

Prevalence and Spectrum of Gastro Esophageal Reflux Disease in Bronchial Asthma

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ABSTRACT

Background: There exists a complex interplay between asthma and gastroesophageal reflux disease. Both these diseases are known to aggravate each other and amelioration of one is necessary for the control of the other. There is a paucity of studies in Indian population on this subject.

Aim: To evaluate the clinical features and the endoscopic findings of the upper gastrointestinal tract in patients with bronchial asthma.

Materials and Methods: Study was conducted at KMC group of hospitals, Mangalore in the Department of chest medicine in association with Department of gastroenterology. Subjects included 50 cases of bronchial asthma and controls were 58 non asthmatic patients with allergic rhinitis and chronic urticaria. All patients were queried about presence or absence of symptoms of upper gastro intestinal tract disorders by gastro oesophageal reflux disease (GERD) questionnaire and all the included patients underwent upper gastro intestinal endoscopy.

Results: The study showed that symptoms of gastroesophageal reflux were significantly more in asthmatics (52%) as compared to the controls (28%). The common presenting features of

gastroesophageal reflux in asthmatics were heartburn (40%) retrosternal pain (24%), nocturnal cough (18%), dyspepsia (16%) and regurgitation (14%) and the above symptoms were significantly more common in asthmatics as compared to controls. Gastroesophageal reflux disease was found to be significantly more common in the asthmatics (58%) as compared to the control group where it was present in 32.75% of the subjects. Clinical or endoscopic evidence of any upper gastrointestinal disorder was found in 68% of the asthmatics as compared to 37.93% of the controls. This difference was found to be statistically significant.

Conclusion: The study showed that gastroesophageal reflux disease was significantly more in asthmatics as compared to the controls. Upper gastrointestinal symptoms were more common in asthmatics as against controls. Clinical or endoscopic evidence of upper gastrointestinal disorder and gastroesophageal reflux disease was found in significantly higher proportion of the asthmatics as compared to the controls. Clinically silent gastroesophageal reflux disease was however seen in both control and asthmatic groups equally with a lower prevalence.

Keywords: Acid peptic disease, Difficult asthmatic, Oesophagitis, Upper GI scopy

INTRODUCTION

Gastro oesophageal reflux is an extremely common clinical problem usually manifested by heart burn and acid regurgitation. These symptoms occur daily in upto 10% of population and intermittently in 15% of otherwise healthy individuals [1]. Apart from typical manifestations, patients with gastro oesophageal reflux may have other manifestations many of which are related to the respiratory tract [2]. Difficult asthmatics need comprehensive evaluation for possible triggers and precipitants that aggravate airway inflammation and airway hyper-reactivity. One of the most important contributing factor is GERD. As the association of gastroesophageal reflux disease and other upper gastrointestinal disorders with asthma has not been done in India this study was planned in asthmatics for upper gastro intestinal disorders by clinical symptoms and endoscopy. There are three potential mechanisms whereby acid refluxing into the oesophagus induces asthma. These include a vagal mediated reflex, heightened bronchial reactivity and microaspiration of gastric acid resulting in bronchoconstriction [3]. On the other hand, physiological alterations in asthma such as increased pressure gradient between thorax and abdomen and flattening of the diaphragm due to hyperinflation and air trapping may potentially impair the anti reflux barrier and promote gastro oesophageal reflux disease [3]. Besides, bronchodilator medications particularly theophyllines increase gastric acid secretion and decrease lower oesophageal sphincter pressure and hence promote gastroesophageal reflux, however, there is debate about these findings [3].

AIM

To evaluate the clinical features and the endoscopic findings of the upper gastrointestinal tract in patients with bronchial asthma.

MATERIALS AND METHODS

Study was conducted at KMC group of hospitals, Mangalore in the department of chest medicine in association with gastroenterology department over a period of 18 months from 2008-2010. Study subjects were 50 cases of bronchial asthma. Controls were 58 non asthmatic patients with allergic rhinitis and chronic urticaria who were admitted for allergy work up. Institutional ethical committee clearance was obtained prior to the study and written informed consent was documented from the study subjects.

Inclusion criteria

Cases of bronchial asthma between the age group of 15 years to 75 years were included. Asthma was diagnosed on basis of clinical symptoms, signs and pulmonary function tests showing airway reversibility of 12 percent and 200 ml in Forced expiratory volume in 1 second (FEV1).

