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ORIGINAL ARTICLE

Gastroesophageal Reflux Disease Among Patients with Chronic Obstructive Pulmonary Disease in Saudi Arabia in Makkah

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Abstract

Background: This study aimed to investigate the prevalence of Gastroesophageal Reflux Disease (GERD) and its factors among patients with Chronic Obstructive Pulmonary Disease (COPD) in Makkah, Saudi Arabia. **Materials and Methods:** Analysis was conducted using electronic health records (EHRs) of 706 adult patients with COPD who visited outpatient pulmonary clinics between August 1, 2023, and September 14, 2024. GERD diagnosis was collected from EHR as well as endoscopic results, and medication use. COPD was defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Data on demographics, pulmonary function tests, the existence of comorbidities, and hospital admissions due to Acute Exacerbations of COPD were collected. Statistical analyses included Chi-Square tests, Kruskal-Wallis tests, and binary logistic regression. **Results:** Among the 706 COPD patients, 186 (26.3%) had a diagnosis of GERD. The mean age of patients with GERD was 66.9 years, with equal gender distribution. The proportion of females was significantly higher in the GERD group compared to those without GERD (50.5% vs. 35.8%, $p < 0.001$). Obesity was more prevalent in the GERD group (49.5% vs. 38.1%, $p = 0.015$), whereas smoking was significantly less common (26.3% vs. 41.5%, $p < 0.001$). Significant factors of GERD among COPD patients included older age >61 years (Odd Ratio: 1.60, 95% CI: 1.11–2.29) and smoking (Odd Ratio: 1.98, 95% CI: 1.37–2.87). **Conclusion:** The study found that 26.3% of patients with COPD also had GERD. Key factors of GERD in this patient population include older age and smoking. These findings highlight the importance of monitoring and managing GERD in patients with COPD to improve clinical outcomes.

Keywords: COPD; Acute Exacerbation COPD; GERD; Gastroesophageal Reflux; Respiratory Therapy

Introduction

Chronic obstructive pulmonary disease (COPD) represents a substantial global health challenge, affecting populations in both developed and developing regions. Predictions suggest that by 2050, COPD will become the third leading cause of disease burden worldwide [1]. This disease, which is both common and preventable, is characterized by persistent and typically progressive airflow obstruction resulting from an abnormal inflammatory response in the lungs to harmful particles or gases [2]. Exacerbations of COPD play a significant role in shaping patients' quality of life

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and can accelerate disease progression, resulting in increased morbidity and greater utilization of healthcare resources [3]. These exacerbations are characterized by acute increases in the frequency and severity of cough, worsening dyspnea, and changes in the quantity and/or nature of sputum [4,5]. The exact mechanisms behind Acute Exacerbations of COPD (AECOPD) remain unclear. It is estimated that respiratory infections account for approximately 50–60% of cases, environmental pollutants for 10%, and 25–35% are of unknown origin [6].

Gastroesophageal reflux disease (GERD) has been proposed as a potential risk factor for COPD exacerbations[7–12]. GERD is a common gastrointestinal disorder characterized by troublesome symptoms and complications arising from the reflux of stomach contents [13]. This condition can contribute to, trigger, or worsen several pulmonary diseases, including chronic cough, bronchial asthma, bronchial pneumonia, and pulmonary fibrosis [14]. The association between GERD and respiratory conditions may be due to microaspiration of gastric contents and bronchospasm induced by vagal nerve irritation from gastric acid [13]. Although the physiological link between GERD and pulmonary diseases has been extensively researched in asthma, it has been less thoroughly examined in other pulmonary diseases, including COPD [7].

A study conducted in Saudi Arabia found that the prevalence of GERD among 1256 individuals in Riyadh city was 45.5% [15]. Similarly, data from the western and eastern regions of Saudi Arabia suggested that patients with GERD were around 39% and 20.9%, respectively [16–19]. Unfortunately, the available published data on the prevalence of GERD in the presence of COPD lags; only one study has explored the relationship between respiratory disorders and GERD, and found that a history of pulmonary symptoms was present in 15% of the study sample. In addition, the study introduced a potential link between GERD and various respiratory disorders [20].

