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Association between gastroesophageal reflux disease and lung function parameters in patients with normal chest X-ray

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ABSTRACT

Background and objectives. Pulmonary manifestations as a potential consequence of extraesophageal GERD symptoms have long been hypothesized. Microaspiration of gastric acid into the respiratory tract and lung parenchyma can cause chronic inflammation or trigger exacerbations, while the vagally mediated esophageal-bronchial reflex plays a role in causing or exacerbating bronchoconstriction. This repeated and chronic condition can lead to a decline in lung function. This study aims to determine the association between GERD and lung function parameters.

Materials and methods. This research is an analytical observational study with a cross-sectional design, involving spirometry and endoscopic examinations on patients diagnosed with GERD at Dr. Wahidin Sudirohusodo Hospital from June 2024 to September 2024. Lung function parameters were assessed using spirometry, while GERD was examined using EGD. Data were analyzed using the chi-square test and Mann-Whitney test.

Results. A total of 100 patients with a normal chest X-ray and symptoms of GERD were included in the study, the majority of whom were under 60 years of age (87%) and female (55%). The mean values of VC, FEV1, and FVC were significantly lower in GERD subjects compared to non-GERD subjects ($p < 0.005$). In GERD patients, restriction abnormalities were more common than normal, with 26 (52%) versus 24 (45%). On the other hand, in patients without GERD, restriction abnormalities were less common than normal, with 16 (32%) versus 34 (68%), and this difference was statistically significant ($p = 0.043$). The Odds Ratio (OR) was calculated to be 2.302.

Conclusions. There is an association between GERD and lung function parameters, where subjects with GERD have a risk of restrictive disorders 2.3 times.

Keywords: GERD, Lung Function Test, Spirometry, Restrictive disorders

Abbreviations:

COPD – Chronic Obstruction Pulmonary Disease
EOS – Extra Esophageal
FEV1 – Forced Expiratory Volume in 1 second
GERD – Gastroesophageal Reflux Disease
IC – Inspiratory Capacity
IOS – Impulse Oscillometry
VC – Vital Capacity
LES – Lower Esophageal Sphincter
OR – Odd Ratio
TLC – Total Lung Capacity
TV – Tidal Volume

INTRODUCTION

The lungs are the primary organs of the respiratory system, and their function is to facilitate the exchange of gases between the environment and the bloodstream [1]. To assess whether a person's lung function is normal, a pulmonary function test must be conducted. This test can be performed using tools such as a spirometer, body plethysmography, or impulse oscillometry (IOS) [2,3]. Spirometry measures both static and dynamic lung volumes and can accurately assess parameters such as vital capacity (VC), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF). While a spirometer cannot provide a specific diagnosis, it can

identify the presence of obstructive and restrictive disorders and estimate the degree of abnormality [3].

Obstructive lung diseases result from the narrowing of the airways, with a hallmark characteristic of decreased FEV1/FVC ratio. Conditions classified as obstructive pulmonary disorders include chronic obstructive pulmonary disease (COPD), bronchiectasis, asthma, small airway disease, and upper airway obstruction. In contrast, restrictive lung diseases are diagnosed based on a normal FEV1/FVC ratio coupled with a reduced vital capacity (VC), which results from decreased total lung capacity (TLC). Diseases that can cause restrictive disorders include interstitial fibrosis, pulmonary edema, pleural effusion, neuromuscular disorders, and severe conditions affecting the thoracic cavity and abdomen [2,3]. In addition to these diseases, factors such as age, environmental exposures, and behaviors particularly smoking can influence lung function, while genetics also play a role in determining the rate of decline in lung function.[3] Recent studies have linked respiratory diseases to gastroesophageal reflux disease (GERD) [3,4].

Gastroesophageal reflux disease is a complex condition characterized by heterogeneous symptoms and diverse pathogenesis.[5] GERD occurs when gastric contents flow back into the esophagus, leading to irritation and inflammation.[6] It commonly causes typical symptoms such as heartburn and chest discomfort (sometimes accompanied by pain and soreness), as well as other symptoms including regurgitation (a sour or bitter taste in the mouth), epigastric pain, dysphagia, and odynophagia [6,7]. Apart from causing esophageal symptoms, GERD can also lead to extraesophageal symptoms (EOS), such as chronic cough, asthma, tooth erosion, laryngitis, non-cardiac chest pain, pulmonary fibrosis, and other pulmonary diseases [7-9].

The prevalence of GERD increases by approximately 4% annually, and the number of doctor visits due to GERD reaches 5.6 million per year. Between 10% and 20% of adults in Western countries, and 5% in Asia, experience GERD symptoms at least once a week.[10] The prevalence of GERD in Asia, including Indonesia, has generally increased in recent years. This rise is attributed to lifestyle changes that increase the risk of developing GERD, such as smoking and obesity [6,10].

