Association between the incidence of gastroesophageal reflux disease and degree of asthma

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ABSTRACT

Background and objectives. Asthma is a non-communicable disease with a high prevalence rate. The prevalence of uncontrolled asthma among asthma patients is inextricably linked to the presence of comorbidities. Gastroesophageal Reflux Disease (GERD) is one of the risk factors for uncontrolled asthma. The Asthma Control Test (ACT) is one of the tools for rapidly assessing the degree of asthma control. The GerdQ questionnaire is a simple diagnostic tool for GERD. This study aims to determine the association between the incidence of GERD and the degree of asthma.

Materials and methods. This case-control study was conducted on asthma patients who had been on controller therapy for at least one month at the outpatient clinics of Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital. All participants completed the ACT and GerdQ questionnaires. The data were analyzed using SPSS version 27.

Results. In this study involving 100 asthma patients who completed a questionnaire, it was found that 52% of the participants were female, and the average age was <40 years. Among the 75 asthma participants who had GERD, 61 (81.3%) experienced uncontrolled asthma, while 14 (18.7%) had controlled asthma. The odds ratio for the association was 9.25, with a p-value <0.0001. The study revealed a negative correlation between the GerdQ and ACT scores (R = -0.411).

Conclusions. There was a significant association between GERD and the degree of asthma. Asthma patients with GERD were 9.25 times more likely to experience uncontrolled asthma. Additionally, lower ACT scores correlate with higher GerdQ scores.

Keywords: asthma, gastroesophageal reflux disease, asthma control test, GerdQ

Abbreviations:

ACT – Asthma Control Test,

BMI – body mass index,

FeNO – fractional exhaled nitric oxide,

FEV1 – forced expiratory volume in one second,

GERD – Gastroesophageal Reflux Disease,

GerdQ – GERD Questionnaire,

GINA – Global Initiatives for Asthma,

HARQ – Hull Airway Reflux Questionnaire,

OSA – obstructive sleep apnea,

PACS – Primary Care Asthma Control Screening Tool,

PPI – proton pump inhibitor

SABA – short-acting beta-agonists

SPSS – Statistical Package for the Social Sciences,

INTRODUCTION

Asthma is a chronic respiratory condition characterized by variable airflow obstruction, heightened sensitivity of the airways, thickening of the airway walls, and increased mucus secretion [1]. It can affect individuals of all ages, from children to adults. In Indonesia, the prevalence of asthma in 2020 was approximately 4.5%, affecting around 12 million people, [2,3].

The assessment of therapy success in asthma patients involves evaluating the degree of asthma control, which includes three categories: controlled asthma, partially

controlled asthma, and uncontrolled asthma. Uncontrolled asthma is characterized by frequent symptoms that disrupt rest, the need for short-acting beta-agonists (SABAs) more than twice a week, and interference with daily activities [4,5]. Additionally, certain comorbidities, such as rhinosinusitis, gastroesophageal reflux disease (GERD), obesity, and obstructive sleep apnea (OSA), contribute to the risk of experiencing uncontrolled asthma [5,6].

GERD is the retrograde reflux of gastric contents into the esophagus, which causes various signs and symptoms, from heartburn/regurgitation to the development of extraesophageal respiratory syndrome [7]. The mechanism by which GERD makes asthma challenging to control or triggers asthma symptoms is not well understood. Previous studies have suggested three mechanisms that explain the relationship between GERD and asthma [8]. GERD causes bronchoconstriction, which provokes vagal reflexes so that acid in the distal esophagus causes a response in the airway. The activation of nerves in the bronchi due to GERD adds to the excessive response that occurs in the airway. Repeated microaspiration occurs, which refluxes into the upper respiratory tract to cause airway obstruction [9,10].

Various instruments, such as the Global Initiatives for Asthma (GINA), Primary Care Asthma Control Screening Tool (PACS), 30-Second Asthma Test, Royal College of Physicians Consensus, Asthma APGAR, Asthma Control Questionnaire, and Asthma Control Test (ACT), can be used to assess the degree of asthma [4]. Because it takes a short time and can be done by patients themselves without the help of health workers, the ACT can be a good choice for evaluating the degree of asthma [11]. In addition, based on the studies of Schatz et al. and Zhou et al., the ACT is more effective and reliable than other instruments [12,13].