To date, the prevalence of GERD among patients with COPD in Makkah has not been thoroughly investigated; this study seeks to fill that gap. Therefore, this study aimed to investigate the prevalence of GERD and its factors among patients with COPD in the outpatient setting in a single center in Makkah.

Materials and Methods

GERD and COPD Definitions

GERD diagnosis was determined based on endoscopic findings, relevant clinical symptoms, and the use of associated medications, all of which were extracted for the entire study sample. The method we used was introduced by Lee et al. and John Hurst to define GERD based on diagnosis, symptoms, and medications related to the condition [21,22]. Operational definition of COPD was according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD's) criteria if the FEV_1/FVC ratio <0.7, Age > 40 years, and a history of smoking.

Study Design and Settings

This retrospective study was conducted at the Security Forces Hospital in Makkah (SFHM) from August 1, 2023, to September 14, 2024. The study was reviewed and approved by the Institutional Review Board at SFHM. Approval ID 0737-220824.

Population Selection

The study involved a retrospective analysis of electronic health records (EHRs) for 706 adult patients who visited the outpatient pulmonary clinics between August 1, 2023, and September 14, 2024. These patients were diagnosed with COPD, as determined by relevant smoking exposure histories and adherence to the GOLD criteria.

Data Collection

Data on demographic characteristics, including age, gender, body mass index (BMI), and smoking status, as well as clinical parameters such as pulmonary function (FEV_1/FVC ratio), presence of comorbidities, hospital admissions due to acute exacerbations of COPD (AECOPD), and medication records, were collected. Data were extracted and entered into a standardized, secure, and Good Clinical Practice (GCP)-compliant electronic database using Microsoft Excel (Version 16, Microsoft Corporation, Washington, USA).

Statistical Analysis Plan

First, we computed frequencies and percentages for categorical variables. Mean and standard deviation (SD) were calculated for the continuous variable to compare the characteristics between COPD patients with and without GERD. Chi-Square was used for categorical variables, and Kruskal-Wallis was used for continuous variables. Second, the medication profiles for all patients were compared via frequencies and percentages. Third, we performed a binary logistic regression analysis to understand the association between general characteristics and the existence of GERD in the COPD population. This included subgroup analysis based on gender to understand the factors contributing to GERD in COPD patients. Gender factor has been considered, as it is a major factor in COPD, which influences treatment plans [23]. Statistical significance was determined using a 95% confidence interval, with a significance level set at 5%. All statistical analyses were conducted using SPSS

(Statistical Package for the Social Sciences, version 30.0, from SPSS Inc.).

Results

Baseline Characteristics of COPD Patients with GERD diagnosis

A total of 706 COPD patients were included in the study, of whom 186 (26.3%) had a diagnosis of GERD. The proportion of females was significantly higher in the GERD group compared to those without GERD (50.5% vs. 35.8%, p<0.001). The mean ± SD age was higher in the GERD group (66.9 ± 10.7 years) than in the group without GERD (64.8 ± 28.7 years), although the difference was not statistically significant (p = 0.056). Obesity was more prevalent in the GERD group (49.5% vs. 38.1%), while smoking was significantly less (26.3% vs. 41.5%, p < 0.001). The mean ± SD of FEV_1/FVC ratio was lower in the GERD group (55.0 ± 10.8 vs. 58.0 ± 9.8, p = 0.015). Additionally, patients with GERD had a higher frequency of AECOPD events (Defined by worsening of respiratory symptoms leading to hospital admission in the last year) (55.3% vs. 30.5%, p < 0.001) and a greater prevalence of comorbidities (94.0% vs. 59.0%, p < 0.001). (Table 1)

Among patients diagnosed with GERD, the most prescribed medications included short-acting beta-agonists (SABA) in 172 patients (92.5%), long-acting beta-agonists (LABA) in 96 patients (52.3%), long-acting muscarinic antagonists (LAMA) in 139 patients (75.4%), inhaled corticosteroids (ICS) in 89 patients (48.3%), and oral corticosteroids in 26 patients (14.6%). Additionally, proton pump inhibitors (PPIs) were prescribed to 172 patients (92.5%). Notably, 18 patients (3.5%) without a diagnosis of GERD were also receiving PPI therapy. A comparative analysis between patients with and without GERD revealed statistically significant differences (p < 0.001) in the prescription rates of all listed medications, except for H2-histamine receptor antagonists, for which no significant difference was observed between the groups (Figure 1).

