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Upper GI EndoscopicManifestations in Bronchial Asthma

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ABSTRACT

AIM :1.To document the various upper gastro-intestinal endoscopic as well as histologic findings of lower esophagus in patients with bronchial asthma.2.To correlate the association with duration and severity of bronchial asthma.3.To document the presence of NERD (Negative Endoscopic Reflux Disease) in patients with bronchial asthma. 4.Endoscopic / histological correlation of esophagus status in patients with bronchial asthma. **MATERIALS AND METHODS:. Inclusion Criteria** :Thirty patients who were diagnosed to have bronchial asthma and having regular follow up in thoracic medicine out patient clinic were included in the study.. **Exclusion Criteria** patients with systematicIllnesses Hypertension, Diabetes Mellitus, Chronic renal failure, Rheumatological diseases. and patients with habits of smoking alcoholism, tobacco ingestion, NSAID intake.Patients at extremes of age.(<13 &>60)Pregnancy, acute exacerbation of symptoms. Routine investigations were taken along with Pulmonary Function Tests. Upper gastro-intestinal endoscopy was done with three biopsy samples were taken for each patient from the gastro oesophageal junction . Histological assessment of the samples were done. **Results:** Various parameters were tabulated and analysed. Out of the 30 paitents. 15 were male (50%) and 15 were female (50%). Of the 30 patients studied 17 had abnormal endoscopy findings thus comprising of 56.67% . Out of the 15 males studied 10 had abnormal findings (66.67%) and out of the 15 female, 7 had abnormal finding (46.67%).. Reflux esophagitis was found in 12 patients (40%) and pulled up gastro-oesophageal junction consistent with hiatus hernia was found in 2 patients (6.67%). **Conclusions:** Prevalence of Reflux esophagitis is more common in asthmatics reconfirmed in this study. Reflux esophagitis is proportional to the duration and severity of bronchial asthma. This study established the Importance of histopathology in negative endoscopic reflux.

KEYWORDS : .

INTRODUCTION: Bronchial asthma is of the diseases that are known to mankind for centuries. Asthma could well be considered an epidemic given the number of people involved. According to WHO, more than 150 million people were afflicted with asthma worldwide resulting in 1,80,000 deaths annually[1] In India the prevalence of 'asthma' was reported as 2.4% in a population study on 73,605 individuals conducted simultaneously at four major centers in India [2] Many of the intrathoracic and extra thoracic condition masquerade and complicate or aggravate bronchial asthma. One among those conditions and is of much curiosity is the gastro intestinal problem that commonly aggravate asthma – gastroesophageal reflux disease. Various studies have been conducted to find out the association of the gastro-esophageal reflux disease with asthma.The latest concept is that*"acid in the lower oesophagus due to reflux can provoke bronchospasm reflexly via vagus nerve, and this response is more pronounced in patients with bronchial asthma and reflux"*[3]This reflux theory is well proved beyond doubt as the most accepted one for this association and so any patient who does not respond to routine asthma medications, or having symptoms of gastro-oesophageal reflux should be evaluated for the same[4]The endoscopic documentation of reflux esophagitis is more relevant because it indicates sequelae of long standing and moderate to serve reflux disease in most of the occasions. As there are only limited studies conducted to establish this association we undertook this study to screen the asthmatic patients with upper gastrointestinal endoscopy and histology to document the reflux associated changes and other finding in these patients.

AIM:1. To document the various upper gastro-intestinal endoscopic as well as histologic findings of lower esophagus in patients with bronchial asthma.2.To estimate the prevalence and magnitude of the reflux associated changes in association with bronchial asthma.3. To correlate frequency of association with duration of bronchial asthma.4.To correlate the frequency of association with severity of bronchial Asthma.5.To document the presence of NERD (Negative Endoscopic Reflux Disease) in patients with bronchial asthma. 6.Endoscopic / histological correlation of esophagus status in patients withbronchial asthma.