The diagnosis of GERD can be effectively made using methods such as the GERD Questionnaire (GerdQ), the proton pump inhibitor test (PPI test), and upper gastrointestinal endoscopy [7]. A GerdQ score of 8 or higher strongly indicates GERD, often correlating with positive results from other diagnostic tests [14]. The DIAMOND study shows the GerdQ has a specificity of 71% and an accuracy of 65% [15]. Additionally, research by Simarmata et al. indicates that higher GerdQ scores are linked to a greater likelihood of esophageal reflux found during endoscopy, emphasizing the GerdQ's clinical value [16].

This study, therefore, investigates the relationship between the incidence of GERD and the degree of asthma, seeking to comprehend the impact of GERD on asthma management and the correlation between the GerdQ score and ACT score.

MATERIALS AND METHODS

Study design: This research is analytic observational research with a case-control design.

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

Study participants/sampling procedure: The population of this study were all asthma patients who had been diagnosed or received asthma treatment therapy for at least 1 month and who were outpatients or inpatients at Wahidin Sudirohusodo Central General Hospital and Hasanuddin University Hospital. The sample of this study was taken from a population that met the inclusion criteria. Inclusion criteria in this study were patients diagnosed with asthma who had received controller therapy for at least 1 month according to GINA guidelines and were willing to participate. Patients meeting the inclusion criteria are then asked to complete the ACT questionnaire. Based on the ACT questionnaire results, patients were divided into two groups: one group for patients with controlled asthma and the other for patients with uncontrolled asthma. Both groups then completed the GerdQ questionnaire. After the results of the GerdQ questionnaire were collected, an analysis was conducted.

Gastroesophageal Reflux Disease: GERD is the retrograde reflux of gastric contents into the esophagus, which causes various signs and symptoms, from heartburn/regurgitation to the development of extraesophageal respiratory syndrome. Diagnosis of GERD is based on symptoms using the GerdQ questionnaire, where a score of 8 or more indicates a diagnosis of GERD.

The degree of asthma: The degree of asthma control was evaluated based on symptoms, frequency, additional symptoms, and medication usage using the Indonesian version of the Asthma Control Test questionnaire. Asthma was considered uncontrolled if the ACT score was 24 or less.

Smoking: Smoking is the activity of smoking or inhaling cigarette smoke using a pipe or cigarette—active smokers or former smokers with a smoking history of 10 years or more.

Obesity: According to the classification of adult weight based on body mass index (BMI) in Asian populations, a BMI ≥ 25.0 kg/m² is considered obese [17].

Food Allergy: Immune responses that cause an abnormal reaction to food intake.

History of Rhinitis: Patients who have had rhinitis since childhood and have family members with a history of rhinitis.

Variables: The independent variable is the degree of asthma, the dependent variable is GERD, and the confounding variables are obesity, food allergies, rhinitis, and smoking.

Data analysis: Data analysis was carried out using SPSS version 27 (Armonk, NY: IBM Corp.). The analysis method consists of descriptive methods and statistical tests. The descriptive method aims to obtain general information about the research sample. The statistical method used was calculating mean and standard deviation and frequency distribution. The statistical test used was Chi-Square. Statistical test results were considered significant if the p-value was <0.05. Spearman's correlation test was also used. The results were supposed to correlate if the p-value was <0.001. The results obtained will be displayed in the form of a narrative supplemented by tables and figures.

RESULTS

Characteristics of participants

This study included 48 male and 52 female participants, ages 18 to 73 years, and a mean age of 41.0 ± 14.0 years. Among the participants, 53.0% were under 40 years old, 33.0% were between 40 and 59 years old, and 14.0% were 60 years or older. The assessment of obesity indices indicated that the BMI ranged from 15.0 to 43.0 kg/m², with a mean BMI of 24.1 ± 5.0 kg/m². Notably, 69.0% of participants had uncontrolled asthma. Out of the 100 asthmatic patients, 75.0% were also diagnosed with GERD. The other comorbidities in this population included 18.0% of participants who were smokers, 90.0% with food allergies, and 88.0% with a history of rhinitis (Table 1).

