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PREVALENCE OF GERD IN BRONCHIAL ASTHMA AND COPD: ASSESSMENT USING FSSG SCALE AND GASTROESOPHAGEAL ENDOSCOPY

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ABSTRACT: BACKGROUND: Gastro-esophageal reflux disease (GERD) is a chronic disorder of the upper gastrointestinal tract with global distribution. GERD often coexists with asthma, COPD and is often responsible for their exacerbations. In India, we do not have any clinical data on GERD either in bronchial asthma or COPD. **OBJECTIVE:** To investigate the prevalence of GERD in adult patients with asthma, COPD and to determine its correlates. **MATERIALS AND METHODS:** A total of 40 subjects each in bronchial asthma and COPD groups underwent assessment with the frequency scale for the symptoms of GERD (FSSG) Questionnaire for GERD. A score of 8 and above was taken as positive for GERD. The confirmation of GERD was done by Gastroesophageal endoscopy to all GERD positive cases. Grading of GERD was done with endoscopy report according to Los Angeles grading. FSSG score was evaluated in detail and the risk factors were analyzed. **RESULTS:** The prevalence of GERD in bronchial asthma patients was 40%, while in COPD cases it was 30%. It was observed that by using FSSG questionnaire, the number of patients showing predominance of regurgitation related symptoms were higher in the asthma group (52%) as compared to the COPD group (37%). In COPD group, the number of patients showing predominance of dysmotility-related symptoms was higher (42%) as compared to asthma group (35%). As the severity of both the diseases increased, the severity of GERD also increased as assessed by Los Angeles grading. **CONCLUSIONS:** According to the current study, more than one-third of adult patients with asthma have GERD and another nearly one third have GERD in COPD cases. Thus high suspicion is required in these cases for the adequate control of either asthma or COPD.

KEYWORDS: GERD, asthma, COPD, FSSG scale, Los Angeles grading.

INTRODUCTION: Gastro-esophageal reflux disease (GERD) is defined as a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.¹ Gastro esophageal reflux (GER) is common in patients with pulmonary disease and is involved in the pathophysiology of exacerbation of asthma and COPD. Acid reflux is a potential trigger of asthma and may also be a complicating factor in difficult-to-control asthma. GER is a potential trigger for supraesophageal manifestations of asthma and COPD.² The prevalence of GERD in asthma patients ranges from 42% to 69% according to the questionnaire for the diagnosis of reflux disease (QUEST).³

In COPD patients, the prevalence of GER has been found to be 37% according to the Mayo clinic GERD questionnaire.⁴ Moreover, GERD has been associated with higher rates of hospitalizations in COPD patients.

The aims of this study were to compare the prevalence of GERD among asthma and COPD patients in a tertiary care hospital. The impact of GERD on the severity of bronchial asthma and COPD was also evaluated.

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MATERIALS AND METHODS: SUBJECTS: The prospective study was done at KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum over a period of 2 years. All patients with confirmed cases of bronchial asthma according to GINA guidelines and COPD, diagnosed according to GOLD Guidelines, were included in the study. A total of 40 cases in each group were included in the study. The grading of bronchial asthma was done according to the Global Initiative for Asthma (GINA) guidelines,⁵ while the grading of Global Initiative for Chronic Obstructive Lung Disease (COPD) was done according to GOLD guidelines.⁶

Patients were excluded if they were chronic smokers, had previous gastric or oesophageal surgery, scleroderma, with malignancy and immune suppressive therapy, and patients on acid suppressive therapy and ACE inhibitors therapy. Ethical clearance was obtained before conducting the study from the Institutional Review Board.

METHODOLOGY: All enrolled patients were given questionnaire which included: Age, gender, cigarette smoking, any other illness, any medication history, any previous surgeries, duration of respiratory disease, and any previous surgery. Then all patients underwent GERD FSSG-SCALE (Frequency Scale for Symptoms of GERD) questionnaire⁷ (Table 1). The FSSG has been proven to be a useful questionnaire for the assessment of GERD. It was used to determine the prevalence and symptoms of GERD⁸. This questionnaire is composed of 12 questions, which are scored to indicate the frequency of symptoms as follows: never = 0, occasionally = 1, sometimes = 2, often = 3, and always = 4. The cut-off score for diagnosis of GERD is defined as 8 points. The unique feature of the FSSG is that the questions cover both acid regurgitation-related symptoms (questions 1, 4, 6, 7, 9, 10, and 12) and gastric dysmotility-related symptoms (questions 2, 3, 5, 8, and 11).

