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Original Research Article

Association of gastro esophageal reflex with chronic asthma and its significance: a prospective study

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ABSTRACT

Background: Many studies have reported that gastro esophageal reflux is significantly more common in asthmatics than in control populations and this appears to apply particularly in childhood. To study the incidence of gastro esophageal refluxes in children which chronic asthma. To identity the clinical characteristic in children with chronic asthma and GER, which would predict reflux, related asthma?
Methods: It is a prospective study of association of GER and chronic asthma using Radio nuclide scintigraphy carried at General pediatric in-patient wards of Niloufer hospital, Hyderabad. A Total of 50 patients with chronic asthma and 15 healthy children were evaluated.
Results: Our study showed an incidence of Gastro Esophageal Reflux (GER) in 42% of chronic asthmatic children. High incidence of reflux (47.6%) under 4 years of age. No significance difference in the incidence of GER in children with seasonal verus Non-Seasonal asthma. About 50% of children with GER had no symptoms i.e. they had silent reflux. Nocturnal symptoms were significantly higher in asthmatic children with Ger (54.8%) than asthmatic children without GER (21%). Children with reflux related asthma suffered more morbidity in terms of recurrence of attacks, severity of chronic asthma (moderate persistent) and sleep disturbance as compared to children with no reflux. Presence of atopic signs was significantly higher in patients with asthma without GER.
Conclusions: GER should be considered as a potentially important contributing factor in any patient with poorly controlled asthma. The asthmatic patient most likely to experience measurable benefit from anti-reflux therapy is the patients with significant nocturnal asthma and who have symptoms of both asthma and of reflux.

Keywords: Chronic asthma, Gastro esophageal reflex, Prospective study

INTRODUCTION

Bronchial Asthma is a heterogeneous and multifactorial syndrome in which reversible airways obstruction may result from activation of different mechanisms. In many patients with such reactive airways, specific causative or provocative factors e.g. Extrinsic allergens, physical agents, chemical irritants, and inhaled or ingested biochemical stimuli can be identified. In others, however, such specific agents are not evident. A number of studies have suggested that in some patients with asthma, Gastro Esophageal Reflux (GER) May be causally related to the

reactive airway condition, and that in others, it is the trigger causing airways to react.[1]

Many studies have reported that gastro esophageal reflux is significantly more common in asthmatics than in control populations and this appears to apply particularly in childhood.[2]

The role gastro esophageal reflux in pathogenesis of bronchial asthma is controversial for bronchial asthma itself can promote gastro esophageal reflux. The situation is further compounded by the observation that the medications used in asthma may also aggravate gastro esophageal reflux. Despite all these controversies, there are reports that medical and surgical treatment of gastro esophageal reflux may improve bronchial asthma significantly.[3]

Thus, gastro esophageal reflux is an important unrecognized provoking factor in recurrent asthma in children and therefore there is a need for evaluation of gastro Esophageal Reflux in such patients as the therapy of reflux can significantly lower the morbidity in selected patients with asthma.[4] The paucity of studies on this subject from India, especially in children, led to the present investigation.

In our study, we evaluated the association of gastro esophageal reflux bronchial asthma, the characteristics in children with chronic asthma and gastro esophageal reflux that would enable a physician to recognize these patients clinically.

METHODS

Our study is a cross sectional study conducted over a period of 1 year from June-2000 to July 2001.

Our study recruited 50 children with chronic asthma. All children with greater than 3 episodes of reversible bronchspasm I.e. acute onset of wheezing and airway obstruction that decrease after therapy were defined as having chronic bronchial asthma and were included in the study. These children were taken up for study 2 weeks after the acute phase of illness had subsided and it was made sure that none of them was on Methylxanthine group of drugs at the time of study.

History regarding the age of onset of 1st episode, recurrence of symptoms, nocturnal cough, nocturnal exacerbation of wheeze. Family history of asthma, role of weather change on asthma and also atopic symptoms like allergic rhinitis, allergic conjunctivitis and atopic dermatitis were elicited.