Exclusion criteria

- 1) COPD patients.
- 2) Asthmatic patients taking any medications known to cause upper gastro intestinal adverse effects like oral steroids and theophyllines.

- 3) Active and ex-smokers with 10 pack years of smoking and above.
- 4) Asthma associated with other systemic diseases like COPD, ischaemic heart disease.
- 5) Cardiac asthma patients.
- 5) Patients with allergic bronchopulmonary aspergillosis.
- 6) Patients requiring intensive care.
- 7) Patients on H2 receptor antagonists or proton pump inhibitors presently or within last 4 weeks.
- 8) Patients on NSAIDS.
- 9) Patients unfit for endoscopy e.g. gross congestive cardiac failure, recent myocardial infarction and those refusing endoscopy.

All patients were queried about presence or absence of symptoms of upper gastro intestinal tract disorders by gastroesophageal reflux disease (GERD) questionnaire. For clinical features of bronchial asthma we used the International Union against Tuberculosis and Lung Disease (IUATLD) asthma questionnaire that has been used and validated in epidemiological studies [4].

All the patients were subjected to baseline investigation which included haemoglobin, total and differential blood counts (TC & DC) and erythrocyte sedimentation rate (ESR), total serum Immunoglobulin E (IgE), pulmonary function tests with post bronchodilator study, chest X- ray, X-ray paranasal sinuses (PNS) and ECG. All the included patients underwent upper gastro intestinal endoscopy.

Endoscopically the following features were studied

1. Presence or absence of erosive oesophagitis using Los Angeles' System which categorizes mucosal injury as grade A, B, C, D.
2. Presence of hiatus hernia.
3. Presence of Barrett's metaplasia.
4. Presence of stricture.
5. Presence of gastric or duodenal erosion.
6. Any other positive findings.

STATISTICAL ANALYSIS

Data analysis was done using Chi-square test with Yates correction and Gaussian test

RESULTS

Fifty asthmatics proven by clinical history and pulmonary function tests were studied. There were 26 males and 24 females. Fifty eight non asthmatic patients taken from the chest ward comprising of 32 males and 26 females served as controls. Most of the subjects in both, case and control groups were found to be in the age group of 20-39 years. The mean age was calculated to be 37.94 ± 15.81 years for the cases and 37.51 ± 15.51 years for the controls. Both the study groups were found to be matched for age and sex.

Symptoms of gastro oesophageal reflux were found to be present in 52% of asthmatics and 28% of the controls. Chi-square test was done to analyse the statistical significance of presence of GERD symptoms in asthmatics. This difference was found to be statistically significant. The most common symptom of gastroesophageal reflux among both groups was heart burn and it was significantly more commonly prevalent among the asthmatics (40% versus 18.9%, $p=0.016$ significant). Among the asthmatics, other predominant symptoms suggestive of gastroesophageal reflux were retrosternal pain (24%), nocturnal cough (18%), dyspepsia (16%) and regurgitation (14%). These symptoms were also significantly more common in the asthmatics compared to the controls ($p < 0.05$) as shown in [Table/Fig-1].

Abnormal findings on upper GI scopy were seen in 42% of asthmatics as compared to 20.83% of controls (Chi-square = 8.04, $p < 0.01$ highly significant). The findings on upper gastrointestinal endoscopy are summarized in [Table/Fig-2]. Oesophagitis was found in 14% of the cases as compared to 5.17% of the controls ($p = 0.213$). Out of the 7 asthmatics having oesophagitis on endoscopy, 2 presented with Grade A, 4 with grade B and 1 with Grade C oesophagitis. Hiatus hernia was found in 8% of asthmatics as compared to 5.2% in controls. This difference was found to be statistically insignificant ($p=0.552$). Endoscopic evidence of gastroesophageal reflux disease (oesophagitis or hiatus hernia) was found in 20% of asthmatics as compared to 10.34% of the controls. Of the 10 asthmatics having gastroesophageal reflux on endoscopy, 7 were found to have symptoms of GERD. The common presenting symptoms in this subgroup were heart burn and nocturnal cough (71.4%), dyspepsia and abdominal bloating (42.8%) and retrosternal pain (28.5%). Gastroduodenal area peptic mucosal damage (gastric or duodenal erosions or ulcerations) was found in 16% of the cases as compared to 8.62% of the controls which was statically not significant.