Then confirmation of GERD was done by using objective evidence with Gastro Esophageal endoscopy to all GERD positive cases obtained by FSSG SCALE Questionnaire method. Grading of GERD was done with endoscopy report according to Los Angeles classification⁹ (Table 2). The severity of oesophagitis was categorized by gastro-oesophageal endoscopy as Grade A to Grade D according to the classification used. Then the severity of GERD was compared with severity of bronchial asthma and COPD cases. Those cases which were confirmed by endoscopy were taken as positive for GERD and were taken for the final analysis.

Statistical Analysis: Data are expressed as the mean (SD). Comparison of parameters between two groups was done by Student's t test. Comparisons among three groups were done by one-way ANOVA with Bonferroni's multiple comparison tests. Differences in frequency between regurgitation and dysmotility symptoms were assessed by the chi-square test. A p value of less than 0.05 was considered significant.

RESULTS: The baseline characteristics are shown in Table 3. The average age in bronchial asthma patients was 44 ± 4.5 years, while in COPD patients it was 58 ± 6.3 years. Majority of the patients in COPD group were smokers, with average pack-years history of 12 ± 3.4 . The BMI was lower in the COPD group as compared to bronchial asthma patients. The main risk factor for bronchial asthma was allergy as evident by the peripheral blood and sputum eosinophilia.

The pulmonary functions were lower in the COPD patients as compared to the bronchial asthma patients with average predicted FEV₁ being $53 \pm 21\%$ in COPD group as compared to $76 \pm 23\%$

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in the bronchial asthma group. The regular treatment given for bronchial asthma patients were inhaled steroids/beta₂ agonists, Montelukast, oral theophyllines, if required and oral steroids during exacerbations. The regular treatment given for COPD was inhaled steroids/beta₂ agonists, inhaled Tiotropium, and oral theophyllines.

The prevalence of GERD in bronchial asthma patients was 40% (16/40), while in COPD patients the prevalence was 30% (12/40). In FSSG questionnaire, the questions are divided into those covering acid regurgitation-related symptoms (Questions 1, 4, 6, 7, 9, 10, and 12) and those for gastric dysmotility-related symptoms (Questions 2, 3, 5, 8, and 11). When regurgitation-related and dysmotility-related symptoms were compared among both the groups, the number of patients showing predominance of regurgitation related symptoms was higher in the asthma group (52%) as compared to the COPD group (37%). The number of patients showing predominance of dysmotility-related symptoms was higher in the COPD group (42%) than in the asthma group (35%) (Fig. 1).

In the present study, the diagnosis of GERD was made depending upon the upper gastroendoscopy findings, and all were classified according to Los Angeles classification⁹. It was observed that as the severity of bronchial asthma increased, the severity of GERD also increased. Similarly in COPD group, as the severity of COPD disease increased, the severity of grading of GERD also increased (Table 4 and Table 5).

This indicates that in both the disorders, as the severity of the diseases increases, the severity of the GERD related symptoms also increases. The presence of GERD was not related to BMI in both the groups. No other risk factors were observed for the presence of GERD in the present study in both the groups. In the present study, all the patients of bronchial asthma and COPD were having stable disease and none of them were having exacerbation of the disease.

Hence we did not evaluate whether the GERD was responsible as a risk factor for the exacerbation of disease. Secondly, obesity was not associated with increased gastro-esophageal reflux in the present study.

DISCUSSION: In the present study the prevalence of GERD in bronchial asthma patients was observed to be 40%, while in COPD patients it was 30%. All the patients were initially evaluated by the FSSG scale for GERD, and were later confirmed by gastro-esophageal endoscopy. The mean age among bronchial asthma patients was 44±4.5 years, while in COPD patients it was 58±6.3 years. Smoking was the main risk factor for the development of COPD, but significant numbers of patients in bronchial asthma group also were smokers.

From the various studies it has been observed that prevalence of GERD varies from 24% to 80%. The method used for diagnosis of GERD in asthmatic patients varies in different studies and this may affect the prevalence rates in different studies. In many of the studies only FSSG scale is used for the diagnosis of GERD. Sontag et al⁷ performed 24-h esophageal pH monitoring on 104 consecutive asthmatic patients, and observed GERD to be 43%. Harding et al¹⁰ studied 26 asthmatic patients and observed that about 62% of patient had showed abnormal acid exposure. Connell et al¹¹ also observed high prevalence of GERD in bronchial asthma patients (72%).

