 7 is indicative of LPR [12].

LPR is a significant disease with debilitating symptoms requiring prolonged treatment with slower recovery as compared to GERD and carries dire possibilities of complications. Central obesity is postulated to be a risk factor considering the pathophysiology of GERD in relation to LPR. The use of the RSI & RFS by Belafsky to screen LPR among patients with central obesity will provide a simple and cost-effective way to establish this hypothesis. A positive correlation will directly contribute to meet the paucity of knowledge and awareness of LPR to avoid cumbersome management of its complications later. To the best of our

knowledge, the much simpler questionnaires by Belafsky has not been used as an independent tool amongst undiagnosed patients who are obese, let alone with central obesity to display characteristics of LPR exclusively by signs and symptoms. The aim of this study is to establish central obesity as a risk factor for LPR by a novel approach just by studying the correlation of RSI & RFS and central obesity.

## 2. MATERIAL AND METHODS

### *2.1 Study design and population*

This was a comparative cross-sectional study done in a tertiary university-hospital in Malaysia. The study proposal was reviewed and approved by the Universiti Sains Malaysia research and ethics committee (study protocol code: USM/JEPeM/19020142). Approved on 9th May 2019. Patient sampling was done amongst scheduled patients to otolaryngology (ORL) clinics between June and October of 2019. These clinics caters for the general pool of patients with first or follow-up visits for a wide array of ORL related diseases.

All patients who were 18 years old and more regardless of central obesity status who met the following exclusion criteria were included in this study. Smokers were excluded in view of smoking effect on laryngeal surface mimicking reflux. Pregnancy as abdominal girth is mis-represented. Patients with diagnosed malignancy as it causes distortion of pharangeal mucosa due to various reasons depending on nature, state and treatment effects. Recent chest infection as it generally affects upper airway. Patients with allergic rhinitis and rhinosinusitis in view of post-nasal drip related laryngeal changes. Patients who received proton pump inhibitor which may provide false negative findings and angiotensin-converting enzyme (ACE) inhibitors which may have cause chronic cough causing laryngeal surface changes. The study proposal was reviewed and approved by the research and ethics committee.

### *2.2 Data collection*

A written consent was taken from the candidates after the aim and methodology as well as the procedure was explained to the candidates. Waist-to-hip ratio will be measured as per guidelines from WHO. Waist circumference measured at the midpoint between lower margin of the last palpable ribs and the top of iliac crest. Hip circumference measured around the widest portion of buttocks. Subjects are to stand at ease with feet close together, arms at sides to ensure equal distribution of weight. Measurement is taken with not stretchable tape without tightness and at the end of normal expiration. The tape should be wound around parallel to the floor. Waist-to-hip ratio of 0.9 and 0.85 for men and women respectively indicates central obesity. The participant filled up RSI/Malay version of Reflux Symptom Index (M-RSI). The physician filled up Reflux Finding Score (RFS). This was carried out using a flexible nasopharyngolaryngoscope (FNPLS) which is a routine, quick and painless office procedure.

### *2.3 Statistical analysis*

All data were recorded using Microsoft Excel 365. The data were then analysed using IBM SPSS for Windows, version 24. Numerical data was presented as mean and standard deviation. Nominal data was presented as frequency and percentage. As the study data was not normally distributed, the Spearman's correlation was employed to determine the association between numerical variables (i.e. Age, BMI, WHR, RSI, and RFS). The strength of associations was as follows: 0-No correlation; 0.1-0.2-poor; 0.3- 0.5-fair; 0.6-0.7-moderate; 0.8-0.9-strong; 0.1-perfect [16]. The numerical data between two independent variables were compared using Mann Whitney test. A p value less than 0.05 indicated a statistical difference.

## 3. RESULTS

A total of 180 participants were recruited. There were 75 males and 105 females (Table 1). Their mean age

was 46±18 years old. Majority of the participants were Malay. Their mean BMI was 27±6.8 $kgm^{-2}$. There were 82 (45.6%) patients with central obesity and 98 (54.4%) patients without central obesity. Mann Whitney test showed a difference between RSI values between patients with and without central obesity (Table 2). The analysis revealed a higher RSI value among patients with central obesity as compared to those who without central obesity. Similarly, Mann Whitney analysis showed there is a difference between RFS values between patients with and without central obesity. The analysis revealed a higher RFS value among patients with central obesity as compared to those without central obesity. As the data are not normally distributed, Spearman's correlation was employed to determine the correlation among RSI, RFS and BMI. There was no significant correlation between BMI and RSI values (Table 3). However, a significant positive linear correlation was observed between RFS and BMI values. The analysis indicated a poor correlation ($r=0.195$, $P<0.05$) between the two study variables. Further correlational analysis indicates no significant association between the two variables and BMI (Table 3). From Spearman's correlation, there is a significant positive correlation between RSI and RFS scores (Table 4). The analysis revealed a fair association ($r=0.406$, $P<0.001$) between the two variables. Further analysis on central-obese patients indicates a significant fair analysis as well (Table 4). On the other hand, there is a significant positive correlation between BMI and WHR scores (Table 5). The analysis revealed a moderate association ($r=0.578$, $P<0.001$) between the two variables. Additional analysis indicates insignificant association between the two study variables among central obesity group (Table 5). Similarly, the analysis also revealed a positive correlation between Age and RFS, but not between Age and RSI (Table 6). The correlation between Age and RFS was fair ($r=0.277$, $P<0.05$). Sub-analysis between the two study variables and participant age reveal poor and insignificant association among central obesity subjects (Table 6).