S No.	Symptoms	Case n=50		Control n=58		Z
		No. of patients	Percentage %	No. of patients	Percentage %	
1.	Heart burn	20	40	11	18.9	2.409 $p=0.016$ sig
2.	Regurgitation	7	14	1	1.7	2.429 $p=0.0151$ sig
3.	Retrosternal pain	12	24	4	6.8	2.494 $p=0.0126$ sig
4.	Odynophagia	6	12	2	3.4	1.692 $p=0.0906$ ns
5.	Dyspepsia	8	16	3	5.2	1.85537 $p=0.0636$ ns
6.	Abdominal bloating	8	16	2	3.4	2.243 $p=0.0248$ sig
7.	Nocturnal cough	9	18	3	5.2	2.115 $p=0.0344$ sig
8.	Nausea	4	8	1	1.7	1.547 $p=0.122$ ns
9.	Hoarseness	3	6	0	0	1.897 $p=0.585$ ns
10.	Water brush	5	10	0	0	2.466 $P=0.0137$ sig

[Table/Fig-1]: Comparison of various presenting gastrointestinal symptoms

S No.	Endoscopy finding	Case n=50		Control n=58		Z
		No. of patients	Percentage %	No. of patients	Percentage %	
1.	Grade A oesophagitis	2	4	2	3.4	0.15 $p=0.879$ ns
2.	Grade B oesophagitis	4	8	1	1.7	1.543 $p=0.122$ ns
3.	Grade C oesophagitis	1	2	0	0	0 $p=1$ ns
4.	Grade D oesophagitis	0	0	0	0	-
5.	Hiatus hernia/ prolapse	4	8	3	5.2	0.595 $p=0.552$ ns
6.	Gastric erosions	6	12	3	5.2	1.28 $p=0.201$ ns
7.	Duodenal erosions	2	4	2	3.4	0.15 $p=0.879$ ns
8.	Candidiasis	2	4	0	0	1.537 $p=0.124$ ns
9.	Others	3	6	0	0	1.895 $p=0.0585$ ns

[Table/Fig-2]: Upper gastrointestinal endoscopy findings in asthmatics and controls

Acid peptic disease (gastroesophageal reflux/hiatus hernia/gastric or duodenal erosions) by upper gastrointestinal endoscopy was found to be present in 34% of asthmatics as compared to 17.24% of the controls [Table/Fig-3] which was statistically significant.

Gastroesophageal reflux disease, defined as presence of symptoms or / and evidence of gastroesophageal reflux on upper gastrointestinal endoscopy was found in 58% of the asthmatics as compared to 32.75% of the subjects in the control group, a statistically significant finding ($p < 0.01$) as depicted in [Table/Fig-4]. Of the 29 asthmatics having gastroesophageal reflux 62% had only symptoms of GERD, 10.34% had only endoscopic evidence of the disease while 24.13% had both clinical and endoscopic evidence of gastroesophageal reflux.

Clinical or endoscopic evidence of any upper gastrointestinal disorder was found in 68% of the asthmatics as compared to 37.93% of the controls ($p < 0.01$) as in [Table/Fig-5].

	Yes	No	Total	Percentage
Asthmatics	17	33	50	34%
Controls	10	48	58	17.24%
Total	27	81	108	

[Table/Fig-3]: Subjects having acid peptic disease on endoscopy
Chi-square = 4.022 $p=0.0449$ significant

	Yes	No	Total	Percentage
Asthmatics	29	21	50	58%
Controls	19	39	58	32.75%
Total	48	60	108	

[Table/Fig-4]: Patients having GERD by symptoms and/or Endoscopy
Chi-square = 6.928 $p=0.0085$ highly significant

	Yes	No	Total	Percentage
Asthmatics	34	16	50	68%
Controls	22	36	58	37.93%
Total	56	52	108	

[Table/Fig-5]: Patients having any upper gastrointestinal disease by symptoms and / or Endoscopy
Chi-square = 9.724 $p=0.0018$ highly significant