Yet another study by Calabrese et al¹² also observed high prevalence of GERD (80%) in bronchial asthma patients. Thus present study is comparable to most of the studies published in the literature. Takenaka et al¹³ used FSSG scale and observed that among the prevalence of GERD among bronchial asthma patients to be 37.4%. Charles et al¹⁴ used the same FSSG scale in 89 patients and

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observed that prevalence of GERD to be 43%. Harding et al¹⁵ performed esophageal pH monitoring on 44 patients with asthma and they observed that 15 patients (34%) had GERD. Calabrese et al¹⁶ investigated 34 consecutive asthmatic patients with ambulatory esophageal pH monitoring and they observed the prevalence of GERD to be 80%. The prevalence of GERD among COPD patients has been reported to be 26.8% than among age-matched healthy controls (12.5%) using FSSG scale.¹⁷ Another recent study by Shimizu et al¹⁸ has observed the prevalence of GERD to be 32.5% in COPD patients using FSSG scale.

In bronchial asthma patients, the typical symptoms detected by the FSSG were an unusual sensation in the throat and burning sensation in the chest. Another study also reported higher prevalence of regurgitation related symptoms in bronchial asthma patients as compared with COPD patients.¹⁸ Possible mechanisms leading to an unusual sensation in the throat are direct acid reflux or acidic gas reflux.

Another mechanism is stimulation of esophageal or laryngeal sensory nerves by gastric acid; because some sensory nerves from these sites terminate in the same region of the central nervous system.¹⁹ Dysmotility-related symptoms were more prominent in the COPD patients. Similar findings have been confirmed in other studies also.¹⁹ A decrease of lower esophageal sphincter pressure is related to the mechanism of GER in both asthma and COPD patients, while dysmotility from the esophagus to intestines seemed to contribute to GER symptoms in COPD.¹⁹

All our patients had confirmed cases of GERD with gastro-esophageal endoscopy, thus ruling out functional dyspepsia. Recently, one study have shown that a history of GERD is associated with frequent exacerbation phenotype in COPD patients.²⁰ Patients who had GER symptoms of reflux or heartburn had significantly more hospitalizations related to their COPD. Therefore, dysmotility to esophagus to intestine possibly affects COPD exacerbation.¹⁸

In the present study comparison between bronchial asthma severity and GERD severity was done and it was observed that majority of patients who had Grade D GERD were associated with severe persistent bronchial asthma. It was also observed that as the severity grade of asthma increased the severity of GERD also statistically increased. This association was statistically significant ($p < 0.0001$). Yasuo et al²¹ studied GERD in bronchial asthma cases using Los Angeles classification, and it was observed that 5%, 10%, 12.5%, and 12.7% patients had Grade A, Grade B, Grade C, and Grade D GERD respectively.

In another study, Ruigomez et al²² observed the risk of asthma development following GERD diagnosis. They observed over a 3 years period, 103 cases of bronchial asthma among 17,190 patients of GERD cases. Thus they estimated an incidence of 6 cases of bronchial asthma per 1000 patients of GERD diagnosed. Among COPD patients, the severity of GERD increased as the severity of COPD grade increased. Recently Bor et al²³ also observed higher prevalence of GERD symptoms in COPD patients as the disease severity increases.

This may be due to the relaxation of the lower esophageal sphincter more as the disease severity increases. Harding et al¹⁵ investigated 105 consecutive asthmatic patients with ambulatory esophageal pH monitoring for GERD, and they observed significant association with smoking history in bronchial asthma patients ($p < 0.0001$). Such association was not observed in the present study.

Also, no other clear association of GERD with other risk factors including BMI and age group was observed in the present study.

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In the present study, all the patients of bronchial asthma and COPD were having stable disease and none of them were having exacerbation of the disease. Hence we did not evaluate whether the GERD was responsible as a risk factor for the exacerbation of disease. Secondly, obesity was not associated with increased gastro-esophageal reflux in the present study. It was also observed that the prevalence of GER was almost to similar extent in patients with alcohol ingestion and those without alcohol ingestion. Thus, it can be assumed that alcohol ingestion had no significant association with increased risk of GER in stable patients with bronchial asthma and COPD.

Due to the high prevalence of GERD in bronchial asthma and COPD, proper treatment should be initiated at the earliest so that appropriate control of bronchial asthma and COPD can be achieved. The goals of treatment include relief of symptoms, healing of esophagitis, prevention of recurrence, and prevention of complications. The principles of treatment include lifestyle modifications and control of gastric acid secretion using drugs or surgical treatment with corrective anti-reflux surgery, if required.²⁴

Multi-drug therapy may be important in bronchial asthma and COPD patients with GERD. The efficacy of proton pump inhibitors may differ between regurgitation-related symptoms and dysmotility related symptoms in asthma patients and COPD patients with GERD.