Most common symptom in this study was frequent clearing of throat with 61.67% followed by excessive throat mucus or post-nasal drip with 59.44%. Heartburn recorded 53.33%, foreign body sensation with 42.22%, hoarseness with 41.67%, both choking sensation and troublesome coughing with 26.11%, coughing after lying down with 24.44 % and lastly difficulty swallowing with 17.22%. Most common laryngeal finding was erythema with 66.67%. 51.67% displayed posterior commissure hypertrophy, 31.67% displayed thick endolaryngeal mucus, 8.9% displayed ventricular obliteration, 6.11% with vocal fold edema, both diffuse laryngeal edema and granuloma found in 3.33% and the least found was pseudosulcus in only 2% of this study population. Of these numbers, only 4 patients fulfilled the criteria of RSI score of 13 or more and RFS score of 7 or more. All 4 were centrally obese, 2 were with BMI more than 25 being overweight and another 2 with BMI more than 30 being obese.

**Table 1:** Demographics of the participants

| VARIABLES | N (%) | MEAN (SD) |
|---|---|---|
| **GENDER** | | |
| **MALE** | 75 (41.7) | |
| **FEMALE** | 105 (58.3) | |
| **AGE** | | 46 (18) |
| **BMI** | | 27 (6.8) |
| **RACE** | | |
| **MALAY** | 163 (90.6) | |

| | |
|---|---|
| **CHINESE** | 11 (6.1) |
| **OTHERS** | 6 (3.3) |
| | |
| **CENTRAL OBESITY** | |
| **YES** | 82 (45.6) |
| **NO** | 98 (54.4) |

Note: Data was presented as frequency (percentage) or mean (standard deviation).

**Table 2:** RSI and RFS scores in patients with and without central obesity

| | **Central Obesity** | | |
|---|---|---|---|
| | **Yes** | **No** | **P value** |
| RSI | 6±8 | 4±8 | 0.036* |
| RFS | 3±3 | 2±4 | 0.007* |

Note: Mann Whitney Test, *statistically significant if P<0.05. Data was presented as median ± inter-quartile range. N=180.

**Table 3:** Correlation between RSI and RFS scores and BMI

| **Correlation between RSI and RFS scores and BMI (N=180)** | | | |
|---|---|---|---|
| | **BMI** | | |
| | **R** | **Strength** | **P value** |
| RSI | 0.038 | Poor | 0.609 |
| RFS | 0.195 | Poor | 0.009* |
| **Correlation between RSI and RFS scores and BMI among central obese patients (N=82)** | | | |
| | **BMI** | | |
| | **R** | **Strength** | **P value** |
| RSI | 0.000 | Poor | 0.998 |
| RFS | 0.132 | Poor | 0.237* |

Note: Spearman's correlation, *statistically significant if P<0.05.

**Table 4:** Correlation between RSI and RFS scores

| **Correlation between RSI and RFS scores (N=180)** | | | |
|---|---|---|---|
| | **RSI** | | |
| | **R** | **Strength** | **P value** |

| | | | |
|---|---|---|---|
| RFS | 0.406 | Fair | <0.001* |
| **Correlation between RSI and RFS scores among central-obese patients (N=82)** | | | |
| | **RSI** | | |
| | **R** | **Strength** | **P value** |
| RFS | 0.356 | Fair | <0.001* |

Note: Spearman's correlation, *statistically significant if P<0.05.

**Table 5:** Correlation between WHR and BMI scores

| **Correlation between WHR and BMI scores (N=180)** | | | |
|---|---|---|---|
| | **WHR** | | |
| | **R** | **Strength** | **P value** |
| BMI | 0.578 | Moderate | <0.001* |
| **Correlation between WHR and BMI scores among central-obese patients (N=82)** | | | |
| | **WHR** | | |
| | **R** | **Strength** | **P value** |
| BMI | 0.179 | Moderate | <0.107* |

Note: Spearman's correlation, *statistically significant if P<0.05.

**Table 6:** Correlation between RSI and RFS scores and age

| **Correlation between RSI and RFS scores and age (N=180)** | | | |
|---|---|---|---|
| | **Age** | | |
| | **R** | **Strength** | **P value** |
| RSI | 0.146 | Poor | 0.050 |
| RFS | 0.277 | Fair | 0.009* |
| **Correlation between RSI and RFS scores and age among central-obese patients (N=82)** | | | |
| | **Age** | | |
| | **R** | **Strength** | **P value** |
| RSI | 0.134 | Poor | 0.229 |
| RFS | 0.181 | Poor | 0.104* |

Note: Spearman's correlation, *statistically significant if P<0.05.