Clinically silent gastroesophageal reflux disease (evidence of gastroesophageal reflux on endoscopy in absence of any symptoms) was found in 8.33% of the asymptomatic asthmatics compared to 7.14% of the asymptomatic controls where as clinically silent gastroduodenal area peptic mucosal damage was seen in 16.66% of asymptomatic asthmatics and 7.14% of the asymptomatic controls both of which were not of statistical significance. Clinically silent acid peptic disease (endoscopic evidence of gastroesophageal reflux/hiatus hernia/gastric or duodenal erosions in absence of clinical features), was found to be present in 25% of all asymptomatic asthmatics as compared to 14.2% of the asymptomatic controls while evidence of any gastrointestinal abnormality on endoscopy of asymptomatic patients was found in 33.33% of asymptomatic asthmatics and 14.2% of asymptomatic controls, both of which were statistically insignificant. In the study group of asthmatics, 74% were having mild asthma while 20% and 6% were found to have moderate and severe asthma respectively. In the subgroup of asthmatics that were diagnosed as having GERD, 68.96% were having mild asthma while 27.5% and 3.44% were found to have moderate and severe asthma respectively.

DISCUSSION

For decades astute clinicians have noted that heavy meal and beverage before reclining may lead to worsening of nocturnal asthma. There was a clinical impression that casual relationship between GERD and asthma existed and some asthma cases were cured by fundoplication surgery [5]. In the present study we

evaluated the clinical features and the endoscopic findings of the upper gastrointestinal tract in patients with bronchial asthma to unearth the extent of interplay between the asthma and GERD.

In our study, it was seen that 52% asthmatics and 28% of controls had one or more symptoms of gastro oesophageal reflux and this difference was found to be significant. A study by Perrin-Fayolle et al., found symptoms of reflux in 65% of 150 consecutive asthmatics [6]. In another study, Kiljander and Laitinen reported GERD symptoms in 51% of 90 asthmatics studied [7].

In our study, common abdominal symptoms found in asthmatics were heartburn (40%), retrosternal pain (24%), nocturnal cough (18%), abdominal bloating and dyspepsia (16%), regurgitation (14%) and odynophagia (12%). These symptoms were also more common in the case group compared to the controls. The difference was found to be statistically significant for heartburn, retrosternal pain, nocturnal cough, dyspepsia and regurgitation. A study of 109 asthmatics and 135 controls in a questionnaire-based, study found that 77% of the asthmatics had heartburn, 55% had regurgitation, and 24% had difficulty with swallowing [8]. Another study reported that 72% of 189 consecutive asthmatics had heartburn, regurgitation and dysphagia were present in 45%, and 22% of asthmatics compared with, 30%, and 5% of controls [9]. This difference in perceived symptomatology and intensity in other studies as compared to our study was difficult to explain. It may be due to difference in diet, body mass index, patient awareness and smoking habits between Indian and western populations.

In the present study, abnormal findings on upper GI scopy were seen in 42% of asthmatics as compared to 20.83% of controls while either clinical or endoscopic evidence of any upper gastrointestinal disorder was found in 68% of the asthmatics as compared to 37.93% of the controls both of which were statistically highly significant. Oesophagitis was seen in 14% of the asthmatics as compared to 5.17% of the controls. Hiatus hernia was found in 8% of asthmatics as compared to 5.17% in controls. Endoscopic evidence of gastroesophageal reflux disease (oesophagitis or hiatus hernia) was found in 20% of asthmatics as compared to 10.34% of the controls. Even though the above findings were seen more commonly in asthmatics as compared to controls, the differences were statistically insignificant. Other findings on endoscopy among the asthmatics were oesophageal polyp, oesophageal diverticuli and gastric polyposis which were seen in one patient each. To the best of our knowledge, these incidental findings have not been reported so far in relation to asthma. Oesophageal candidiasis was observed in 2 of the 50 asthmatics who were subjected to endoscopy. Both these patients who presented with candidiasis were on long term inhaled corticosteroids. In a similar study to determine whether gastroesophageal reflux in asthmatics results in oesophagitis, endoscopy and oesophageal biopsy were performed on 186 consecutive adult asthmatics [10]. Oesophageal erosions or ulcerations as seen on endoscopy were present in 39% of consecutive asthmatics and 13% had Barrett's oesophagus. Also, 58% of asthmatics were found to have a hiatus hernia [8]. A study by May et al., of 28 patients with severe asthma who were routinely examined with upper gastrointestinal (UGI) x-ray films 64% were found to have hiatus hernia and 46% were found to have demonstrable gastroesophageal reflux [11]. A higher percentage of asthmatics having oesophagitis, hiatus hernia and Barrett's oesophagitis as compared to our study is perhaps due to the fact that only severe asthmatics were included in the mentioned study while our study also had asthmatics with mild to moderate disease.