Reflux symptoms like vomiting, feeding difficulties, retrosternal pain was elicited either from the patient or from the mother. Height, weight and mid arm circumference of all children were recorded. Chest X-ray and peripheral blood smear for absolute eosinophil count was done in all patients.

Exclusion criteria

Subjects with pulmonary tuberculosis, Emphysema, chronic bronchitis bronchiestasis, known heart diseases, neurological disorder like cerebral palsy or mental retardation were excluded.

Control group

The control group consisted of 15 asymptomatic healthy children not taking any drugs, drawn from the outpatient department after due consent.

After overnight fasting, the subject was given 500 micro curies of TC-sulphur colloid mixed with milk or fruit juice orally. A drink of water or plain milk / juice was given to clear radiotracer from the esophagus, the younger patients were sedated, if required with promethazine administrated orally (0.25 mg/kg), which do not promote GER. Then the patient was placed supine under the gamma camera, with the stomach in the lower part of the field of view. Dynamic images were obtained at one frame per 30 seconds for 1 hour. Scintiscan was taken as positive for GER, when tracer was seen in esophagus in more than 2 frames. The test was taken as negative if no tracer was seen into esophagus from the stomach.

Statistical analysis

Statistical analysis included Chi-Square test, probability ‘t’ Test.

RESULTS

Table 1: Incidence of GER.

Subject	Scan +ve	Scan –ve	Total
Study group	21 (42%)	29(58%)	50
Control group	0	15	15

21 patients out of 50 i.e. 42% showed Gastro Esophageal reflux by scintiscan while none of the controls showed any evidence of reflux and lung scans done 24 hours after the study showed no evidence of radioisotope in lung fields in both study and control groups. Lung scans done 24 hours after the study shared no evidence of radioisotopes in lung fields in both study and control group.

There was no significant correlation between mean age of onset of asthma and reflux positivity. Similarly, patients with non-seasonal occurrence of asthma did not have any significant reflux compared to patients with seasonal occurrence of asthma. Presence of atopic signs was significantly higher in patients with asthma without GER ($p<0.05$).

Table 2: Relation between clinical characteristics of asthmatic children with reflux.

	Scan +ve	Scan –ve	
Mean age of on set	2 years	3 years	P=NS
Seasonal occurrence of asthma	12 (57.1%)	20 (68.97%)	P=ns
	0	8	P<0.05

Table 3: Relationship between symptoms of reflux and gastro esophageal reflux.

Scan	Reflux symptoms	
	Positive	**Negative**
Positive	11 (52.3%)	10 (47.7%)
Negative	9 (31%)	20 (69%)

Out of 21 children who had reflux by scanning, only 11 had reflux symptoms. Absence of reflux symptoms did not significantly correlate with negative scan ($X^2 = 2.3$).

Table 4: Relationship between nocturnal symptoms and gastro escophageal reflux.

Scan	Nocturnal symptoms	
	Present	**Absent**
Positive	17	4
Negative	14	15

P<0.05

Out of 21 children who had reflux, 17 experienced nocturnal cough and exacerbation of wheeze. There was significant correlation between nocturnal symptoms and presence of reflux by scan (p<0.05) significant.

Table 5: Relationship between reflux symptoms and nocturnal symptoms.

Reflux symptoms	Nocturnal symptoms	
	Positive	**Negative**
Positive	17	14
Negative	2	17

Out of 31 children who had nocturnal symptoms, 17 children also experienced reflux symptoms. Presence of nocturnal symptoms had significant correlation with reflux symptoms (p<0.01).

Table 6: Chest X-ray changes in asthmatic children with gastro esophageal reflux and without gastro esophageal reflux.

Chest X-ray changes	Scan +ve	Scan –ve
Hyper inflations	10	20
Atelectasis	4	6
Infiltrates	7	3

Majority of children showed hyperinflation changes in chest X-ray. Presence of infiltrates in chest X-ray was significantly higher in patients with GER (p<0.05).

Table 7: Absolute eosinophil count in relation to GER.

Group	Number	Mean	SD	
GER+ve	21	296.56	23.7391	None
GRE–ve	29	518.07	191.69	Significant

There was no significant correlation between absolute eosinophilic count and presence of reflux.