MATERIALS AND METHODS: The study was conducted in Government Mohan Kumaramangalam Medical college Hospital, Salem, during the period of February2008 to September 2009.and protocol of the study was submitted to the ethical committee of the hospital and the approval was obtained .Thirty patients who were diagnosed to have bronchial asthma and having regular follow up in thoracic medicine out patient clinic were included in the study. **Inclusion Criteria :**Patients who had been diagnosed to have bronchial asthma earlier by history and pulmonary function tests and were on regular follow up. Patients who do not have satisfactory control of the symptoms in spite of regular treatment. Patients who experience frequent nocturnal episodes of asthmatic attacks.Patients who have symptoms of gastro-oesphageal reflux disease. For thesepatients , during exacerbation of symptoms, spirometry is performed both before and after bronchodilator administration. A 12% increase (calculated from prebronchodilator values) and a 200ml increase in either FEVI or FVC defines a positive bronchodilator response and indicates reversibility of obstruction. **Exclusion Criteria** patients with systematic Hypertension, Diabetes Mellitus, Chronic renal failure, Rheumatological diseases. patients who have other cardio respiratory disease like pulmonaryTuberculosis, Chronic obstructive Pulmonary Diseases Coronary artery disease, Congestive Cardiac Failure, Valvular Hear disease etc. Patients with habits of smoking alcoholism, tobacco ingestion, NSAID intake.Patients at extremes of age.(<13 &>60)Pregnancy, acute exacerbation of symptoms.The patients were admitted in medical wards and detailed history taking and clinical examination was carried out. **Laboratory Investigations:** Routine investigations were taken along with Pulmonary Function Tests. In this study ,**GINA (Global Initiative for Asthma) classification of Asthma Severity** is used to classify patients.Upper GI endoscopy is carried out in all the patients using PENTEX VIDEO ENDOSCOPY SYSTEM. Endoscopic rapid screening of upper GI tract Three biopsy samples were taken for each patient from the gastro oesophageal junction . Histological assessment of the samples were done to find out the prevalence of histopathologicchanges..Basal cell thickness, Length of papillae, and Dysplasia In situ (DIS) were semiquantitatively scored as 0 (absent), 1 (mild) and 2 (marked) on hematoylin- eosin stained slides

obtained from each biopsy site.

Results: *Study population* : 15 males and 15 females. *Age Group*: Less than 20yrs :4; 20-29yrs : 6; 30 -39yrs :7 ; 40-49 yrs: 8 ; Above 50: 5 . *Abnormal Endoscopy findings*: 17 Male:10 ; Female: 7 . Less than 20yrs : 1; 20-29yrs :4; 30 -39yrs :5 ; 40-49 yrs:4 ; Above 50:3. Abnormal Endoscopy findings and duration of illness: Less than 5 years : Male 3 ; female 2 . 5years and above : male 7 ; female 5. Incidence of abnormalities Number . Of patients – 30 **:** Grade I esophagitis :11 ; Grade II:1 ; GradeIII:0 ; Candidiasis:1 ; Antral gastritis:5 ; Hiatus Hernia:2 and Duodenitis :2.Endoscopy Findings: Abnormal: 12 ; normal :8 ; Histopathology : positive 20; Negative :10**.**Abnormal endoscopy findings vs severity of asthma: Mild and moderate persistent asthma :21 with Reflux associated lesion: 13. Severe persistentasthama : 9 with Reflux associated lesion:4; Reflux esophagitis versus severity of asthma : Mild and moderate: 7 out of 21 (33.33%) ; Severe persistent: 9 out of 5 (55.55%).Comparative analysis Prevalence of reflux oesophagitis in asthmatics**:** S.J.Sontag et al: 39% . Kiljander et al: 38% . Our study:40%

Reflux esophagitis versus duration of illnessEndoscopy positivity versus basal cell thickness score

Duration of Asthma	Total Number	Reflux Associated Lesion
Less than 5 years	13	4
More than 5 years	17	8

No. of Patients with positive Endoscopy	Basal Cell Thickness Score	No.of patients
12	0	0
	1	8
	2	4

Endoscopy Negativity Versus Basal Cell Thickness Score Endoscopy Positivity versus Length of Papillae

No. of Patients with Negative Endoscopy	Basal Cell Thickness Score	No.of patients
18	0	0
	1	5
	2	2

Endoscopy Negativity Versus Papillary ElongationEndoscopy Invasion Positivity Versus Eosinophil

No.of Patients with negative Endoscopy	Papillary Elongation Score	No.of patients
18	0	0
	1	6
	2	0

No. of patients with Positive Endoscopy	Eosinophil Invasion Score	No.of patients
12	0	0
	1	0
	2	12

Endoscopy Negativity Versus Eosinophil Invasion Endoscopy Positivity Versus Neutrophil Invasion

No . Of patients with Negative Endoscopy	Eosinophil Invasion Score	No. of patients
18	0	0
	1	0
	2	8