TABLE 1. GENERAL CHARACTERISTICS OF COPD PATIENTS INCLUDED IN THE STUDY

Variable	COPD with GERD		COPD without GERD		Chi-square or t-test
	N=186	26.3%	N = 520	73.7%	
Female	94	50.5	186	35.8	<0.001
Males	92	49.5	334	64.2	<0.001
Age (Mean and SD)	66.9	10.7	64.8	28.7	0.056
BMI					
Underweight	7	3.8	20	3.8	0.015
Normal	31	16.6	115	22.1	
Overweight	56	30.1	187	36.0	
Obese	92	49.5	198	38.1	
Smoking status					
Smokers	49	26.3	217	41.5	<0.001
Ex-smokers	75	40.3	183	35.2	
Non-smokers	62	33.4	120	23.3	
FEV_1/FVC% (Mean and SD)	55.0	10.8	58.0	9.8	0.015
GOLD stages					
GOLD stage 1	28	15.1	77	14.8	0.086
GOLD stage 2	87	46.8	280	53.9	
GOLD stage 3	45	24.2	103	19.8	
GOLD stage 4	26	14	60	11.5	
AECOPD in the last year (Yes)	103	55.3	159	30.5	<0.001
Number of patients with comorbidities	175	94.0	307	59.0	<0.001

Footnote: *Data were analyzed as frequency and percentages unless otherwise specified. Abbreviations: COPD; Chronic Obstructive Pulmonary Disease, GERD; Gastroesophageal Reflux Disease, N; number, SD; standard deviation, BMI; Body Mass Index, FEV1; Forced Expiratory Volume in One Second, FVC; Forced Vital Capacity, GOLD; Global Initiative for Chronic Obstructive Lung Disease, AECOPD; Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Variable AECOPD in the last year reported the number of patients with COPD and GERD. Variable comorbidities reported the number of patients who have comorbidities.*