In our study, gastroesophageal reflux defined as any abnormal reflux parameter, be it clinical or endoscopic was found in 58% of the asthmatics as compared to the control group where it was present in 32.75% of the subjects ($p < 0.01$). Sontag et al., in three studies conducted in the same centre found that 90% of asthmatics have at least one parameter needed to be considered

as having gastroesophageal reflux disease (GERD) [9,10,12]. reflux symptoms, oesophageal mucosal disease, or abnormal acid reflux. This difference in prevalence of GERD in the two studies may be due to the fact that acid reflux using pH monitoring probes has not been done in our study.

Clinically silent gastroesophageal reflux disease (evidence of gastroesophageal reflux on endoscopy in absence of any symptoms) was found in 8.33% of the asymptomatic asthmatics compared to 7.14% of the asymptomatic controls ($p=1$ not significant). In their study, Irwin et al., reported that GERD was clinically silent in 24% of asthmatics [13]. Harding et al., also examined the prevalence of gastroesophageal reflux in 26 asthma patients without reflux symptoms using oesophageal manometry and 24-hour oesophageal pH testing [14]. The prevalence of abnormal 24-hour oesophageal pH tests in asthma patients without reflux symptoms was 62%. A lower incidence of occurrence, of clinically silent gastrointestinal disease in our study may be due to higher sensitivity of pH tests in detecting reflux which was not done in our study. Clinically silent gastroduodenal area peptic mucosal damage was seen in 16.66% of asymptomatic asthmatics and 7.14% of the asymptomatic controls ($p > 0.05$). Clinically silent acid peptic disease was present in 25% of all asymptomatic asthmatics as compared to 14.2% of the asymptomatic controls ($p > 0.05$). Evidence of any gastrointestinal abnormality on endoscopy of asymptomatic patients was found in 33.33% of asymptomatic asthmatics and 14.2% of asymptomatic controls which was not significant.

In our study, gastroduodenal area peptic mucosal damage (gastric or duodenal erosions or ulcerations) was found in 16% of the cases as compared to 8.62% of the controls ($p=0.2399$, not significant). The commonest site of peptic damage in our study was the stomach (66%). Cherniavskaia et al., from Russia, examined 260 patients with bronchial asthma, gastroduodenal area peptic erosions were revealed in 26.9% [15]. The commonest site of an ulcerative process was in the duodenum (90%) and it was associated with reflux oesophagitis in 84.1% of the cases. In two more studies at the same centre, gastroduodenal erosions were endoscopically diagnosed in (22.5%) [16] and (21.9%) [17] of the studied asthmatic patients. However, the difference in the most common site of erosions was difficult to explain. It may be due to difference in dietary habits, alcoholic and beverage consumption habits between Indians and Russians. There is paucity of data of GERD and asthma in the adult Indian population though there are numerous studies in paediatric age group. One study of GERD in difficult asthmatics showed the prevalence to be as high as 70% and endoscopy, oesophagitis was documented in 46.4% of cases [18].

LIMITATION

Some of the findings like clinically silent gastroesophageal reflux disease and gastroduodenal area peptic mucosal damage were prevalent without clinical significance in both the groups. This could be due to the fact that the control group in our study were not normal subjects but patients who were non asthmatic but with allergic rhinitis and chronic urticarial. This in fact is also one

of the limitations of our study. The other limitation is the absence of 24-hour oesophageal pH tests which has probably resulted in lower prevalence of silent GERD in our study as compared to other studies.

CONCLUSION

The study showed that symptoms of gastroesophageal reflux were significantly more in asthmatics as compared to the controls. The upper gastrointestinal symptoms and endoscopic evidence of gastroesophageal reflux disease (oesophagitis or hiatus hernia) were more common in asthmatics as against controls. Gastroduodenal area peptic mucosal damage on endoscopy was found more common in asthmatics as compared to the controls with the stomach being the most common site of ulceration. Clinically silent gastroesophageal reflux disease was also seen in both control and asthmatic groups equally with a lower prevalence. As asthma and GERD have significant association with clinical, pathologic and therapeutic implication careful routine enquiries must be made by the physicians in asthmatics for GERD symptoms. Even with no history of GERD, one must be alert for the difficult asthmatic with silent reflux. Identification of the exact GERD trigger and aggressive medical treatment with lifestyle modification significantly improves asthma control.

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