In conclusion, in the present study, more than one third of adult asthmatic patients and nearly one-third of COPD patients have GERD. These patients do not often have typical reflux symptoms such as heartburn or regurgitation. However, the presence of typical reflux symptoms in an asthmatic or COPD patient does not seem to guarantee the presence of pathologic acidic esophageal reflux.

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Table 1: Questions of FSSG*

Questions
1. Do you get heart burn?
2. Does your stomach feel bloated?
3. Does your stomach ever feel heavy after meals?
4. Do you sometimes sub consciously rub your chest with your hand?
5. Do you ever feel sick after meals?
6. Do you get heart burn after meals?
7. Do you have unusual sensation in the throat?
8. Do you feel full while eating meals?
9. Do something gets stuck while swallow?
10. Do you get bitter coming up in to your throat?
11. Do you burp a lot?
12. Do you get heart burn if you bend over?

FSSG* - The frequency of scale for the symptoms of GERD.

Symptom Scale: Each question was scored as:

Never=0,

Occasionally=1,

Sometimes=2,

Often=3,

Always=4.

If score >8 then GERD was considered to be POSITIVE.

Table 2: Los Angeles grading of GERD:

Grade A – Mucosal break = 5mm in length

Grade B – Mucosal break >5mm

Grade C – Mucosal break continuous between >2 mucosal folds

Grade D – Mucosal break > 75% of esophageal circumference.

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Table 3: Characteristics of patients having Bronchial Asthma and COPD:

	Bronchial Asthma	COPD
Frequency of GERD	40% (16/40)	30% (12/40)
% of GERD		
Age (Years)	44 ±4.5	58 ±6.3
Sex (M/F)	6/10	9/3
BMI	20.4 ±1.2	18 ±2.4
Smoking pack-years	7 ±2	12 ±3.4
Peripheral eosinophilia, %	6.4 ±2.6	3.3 ±1.4
Sputum, %		
Neutrophils	45 ±10.5	53 ±5.9
Eosinophils	34.2 ±6.7	4.5 ±4.2
Pulmonary Functions:		
FEV ₁ , L	2.1 ±2.3	1.7 ±0.98
FVC, L	3.4 ±1.9	2.8 ±1.08
FEV ₁ % predicted, %	76 ±23	53 ±21
FEV ₁ /FVC, %	67 ±25	51 ± 21
Acid regurgitation related symptoms (Questions -1, 4, 6, 7, 9, 10 and 12)	21 (52)	15 (37)
Dysmotility related symptoms (Questions -2, 3, 5, 8 and 11)	14 (35)	17 (42)

Table 4: Comparison between Asthma severity and GERD severity:

Asthma Grades	GERD				Negative	Total
	A	B	C	D		
Intermittent persistent (Grade 1)	1	0	0	0	7	8
Mild persistent (Grade 2)	0	1	0	0	8	9
Moderate persistent (Grade 3)	0	1	3	1	5	10
Severe persistent (Grade 4)	1	1	3	4	4	13
Total	2	3	6	5	24	40

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Table 5: Grading of COPD and GERD severity:

COPD Grades	GERD				Negative	Total
	A	B	C	D		
Mild (Grade 1)	-	1	-	-	10	11
Moderate (Grade 2)	1	-	1	-	9	11
Severe (Grade 3)	-	1	2	2	5	10
Very Severe (Grade 4)	-	-	2	2	4	8
Total	2	2	5	3	28	40

Figure 1: Chief symptoms of asthma patients (n = 16), COPD patients (n = 12) with GERD in relation to Regurgitation related symptoms or Dysmotility related symptoms

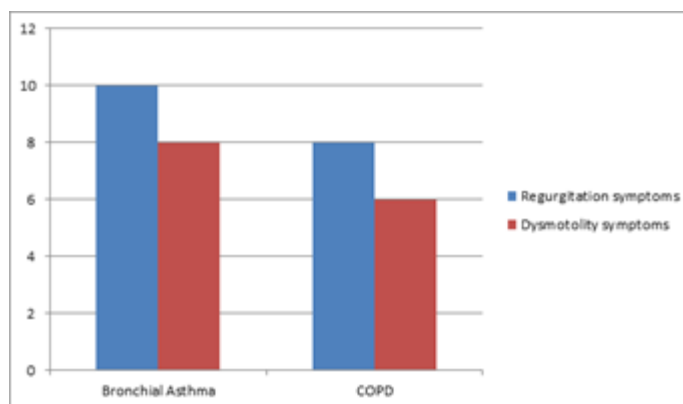


Figure 1

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