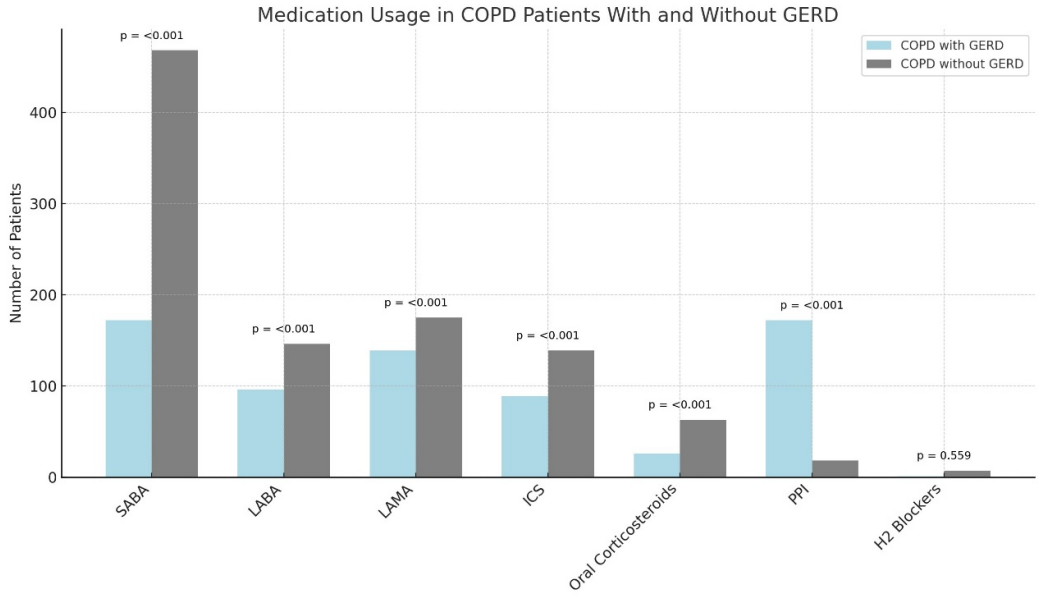

FIGURE 1. MEDICATION USAGE LIST AMONG COPD PATIENTS WITH OR WITHOUT GERD. THE P-VALUE WAS COMPUTED USING THE CHI-SQUARE TEST TO COMPARE THE FREQUENCIES OF MEDICATION USAGE BETWEEN COPD PATIENTS WITH OR WITHOUT GERD. SABA; SHORT-ACTING BETA-AGONIST, LABA; LONG-ACTING BETA-AGONIST, LAMA; LONG-ACTING MUSCARINIC ANTAGONIST, ICS; INHALED CORTICOSTEROID, PPI; PROTON PUMP INHIBITORS, H2 BLOCKERS; H2-HISTAMINE RECEPTOR ANTAGONISTS.

Gender Differences Among COPD Patients with GERD

The mean ± SD of the age variable was 67.2 ± 11.4 years for females and 66.5 ± 10.1 years for males, with no statistically significant difference between the two groups (p = 0.21). In terms of BMI categories, a greater proportion of females were classified as obese compared to males (53.2% vs. 45.7%, p = 0.66). Regarding smoking status, the prevalence of current smokers was higher among males than females (34.8% vs. 18.1%, p = 0.001). The mean ± SD of FEV_1/FVC ratio was 54.9 ± 11.0 for females and 55.1 ± 10.7 for males. Regarding GOLD stages, 42.6% of females were categorized as GOLD 2, which was comparable to 51.1% of males in the same category. In the preceding year, 48 female patients (51.1%) and 55 male patients (59.8%) experienced AECOPD. The number of patients with existing comorbidities was higher in both female and male patients (96.8% vs.91.3%), respectively. (Table 2)

The analysis of medication usage among COPD patients with GERD revealed comparable patterns between females and males. The use of bronchodilators, including SABA, LABA, and LAMA, was high across both groups, with no significant differences observed (e.g., LAMA use: 93.6% in females vs. 94.6% in males, p = 0.78). ICS were also similarly prescribed (75.5% in females vs. 73.9% in males, p = 0.79). Although a higher percentage of males received oral corticosteroids compared to females (40.2% vs. 27.7%), the difference did not reach statistical significance (p = 0.07). PPIs were widely used in both groups (females: 92.6%, males: 92.4%, p = 0.96). (Figure 2).

Factors Associated with GERD Among COPD Patients.

Binary logistic regression analysis identified factors significantly associated with GERD among COPD patients. Female gender was associated with a lower likelihood of having GERD (OR = 0.54, 95% CI: 0.38–0.76, p < 0.001). Similarly, a history of AECOPD admissions in the last year was associated with lower odds of GERD (OR = 0.35, 95% CI: 0.25–0.50, p < 0.001), with similar patterns observed in both female and male subgroups. In contrast, age over 61 years was significantly associated with an increased odds of GERD (OR = 1.60, 95% CI: 1.11–2.29, p = <0.001), with the effect more in males (OR = 1.89, 95% CI: 1.13–3.17, p = 0.015). Smoking was also a significant risk factor (OR = 1.98, 95% CI: 1.37–2.87, p < 0.001), particularly among females (OR = 2.32, 95% CI: 1.26–4.25, p = 0.007); however, it did not reach significance in males (p = 0.060). (Table 3)

TABLE 2: GENDER DIFFERENCES AMONG COPD PATIENTS WITH GERD

Variable	Female		Male		Chi Square
	N	%	N	%	
	94	50.5	92	49.5	
Age (Mean and SD)	67.2	11.4	66.5	10.1	0.21
BMI					
Underweight	4	4.3	3	3.3	0.66
Normal	16	17	15	16.3	
Overweight	24	25.5	32	34.8	
Obese	50	53.2	42	45.7	
Smoking status					
Smokers	17	18.1	32	34.8	0.001
EX-smokers	24	25.5	51	55.4	
Non-smokers	53	56.4	9	9.8	
FEV_1/FVC ratio (Mean and SD)	54.9	11.0	55.1	10.7	0.49
GOLD stages					
GOLD stage 1	15	16	13	14.1	0.66
GOLD stage 2	40	42.6	47	51.1	
GOLD stage 3	26	27.7	19	20.7	
GOLD stage 4	13	13.7	13	14.1	
AECOPD in the last year (Yes)	48	51.1	55	59.8	0.66
Number of patients with comorbidities	91	96.8	84	91.3	0.11