## 4. DISCUSSION

Obesity and its myriad of associated diseases have registered a secular trend with increasing incidences prompting more studies to help mitigate its rise. Links to GERD, Barrett's esophagus, adenocarcinoma of esophagus, OSA, and asthma has been widely published [17], [18]. Central obesity independent of classical

obesity based on BMI, show a higher incidence of GERD. High visceral fat in the abdominal area as opposed to truncal distribution; predisposes to increased intragastric pressure that can directly affect the lower esophageal sphincter causing reflux over time [5]. The visceral fat contains adinopectin which is a protein capable of apoptosis by its immunomodulatory and inflammatory properties. Increase in adinopectin is inversely related to obesity, which is related to incidence of Barrett's esophagus. Similarly, by way of humoral mechanism, leptin, which is secreted by adipose cells, are mitogenic with proliferative capacity resulting in susceptibility of mucosal lining to cancer [17]. A local survey in 2006 among Malaysian adults had registered an alarming 17.4% in prevalence of central obesity. As stated above this number is bound to be exponential as it's a disease directly influenced by advancement of socioeconomic condition [19]. A recent data by placed hiatus hernia and overweight as isolated risk factors for LPR. GERD remains the consistent risk factor for LPR which gives reproducible proof using the dual-probe pH monitoring [4], [15]. Despite convincing association with many afore-mentioned diseases, high BMI does not correlate to incidences of LPR as reported in a Malaysian study by [13]. This conclusion has been partly similar in this study as well as there was poor correlation observed between RSI and high BMI. However, LPR signs through RFS displayed a positive correlation with high BMI. Pertaining to the core objective of this study, a significant positive correlation was derived between both RSI and RFS with central obesity. This outcome may seem predictable in view of the interrelated occurrence of central obesity and high BMI as derived in this study where a positive correlation was seen between waist-to-hip ratio and BMI, nevertheless it provides an objective evidence to signify the adversity of central obesity especially in otolaryngology. Various studies have been done to proof relations between obstructive sleep apnea, chronic suppurative otitis media and voice disorder with LPR [20], [21]. Hence, giving due importance in establishing central obesity as a risk factor is relevant.

Age was not a significant factor in determining the outcome RSI and only showed fair significance in RFS. This is similar even among central obese patients alone as shown in this study. Perhaps the relative simplicity of the components of RSI in eliciting the correct response further establishes the score as reliable and suitable among the general population regardless of experience and maturity. LPR manifests differently although the core concepts of both LPR and GERD lies on reflux mechanisms. Heartburn and regurgitation are characteristic of GERD, which the LPR patients may not suffer from. GERD patients often complaint of nocturnal symptoms with supine position as opposed to daytime and upright position related symptoms in LPR [22]. Laryngeal examination provides significant information to diagnose LPR; however careful correlation must be drawn from the history, as the changes in the larynx may be multifactorial as detailed in the exclusion criteria of this study. One such cause is often attributable to upper airway related disorders such as nasal and paranasal inflammatory diseases with post-nasal drip [23].

In this study, only 4 patients fulfilled the cut off mark of 13 for RSI and 7 for RFS which supports the diagnosis of LPR. However, the analysis has shown linear positive correlation between the scores and central-obese patient which should safely allow a causal inference to be made towards risk of developing LPR even with insufficient cumulative scores. Studies using empirical treatment with proton pump inhibitors displayed positive outcome in terms of resolution of LPR symptoms which translates well into the RSI score, however laryngeal findings often display insignificant differences post treatment [24]. Having said that, the RFS as a diagnostic tool in conjunction with RSI still holds true. Concluded the relevance of RSI and RFS is still significant despite the poor specificity; 37.5% and 18.8% respectively due to the practical feasibility of these test in terms of cost, simplicity and patient compliance [10].

Complication resulting from longstanding and untreated LPR is difficult to establish as the exact cause and effect may be multi-factorial. Nevertheless, conditions such as vocal cord granuloma, paroxysmal

laryngospasm, laryngeal stenosis, and laryngeal carcinoma are increasingly being associated with LPR [3]. Medical treatment of LPR are also implicated with slower recovery and even resistance to proton- pump inhibitors [25]. This emphasizes the importance of awareness and early detection. This study primary drawback would be the absence of pH probe monitoring of the patients who scored high values in RSI and RFS and were central-obese. The confirmation would have contributed significantly to the validity of these tools in diagnosing LPR.

## 5. CONCLUSION

Central obesity is proven as a positive risk factor for LPR, which is important as the prevalence of both this condition is rising. The direct inter-dependence of this entity requires active intervention from both the medical personnel and the society as the management revolves greatly in lifestyle modification. The Belafsky scores of RSI and RFS are a reliable screening and diagnostic tool in detecting LPR among central-obese patients.

## 6. Acknowledgement

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## 7. Conflict of Interest

All contributing authors in this stufy declared no conflict of interest.

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