No.of patients with positive Endoscopy	Neutrophil Invasion Score	No.of patients
12	0	0
	1	0
	2	12

Oesophageal Muscosal Status

	Sontag et al.	This Study
Normal (No oesophagitis/No Barrett's)	57.5%	33.33%
Oesophagitis without Barrett's	29.6%	66.67%
Barrett's without Oesophagitis	3.2%	Nil
Barrett's with Oesophagitis	9.7%	Nil

Clinical Stage	Endoscopic Oesophagitis		Histopathologic Oesophagitis	
	Tug et al	This study	Tug et al	This study
Mild &Moderate Persistent (n=21)	27%	33.3% (n=7)	55%	61.9% (n=13)
Severe Persistent (n=9)	18%	55.5% (n=5)	36%	77.7% (n=7)

Endoscopy Vs asthma symptoms and clinical stage - Comparative Analysis

	Endoscopic Oesophagitis		Histopathologic Oesophagitis	
	Tug et al	This study	Tug et al	This study
Nocturnal attacks + (n = 12)	24%	58.33% (n=7)	47%	75% (n=9)
Nocturnal attacks - (n=18)	17%	27.7% (n=5)	35%	61.1% (n=11)

HISTOPATHOLOGICAL FINDING : In this study, we included the histopathological correlation of reflux oesophagitis. Histopatho logical changes consistent with GERD were present in all the 12 patients with refluxoesophagitis.Out of the 18 patients who were endoscopically negative for reflux esophagitis , 8 had findings consistent with GERD. (5 male : 3 female) (44.4%).Tug et al conducted a study on the association between severity and stage of asthma symptoms in a distinctive period and gastroeso phagealreflux[5]. Histopathological diagnosis was based on the definition given by Ismail – Beigi et al In this study, the prevalence of Endoscopic oesophgitis is 33.3% (n=7) and histopathologica loesophagitis is 61.9% (n=13) in patients with mild and moderate persistent asthma.In patients with severe asthma, the endoscopic prevalence is 55.5% (n=5) and histopathologic prevalence is 77.7%(n=7). In patients without nocturnal attacks the prevalence is 27.7% (n=5) and 61.1%(n=11) respectively. The prevalence of both endoscopic and histopathological reflux is higher in higher in patients with nocturnal symptoms. But these values are higher compared to study by Tug et al.SimilarlyKiljander et al conducted a study about the prevalence of GERD in adult asthmatics in which they used 24 hour pH metry as the standard. The prevalence of reflux oesophagitis in their study was 36%.[6] Reflux oesophagitis is the sequelac and indicator of long standing and moderate to severe gasto-oestophagealreflux. There is significant difference present in the prevalence of reflux esophagitis between males and females. Out of the 15 males 7 had reflux esophagitis (46.67%) whereas in females 5 out of 15 had reflux esophagitis (33.33%).The prevalence of reflux esophagitis is higher in long standing and severe asthmatics. In this study reflux oesophagitis was present in 23.33% of patient with less than 5 years of disease and 33.3% of patients with 5 years or more of disease durtion. Similarly out of the 21 patients with mild and moderate persistent asthma 33.33% (n=7) had reflux oesophagaitis whereas out of the 9 patients with severe persistent asthma 55.55% (n=5) had reflux esophagitis.Thus this study clearly indicates that reflux esophagitis is a common association in bronchial asthma patients with long standing and / or degree of disease. In our study the prevalence of NERD (Negative Endoscopic Reflux Disease) is 44.44%. which is statistically significant.

DISCUSSION: Out of the 30 patients, 17 had abnormal endoscopy finding (56.67%).Out of the 15 males studied, 10 had abnormal findings (66.67%).Out of the 15 females studied , 7 abnormal findings (46.67%).There is a slightly higher prevalence of abnormal endoscopy findings in males with a ratio of 1.43:1. Abnormal endoscopy findings were not well correlated with the age group of