Footnote: *Data were analyzed as frequency and percentages unless otherwise specified. Abbreviations: COPD; Chronic Obstructive Pulmonary Disease, GERD; Gastroesophageal Reflux Disease, N; number, SD; standard deviation, BMI; Body Mass Index, FEV_1; Forced Expiratory Volume in One Second, FVC; Forced Vital Capacity, GOLD; Global Initiative for Chronic Obstructive Lung Disease, AECOPD; Acute exacerbation Chronic Obstructive Disease, Variable AECOPD in the last year reported the number of patients within the COPD with GERD. Variable comorbidities reported the number of patients who have comorbidities.*

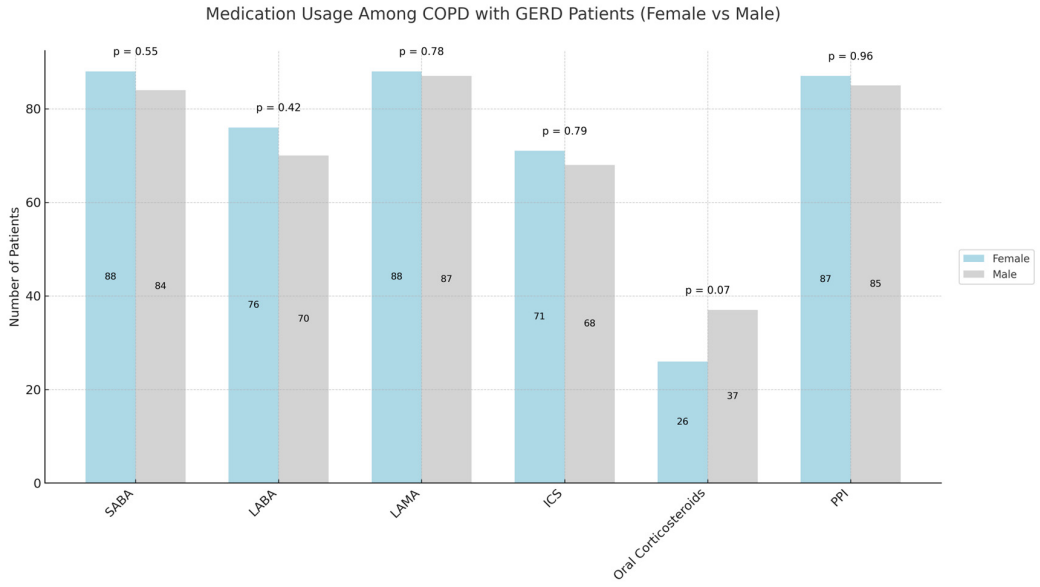

FIGURE 2. MEDICATION USAGE LIST AMONG BOTH FEMALE AND MALE COPD PATIENTS WITH GERD. THE P-VALUE WAS COMPUTED USING THE CHI-SQUARE TEST TO COMPARE THE FREQUENCIES OF MEDICATION USAGE BETWEEN GENDERS. SABA; SHORT-ACTING BETA-AGONIST, LABA; LONG-ACTING BETA-AGONIST, LAMA; LONG-ACTING MUSCARINIC ANTAGONIST, ICS; INHALED CORTICOSTEROID, PPI; PROTON PUMP INHIBITORS.