Pulmonary manifestations as a potential consequence of extraesophageal GERD symptoms have long been hypothesized [11]. This hypothesis is based on the history of patients with asthma or chronic cough, particularly nocturnal cough, who report experiencing gastroesophageal reflux before an attack occurs.[9] The mechanisms underlying the extraesophageal manifestations of GERD, which are currently being explored, include: 1) direct aspiration of refluxate into the upper airway, and 2) a vago-vagal reflex triggered by acidification in the distal esophagus and microaspiration.[6]

Microaspiration of gastric acid into the respiratory tract and lung parenchyma can lead to chronic inflammation or exacerbate existing conditions, while the vagally mediated esophageal-bronchial reflex plays a role in causing or worsening bronchial constriction. This chronic and recurrent condition can result in a decline in lung function, manifesting as obstruction, restriction, or a mixed pattern [12,13]. Research by Nazemiyeh et al. comparing lung function between GERD and non-GERD patients found a significant decrease in the FEV1/FVC ratio and increased airway resistance in GERD patients [14].

Understanding lung function parameters can help assess the risk of lung function decline in GERD patients. Additionally, research on lung function in GERD patients has not been conducted in Indonesia especially in Makassar. This study aims to explore the association between GERD and lung function parameters.

MATERIALS AND METHODS

Study design: This research is analytic observational research with a cross sectional design.

Study site/setting: This study was conducted from June 2024 to September 2024 at the Wahidin Sudirohusodo Central General Hospital and Hasanuddin University Hospitals.

Study participants/sampling procedure: The population for this study consisted of all patients diagnosed with GERD at the Gastrocenter HAM AKIL, Dr. Wahidin Sudirohusodo Hospital, from June 2024 to September 2024. All participants who met the inclusion criteria, received information about the study's objectives, and their anonymity, confidentiality, voluntary nature of participation, and the right to refuse or withdraw consent at any moment were assured without consequence. This allowed them to clarify any questions they had about their involvement. Thus, all participants provided their free and informed consent in writing. The participants included in this study were diagnosed with GERD at the Gastrocenter HAM AKIL, Dr. Wahidin Sudirohusodo Hospital, Makassar. They were over 18 years old, willing to participate in the research, and had signed the informed consent. Additionally, patients with normal chest x-ray and did not have a history of asthma, COPD, pulmonary tuberculosis, pleural effusion, or chronic cor pulmonale.

Data analysis: Data were analyzed using SPSS version 25. Descriptive statistical tests and frequency distribution were applied for the analysis. The statistical tests used included the Kolmogorov-Smirnov test to assess data normality, Chi-square test, and Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant. The results obtained will be displayed in the form of a narrative supplemented by tables and figures.

RESULTS

Characteristics of participants

This study included 100 subjects, comprising 45 male subjects (45%) and 55 female subjects (55%), aged between 19 and 79 years, and a mean age of 39.5 ± 14.2 years. The average age of participants was less than 60 years, with 87 subjects (87%) under 60 years and 13 subjects (13%) over 60 years. The assessment of obesity indices indicated that the body mass index (BMI) ranged from 15.5 to 36.2 kg/m², with a mean BMI of 24.2 ± 4.5 kg/m². Among the 100 subjects, 58 (58%) had normal lung function parameters, and 42 (42%) had restrictive disorder. There were no subjects with obstructive disorders in this study (Table 1).

Association between GERD and Lung Function Parameters

The results (Table 2) show that the mean FEV1/FVC ratio was significantly higher in GERD subjects compared to non-GERD subjects ($p < 0.05$). In contrast, the mean values of VC, FEV1, and FVC were significantly lower in GERD group than in the non-GERD group ($p < 0.005$).

In this study, a significant association was found between restrictive disorders and GERD. As shown in Table 3, restrictive disorders were more prevalent in GERD subjects compared to those with normal lung function, with 26 subjects (52%) having restrictive disorders versus 24 subjects (45%) with normal function. In contrast, among non-GERD subjects, restrictive abnormalities were less common, with 16 subjects (32%) having restrictive disorders and 34 subjects (68%) having normal lung function, a difference that was statistically significant ($p = 0.043$). The calculated odds ratio (OR) was 2.302, indicating that GERD subjects have a 2.3 times higher risk of developing restrictive disorders compared to non-GERD subjects.