the patients. But it has correlation with the duration of the illness.Out of the 13 patients with disease duration less than 5 years , 5 had abnormal findings (38.46%), where asot of the 17 patients with disaease duration more than 5 years , 12 had abnormal findings (70.5%).Among abnormal findings , reflux oesophagitis stands first with pervalence of 40% (n=12) among which Grade I oesophagitis is 36.67% (n=11) and Grade II is 3.3% (n=1).Reflux oesophagitis was slightly more prevalent in males than in females with a ratio of 1.4:1.Out of the 15 males , 7 had reflux oesophagitis (46.67%) & out of the 15 females 5 had reflux oesophagitis (33.33%).Pulled up gastro oesophageal junction consistent with hiatus hernia was found in 2 patients (6.67%). Out of this one had reflux oesophagitis. Prevalence of reflux oesophagitis was slightly higher in longstanding asthmatics. Out of the 13 patients with disease less than 5 years 4 had reflux oesophagitis (30.8%). Out of the 17 patients with disease duration more than 5 years, 8 had reflux oesophagitis (41.18%).Reflux oesophagitis was slightly more prevalent in diseases of severe degree. Out of the 21 patients with mild and moderate persistent asthma , 7 had reflux oesophagitis (33.33%). where as out of the 9 patients with severe persistent asthma , 5 had reflux oesophagitis (55.55%).Histopathological findings consistent with GERD were present in all the patients with reflux oesophagitis. Out of the 18 patients who do not had reluxoesophagitis (NERD), 8 patients had histopathological findings consistent with GERD (44.44%) (NERD – higher percentage in this study). In patients with mild and moderare persistent asthma, the pervalence of endoscopic is 33.3% (n=7) and histopathologicoe sophagitis is 613.9% (n=13).In patients with severe persistent asthma, the prevalence of endoscopic oesophagitis is 55.5% (n=5) and histopathologicoesophagitis is 77.7%(n=7).In patients with nocturnal attacks, the prevalence of endoscopic oesophagitis is 58.3% (n=7) and histopathologicaloesophagitis is 75%(n=9). In patients without nocturnal attacks, the prevalence is 27.7% (n=5) and 61.1% (n=11) repectively.Total prevalence of reflux oesophagitis (Endoscopy And Histology Wise) is 66.67% (n=20).OTHER LESIONS:Hiatus hernia was present in only 2 patients (6.67%) in this study. Out of these , one patient had reflux esophagitis. But the western literature quotes the presence of hiatus hernia to the tune of upto 45% in various series. Oesophageal candidiasis was present in only one patient which was statistically insignificant. 5 of the 30 patients had Antral gastritis (Male 3: Female :2) and two male patients had gastric ulcer (6.67%). Duodenitiswas present in 3 cases (2 female and one male). These disorders could be explained by the hyperacidity by the stress due to the disease or steroid intake.

This study was primarily aimed at finding out the prevalence of reflux associated changes by upper gastrointestinal endoscopy.. Since reflux esophagitis is one of the conditions which hinders with effective asthma treatment, we selected the cases who do not have adequate control of asthma in this study. Thorough questionnaire was put to evaluate the gastrointestinal symptoms. Gastro-oesophageal reflux disease is one of the conditions which triggers or worsens the asthmatic condition and hinders with the effective treatment. Physiological reflux , though produces bronchocon striction by reflex vagal stimulation, is not strong enough to produce symptoms of asthma in normal individuals. Acid reflux triggers asthmatic attacks or worsens the symptoms of asthma in the asthmatic patients. This effect is more pronounced in the patients have reflux esophagitis.

S.J. Sontag, T.G. Schnell and co-workers conducted endoscopic evaluation in a asthmatic patients who attended the asthma clinic. In their study 39% of the patients with asthma had esophagitis of Barrett's oesophagus or both. There was no difference in the oesophageal mucosal status between asthmatics who required and those who did not require bronchodilators. 58% of asthmatic had a hiatal hernia. They concluded that esophagitis is common and independent of the use of bronchodilator therapy in asthmatics[7]Sontag et al reported a prevalence of 39% of oesophafitis and / or Barrett's oesophagus in their study of asthmatic patients. In this study of 30 patients, 7 males and 5 females had reflux oesophagiti. (23.3% and 16.67% respectively). Comprising a total of 40% of oesophagitis in this study.Studies by Indian authors Agarwal et al also reported similar range of prevalence of reflux oesophagitis in asthmatic patients.

Conclusion:

The finding that prevalence of Reflux esophagtits is more common in asthmatics reconfirmed in this study.Refluxesophagitis is present in significant proportion of bronchial asthma patients of long standing illness and more severe disease pattern. Since presence of reflux esophagitis worsens the disease pattern and hinders with effective control , these patients do not have satisfactory control of their asthma symptoms.This study established the Importance of histology in negative endoscopic reflux. Significant number of patients with negative endoscopy had histopathological evidence of esophagitis, thereby proving the role of biopsy in GERD..

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