TABLE 3. FACTORS ASSOCIATED WITH GERD AMONG COPD PATIENTS

Variable/Factor	All patients (n=186) OR (95% CI)	P-value	Female (N=94) OR (95% CI)	P-value	Male (N=92) OR (95% CI)	P-value
Gender/ Female	0.54 (0.38 – 0.76)	<0.001	-	-	-	-
Age/ >61	1.60 (1.11 – 2.29)	<0.001	1.37(0.81-2.31)	0.232	1.89(1.13-3.17)	0.015
Smoking status/ Smoker	1.98 (1.37- 2.87)	<0.001	2.32 (1.26-4.25)	0.007	1.58 (0.98-2.56)	0.060
AECOPD admission in the last year	0.35 (0.25 – 0.50)	<0.001	0.39 (0.23-0.66)	<0.001	0.30(0.19-0.42)	<0.001

Footnote: *N; Number, OR Odd ratio, AECOPD; Acute exacerbation of chronic obstructive pulmonary disease. CI: confidence intervals. Reference groups for the binary logistic regression were as follows: Male was the reference group for gender, Age below 60 was the reference group for age >61, Non-smokers was the reference group for smoking status, and having no admission in the last year was the reference group for AECOPD admission in the previous year.*

Discussion

This study investigated the prevalence of GERD and its factors within a defined COPD cohort in Saudi Arabia, using real-world clinical data. The main findings of this study show that over 26.3% of patients diagnosed with COPD also suffered from GERD. Key potential factors of GERD in this patient population included smoking and older age.

The global prevalence of GERD among patients with COPD, primarily assessed using self-reported questionnaires, has been estimated to affect between 19% and 29% of adults, with geographical variation in prevalence estimates [24–26]. Additionally, GERD symptoms have consistently been reported to be more prevalent in patients with COPD than in the general population [24,27]. In our study, the prevalence of GERD in the COPD cohort was 26.3%, which is consistent with global prevalence estimates. However, the prevalence observed in our study is significantly lower than that reported in local studies conducted across various regions in Saudi Arabia, which investigated GERD symptoms in the general population [28–31]. This may be due to the size of the population in our study and could also be attributed to the underreporting of comorbidities in patient records. Nevertheless, the data provide significant insights into the basis of GERD prevalence among COPD populations.

Whilst the reasons behind the differences in the national prevalence rates of GERD between those with and without COPD are unclear, the discrepancies in the prevalence of GERD symptoms across Saudi regions may be explained in part by regional differences in the presence of the risk factors associated with GERD, which may include family history of GERD, smoking, obesity, sedentary lifestyle, drinking tea, and greasy and fast food intake[32]. Additionally, regional food ingredients and habits are different across Saudi Arabia; this may directly or indirectly impact the prevalence of GERD [33–37].

Our clinical data findings are highly relevant to the delivery of COPD clinical care in Saudi Arabia. As no prior data present GERD in the COPD community, this research highlights the importance of monitoring comorbidities, such as GERD, in patients with COPD. Additionally, the study will help clinical practitioners identify risk factors associated with the coexistence of GERD and COPD in clinical practice [38,39]. It also underscores the significance of using validated Arabic surveys to screen for GERD in outpatient clinics [40]. Patients included in this study were from a clinical population receiving COPD care at outpatient pulmonary clinics in Makkah, which allowed for the assessment of GERD prevalence using real-world clinical data. However, the findings of this study must be interpreted with caution due to several limitations. Firstly, the small sample size, with all patients being from a single city in Saudi Arabia. Whilst this may increase the risk of bias and reduce the variation and diversity of the study population, it may also limit the generalizability of the findings. However, our study is among the first to investigate the prevalence of GERD in COPD using real-world clinical data, in addition to the current efforts using validated questionnaires.

Secondly, routine EHR data is not primarily collected for research purposes. Therefore, retrospective analyses of routinely collected clinical data may introduce selection and detection bias due to incompleteness or inconsistencies in data capture and coding. To mitigate these potential biases, we used inclusion criteria that incorporated both clinical diagnosis and medications commonly used for patients with GERD.

Ultimately, despite these limitations, our findings offer valuable clinical and research insights by providing empirical data on the prevalence and factors associated with GERD in patients with COPD residing in Saudi Arabia. Additional research is needed to further examine the relationship between GERD and COPD, as well as the implications of their coexistence from patient, clinical, and economic perspectives.

Conclusions

Our findings showed that 26.3% of the Saudi COPD patients in our study also had GERD, with smoking and older age as identified risk factors. These findings highlight the need to further investigate the implications of GERD co-existence with COPD patients.

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Not Applicable

Conflict of Interest

None

Data Availability

All data available within the manuscript.