Association Between the Incidence of Gastroesophageal Reflux Disease and The Degree of Asthma

A significant association was found between GERD and the severity of asthma ($p < 0.0001$). The proportion of uncontrolled asthma was notably higher in participants with GERD (81.3%) compared to those without GERD (32.0%) (Table 2). Conversely, a greater percentage of controlled asthma cases was observed in non-GERD participants (68.0%) than in those with GERD (18.7%). Among the 75 participants diagnosed with GERD, 61 (81.3%) had uncontrolled asthma, while 14 participants (18.7%) had controlled asthma. In contrast, the rate of uncontrolled asthma among the 25 participants with asthma who did not have GERD was lower, at 32.0%. Based on the odds ratio (OR) of 9.259, participants with asthma and GERD were found to have a 9.25 times greater risk of experiencing uncontrolled asthma compared to those with asthma who do not have GERD (Table 2).

A significant negative correlation was found between the GerdQ and ACT scores ($p < 0.001$). This indicates that as the GerdQ score increases, reflecting more severe GERD symptoms, the ACT score decreases, indicating worse asthma control (Table 3).

In other words, more severe GERD symptoms are associated with worsened asthma control. The correlation coefficient value of R = -0.411 suggests a moderate negative relationship between the severity of GERD and the degree of asthma control (Figure 1).

DISCUSSION

Asthma is a chronic inflammatory disorder of the lungs characterized by reversible airway constriction and bronchospasm, which can be triggered by various factors [4]. Effective management of asthma symptoms is crucial, and this can be assessed using different metrics and validated questionnaires, such as the ACT. The ACT questionnaire measures asthma management and treatment effectiveness over a specified period, without the need for spirometry or additional tools [18,19]. The ACT is an effective resource because it is user-friendly for patients, requires only a short amount of time to complete, has been validated, and demonstrates greater reliability compared to many other questionnaires [12,19]. GERD refers to the backward flow of gastric contents into the esophagus, leading to various symptoms, including heartburn and regurgitation. It can also contribute to the development of extraesophageal respiratory syndrome [10,20]. Diagnosing GERD can be achieved through several methods, including the GerdQ questionnaire, proton pump inhibitor (PPI) test, or upper gastrointestinal endoscopy. The GerdQ questionnaire has been validated, with a score of 8 or higher indicating that a patient is more likely to have GERD [15,21].

This study identified a significant relationship between GERD and the level of asthma control (p < 0.0001). A considerable proportion of patients with uncontrolled asthma also had GERD, with 81.3% of these individuals experiencing poor asthma control compared to only 32.0% in patients without GERD. These findings align with the research conducted by Liang et al. in 2013, which involved asthma patients and utilized logistic regression analysis. In that study, 50.9% of patients diagnosed with GERD, as determined by the Reflux Diagnostic Questionnaire (RDQ), were significantly associated with the incidence of uncontrolled asthma (p < 0.001) [8]. GERD can result in the repeated aspiration of stomach contents, which may accumulate in the airways and cause obstruction. This obstruction can worsen asthma symptoms, leading to more frequent use of reliever medications and lower scores on the ACT among patients with poor asthma control [22]. This study, along with previous research, evaluated the same group of asthma patients diagnosed with GERD and assessed their asthma control using the ACT questionnaire [8].

Kurokawa et al. conducted a study on a group of asthma patients from 2018 to 2020, they identified a strong association between reflux symptoms and poor asthma control. A key difference between their study and the current investigation is the questionnaire used to evaluate reflux symptoms; Kurokawa et al. employed the Hull Airway Reflux Questionnaire (HARQ) [23]. Despite this difference, both studies reached similar conclusions regarding the relationship between asthma severity and reflux symptoms or GERD events. Frequent reflux episodes in asthma patients with GERD can lead to prolonged relaxation of the lower esophageal sphincter, resulting in repeated acid aspiration. This irritation of the upper airway can exacerbate asthma symptoms, contributing to uncontrolled asthma conditions [24].