DISCUSSION

Gastroesophageal Reflux Disease has been associated with various respiratory diseases, either as a direct cause or as a risk factor for the inability to control or the worsening of the disease.[8] The prevailing hypothesis is that it results from the direct contact of the refluxate with the upper airways, and due to vagal reflexes limited to the lower esophageal sphincter. Microaspiration can induce bronchospasm and bronchial hyperresponsiveness [4,8]. Additionally, the potential mechanism of acid aspiration into the airways and lung parenchyma, or alveolar tissue, may lead to chronic inflammation, which could progress to fibrosis of lung [8,15].

In this study, the mean values of VC, FEV1, and FVC were significantly lower in GERD subjects compared to non-GERD subjects ($p < 0.005$). These findings are consistent with research conducted by Bonacin et al. (2012) in Croatia, which found statistically significant differences between the GERD and non-GERD groups in FVC ($p = 0.034$) and FEV1 ($p = 0.002$). However, in their study, the FEV1/FVC ratio was lower in GERD subjects compared to non-GERD subjects ($p = 0.001$).[12] This result contrasts with our findings, where the FEV1/FVC ratio was higher in GERD subjects compared to non-GERD subjects. This discrepancy may be explained by the fact that the most common pattern of lung abnormalities observed in GERD subject in our study was restrictive disorders.

The results of this study indicate a significant association between GERD and restrictive disorders ($p < 0.05$). Based on the odds ratio (OR), GERD patients have a 2.3 times greater risk of developing restrictive disorders compared to those without GERD. A study consistent with these findings is that of Ali ER et al. (2016), which reported an increase in airway resistance among several GERD patients.[15] Additionally, an epidemiological study by Rascon-Aguilar et al. (2006) in patients with reflux esophagitis found a modest increase in the risk of idiopathic pulmonary fibrosis (OR = 1.36) and pneumonia (OR = 1.15) [14].

The strength of this study lies in being the first in Indonesia especially in Makassar to analyze the association between GERD and lung function parameters in GERD and non-GERD subjects with normal chest x-ray. The limitation of this study is the small sample size and cannot analyze the association between the severity of GERD based on LA classification and lung function parameters. The patients did not undergo follow-up assessments to evaluate the long-term effects of GERD on respiratory function. Given the substantial impact of GERD on pulmonary health, cohort studies are needed to explore the susceptibility to pulmonary diseases in GERD patients.

CONCLUSION

GERD is associated with lung function parameters, which subjects diagnosed with GERD being 2.3 times more likely to experience restrictive disorders.

Conflict of interest: None declared

Authors' CONTRIBUTIONS: SAS, HI, and AML (idea, planning, availability, materials, gathering and processing of data, interpretation and analysis, literature search, and writing of manuscripts). SAS, SB, HI, AML, and HR (idea, design, supervision, evaluation and

interpretation, and literature search). AS (concept, design, critical review). SAS (Concept, Design, Analysis and Interpretation, Critical Review)

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Informed consent: Informed consent was obtained from all participants in the study.

Ethics approval and consent to participate: This study was approved by the Ethics Committee for Biomedical Research on Humans at the Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia, based on recommendation letter number 457/UN4.6.4.5.31/PP36/2024, dated June 21, 2024.

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TABLES

Table 1. Characteristics of the study population (n = 100)

Variable	Category	n	%
Gender	Female	55	55
	GERD	31	31
	Non-GERD	24	24
	Male	45	45
	GERD	19	19
	Non-GERD	26	26
Age	<60 years	87	87
	>60 years	13	13
	Minimum 19 years		
	Maximum 79 years		
	(mean 39.5 ± 14.2)		
BMI	Obese	36	36
	Non-Obese	64	64
	Minimum 15.5		
	Maximum 36.2		
	(mean 24.2 ± 4.5)		
GERD	Yes	50	50
	No	50	50
Spirometri	Normal	58	58
	Restriction	42	42

Table 2. Comparison of GERD to Lung Function Parameters

Parameters	GERD	n	Mean	SD	p
VC (%)	Yes	50	72.6	13.3	0.003
	No	50	79.7	16.3	
FEV1 (%)	Yes	50	70.7	11.8	0.000
	No	50	84.8	15.0	
FVC (%)	Yes	50	72.9	14.8	0.000
	No	50	82.4	13.5	
FEV1/FVC (%)	Yes	50	103.0	13.9	0.031
	No	50	99.1	9.9	
Mann-Whitney test (p<0.05)					

Tabel 3. Association between GERD and Lung Function

GERD		Spirometry: Restrictitive	Spirometry: Normal	Total	p	OR
Yes	n	26	24	50	0,043	2,302
	%	52.0%	48.0%	100.0%		
No	n	16	34	50		
	%	32.0%	68.0%	100.0%		
Total	n	42	58	100		
	%	42.0%	58.0%	100.0%		

Chi square test ($p<0.05$)