Author Contributions

Each author significantly contributed to the reported work, whether through the conception, study design, execution, data acquisition, analysis, interpretation, or a combination of these areas. They participated in drafting, revising, and critically reviewing the article, provided final approval for the version to be published, agreed on the journal for submission, and accepted responsibility for all aspects of the work.

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انتشار مرض الارتجاع المعدي المريئي بين مرضى الانسداد الرئوي المزمن في مكة المكرمة، المملكة العربية السعودية

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المستخلص

الخلفية: هدفت هذه الدراسة إلى استقصاء مدى انتشار مرض الارتجاع المعدي المريئي (GERD) والعوامل المرتبطة به بين مرضى الانسداد الرئوي المزمن (COPD) في مدينة مكة المكرمة، المملكة العربية السعودية.

المواد والطُرق: تم إجراء التحليل باستخدام السجلات الصحية الإلكترونية (EHR) لـ ٧٠٦ من مرضى الانسداد الرئوي المزمن البالغين الذين راجعوا عيادات الأمراض الصدرية الخارجية خلال الفترة من ١ أغسطس ٢٠٢٣ حتى ١٤ سبتمبر ٢٠٢٤. تم الحصول على تشخيص مرض الارتجاع المعدي المريئي من السجلات الصحية الإلكترونية بالإضافة إلى نتائج التنظير واستخدام الأدوية. تم تعريف مرض الانسداد الرئوي المزمن وفقًا لمعايير المنظمة العالمية للانسداد الرئوي المزمن (GOLD). شملت البيانات التي تم جمعها معلومات ديموغرافية، واختبارات وظائف الرئة، ووجود أمراض مصاحبة، وحالات الدخول للمستشفى بسبب التفاقم الحاد للانسداد الرئوي المزمن. شملت التحليلات الإحصائية اختبار كاي التربيعي، واختبار كروسكال واليس، والانحدار اللوجستي الثنائي.

النتائج: من بين ٧٠٦ مريضًا بالانسداد الرئوي المزمن، تم تشخيص ١٨٦ مريضًا (٢٦,٣٪) بمرض مرض الارتجاع المعدي المريئي .بلغ متوسط أعمار المرضى المصابين بالـ مرض الارتجاع المعدي المريئي نحو ٦٦,٩ عامًا، مع تساوٍ في

التوزيع بين الجنسين. كانت نسبة الإناث في مجموعة مرض الارتجاع المعدي المريئي أعلى بشكل ملحوظ مقارنةً بمن لا يعانون من مرض الارتجاع المعدي المريئي ٥٠,٥٪ مقابل ٣٥,٨%، (p<٠,٠٠١) .كما كان انتشار السمنة أعلى في مجموعة مرض الارتجاع المعدي المريئي ٤٩,٥٪ مقابل ٣٨,١%، (p=٠,٠١٥)، بينما كان معدل التدخين أقل بشكل ملحوظ ٢٦,٣٪ مقابل ٤١,٥%، p<٠,٠٠١ .من العوامل المرتبطة بشكل كبير بوجود مرض الارتجاع المعدي المريئي بين مرضى الانسداد الرئوي المزمن: العمر الأكبر من ٦١ سنة (نسبة الأرجحية: ١,٦٠، فاصل الثقة ٩٥٪: ١,١١–٢,٢٩)، والتدخين (نسبة الأرجحية: ١,٩٨، فاصل الثقة ٩٥٪: ١,٣٧–٢,٨٧).

الاستنتاج: أظهرت الدراسة أن ٢٦,٣٪ من مرضى الانسداد الرئوي المزمن يعانون أيضًا من مرض الارتجاع المعدي المريئي .وتشمل العوامل الرئيسة المرتبطة بالارتجاع المعدي المريئي في هذه الفئة من المرضى كِبر السن والتدخين. وتبرز هذه النتائج أهمية المتابعة الدقيقة وإدارة مرض الارتجاع المعدي المريئي بين مرضى الانسداد الرئوي المزمن لتحسين النتائج السريرية.

الكلمات المفتاحية: الانسداد الرئوي المزمن، التفاقم الحاد للانسداد الرئوي، GERD، الارتجاع المعدي المريئي، الرعاية التنفسية