A study by Singh et al. from 2021 to 2023 involved a sample of asthma patients diagnosed with the condition. The study took place at a polyclinic and utilized correlation tests to explore the relationship between asthma and GERD. The assessment of asthma control was measured using the ACT questionnaire, as well as evaluating forced expiratory volume in one second (FEV1) and fractional exhaled nitric oxide (FeNO) levels. The findings indicated that GERD is considered a contributing factor to the assessment of asthma severity [25]. The ACT was found to be less accurate than the assessments using FEV1 and FeNO. However, it is important to note that the study only assessed asthma severity through the ACT, and no comparison was made regarding the accuracy of other measurement methods. Furthermore, acid exposure in the esophagus can lead to decreased peak expiratory flow, which increases airway resistance. The lower pH levels in the esophagus, due to ongoing acid reflux, also act as a trigger for increased airway hyperresponsiveness, a fundamental mechanism underlying asthma [26,27].

This study identified a significant negative correlation between the GerdQ score and the ACT score; specifically, as the GerdQ score increases, the ACT score decreases. This finding indicates that patients diagnosed with GERD who experience severe reflux symptoms tend to have poorer asthma control. The correlation coefficient suggests a moderate relationship ($R < 0.500$) between the severity of reflux symptoms in GERD and the degree of asthma control. These results are consistent with the study conducted by Harding et al. from 1984 to 1994, which examined the connection between respiratory symptoms in asthma patients and acidic events in the esophagus, using a 24-hour esophageal pH monitoring approach [28]. The accumulation of substance P in the airways due to repeated acid exposure from reflux leads to the contraction of smooth muscles in the bronchi and increases vascular permeability, ultimately causing edema in the airway mucosa. Both of these conditions contribute to the onset of asthma symptoms and, if they occur repeatedly, can result in uncontrolled asthma in affected patients [29,30]. This

study's findings reinforce the notion that GERD can trigger respiratory symptoms in individuals with asthma.

CONCLUSION

Patients with asthma and GERD have a 9.25-fold increased likelihood of experiencing uncontrolled asthma.

Conflict of interest: None declared

Author's contributions: AAZM, MHI, and AML (idea, planning, availability, materials, gathering and processing of data, interpretation and analysis, literature search, and writing of manuscripts). WIN, SB, MHI, AML, and HR (idea, design, supervision, evaluation and interpretation, and literature search). AAZ (concept, design, critical review). WIN (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: The study was approved by the Ethics Review Committee of the Faculty of Medicine, Hasanuddin University, Makassar, Indonesia under reference number 555/UN4.6.4.5.31/PP36/2024.

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TABLES

Table 1. Characteristics of study (n = 100)

Variable	Category	n	%
Sex	Female	48	48.0
	Male	52	52.0
Age (years)	<40	53	53.0
	40-59	33	33.0
	≥ 60	14	14.0
BMI	Obese	32	32.0
	Non-obese	68	68.0
Comorbid	Smoking	18	18.0
	Food Allergy	90	90.0
	History Rhinitis	88	88.0
GERD	Yes	75	75.0
	No	25	25.0
Degree of Asthma	Uncontrolled asthma	69	69.0
	Controlled asthma	31	31.0

Table 2. Association between GERD and the degree of Asthma

GERD	The Degree of Asthma		OR	*p-value*
	Uncontrolled asthma	Controlled asthma		
Yes (n, %)	61 (81.3)	14 (18.7)	9.259	<0.0001
No (n, %)	8 (32.0)	17 (68.0)		

Table 3. Correlation between GERDQ score and ACT score

Variable	ACT score		
	n	R	p
GerdQ score	100	-0.411	<0.0001

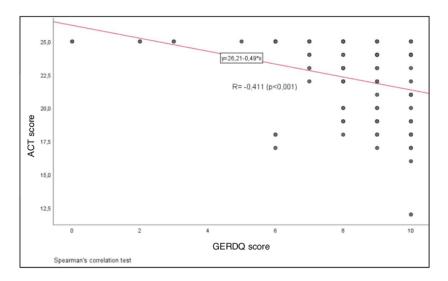Note: Spearman's Correlation test; R = Correlation coefficient

FIGURE

Figure 1. Spearman's Correlation Test