Table 8: Severity of chronic asthma and GER.

Severity of Asthma	Scan +ve	Scan –ve
Moderate persistent	10 (47.62%)	5 (17.2%)
Mild Persistent	7 (33.35%)	10 (34.4%)
Mild intermittent	4 (19.1%)	14 (48.28%)
Total	21	29

There was significant correlation between presence of reflux and more severe chronic asthma (P<0.05).

Table 9: GER versus morbidity of asthma.

	Scan +ve	Scan –ve	P value
No. of children-recurrence of attack (>5 yr)	18 children	10 children	P<0.01
Average duration of stay in hospital	4 days	4 days	P=not significant
Sleep disturbance> twice/week	10 children	5 children	P<0.05
Missed school days>9 per year	18 children	12 children	P<0.01

Recurrence of asthma, sleep disturbance, No. of missed school days were significantly higher than in patients with GER than in patients without GER. There was significant correlation between presence of reflux and more severe chronic asthma (p<0.05).

DISCUSSION

In order to eliminate the possibility of reflux secondary to the asthmatic state, the test was done in subjects 2 weeks after the acute phase of illness, thus they were relatively asymptomatic at the time of study and also none of the subjects were on methylxanthine group of drugs. It has long been believed that bronchodilators reduce the tone in the LES. Although Hubert et al failed to demonstrate an increase in Gastro Esophageal Reflux assessed by pH monitoring when anhydrous theophylline was added, Ekstrom and Tibbling reported a 24% increase in the amount off gastro Esophageal Reflux accompanying theophylline.[4,5] In view of the conflicting reports we have

avoided drugs to eliminate drugs to eliminate drug induced reflux in our study.

In our study, we used scintiscanning to detect GER as it was more sensitive than conventional methods like barium esophagography, endoscopy, biopsy and manometry. Its sensitivity was proven to be 78.54% by Kashyap et al, 90% by Robert et al as against the sensitivity of 40-60% of conventional methods.[6] Also it was non-invasive, convenient, equipment was available in nuclear department and exposure to radioactivity was only 5 mred (versus 20 mred fluoroscopy) thus prolonged monitoring was feasible.

In our study incidence of GER in asthmatic children was 42% while none of controls showed reflux. This is comparable to incidence published in other studies like Chopra et al who reported an incidence of 38.75%, Sontag et al who found an incidence of 39% and Dalnegro et al who observed the incidence as 83.3%.[7-9]

There is an increased incidence of GER in asthmatic children when compared to normal population. The quoted figures vary between 34-89%.

Pulmonary scintigraphy done 24 hours following ingestion of radio labelled meal showed no evidence of any radioisotopes in lung fields. Thus, role of micro aspiration cause asthma could not be established in our study. Ruth M et al in their study have shown that pulmonary scintigraphy is low sensitivity and has a diagnostic yield below 20%, but a positive test result is of great diagnostic value.[10]

The male to female ration in our study was 1.6:1 and three was no significant correlation between sex and efflux $x^2=0$.

While evaluating clinical characteristics of asthmatic children, we found that, age of onset of asthma was not statistically significant in reflux +ve and reflux -ve patients. This finding was in contrast to study by Dennis et al where the age of onset in children with recurrent pulmonary disease due to GER was less than one year.

Reflux symptoms versus scan positivity. There was no significant correlation between symptoms and presence reflux. 11 patients out of 21 who were scan positive for reflux experienced symptoms while 10 with reflux did not experience and symptoms. Thus about 50% suffered silent reflux. It could be because the presenting gastrointestinal symptoms of GER are often not clearly defined in the history because they are frequently subtle and even when children are old enough to provide reliable history, they may not localize thee complaints to the GIT tract. Klauser et al showed the clinical diagnosis of GORD by history had a sensitivity of 78% and specificity of 60%.[11]

There was significant positive correlation between presence of reflux and nocturnal occurrence of symptoms. Out of 21 children who had reflux 17 experienced nocturnal symptoms while only 4 out of 29 reflux negative patients experienced nocturnal symptoms. This positive correlation was proved in the study by Chopra et al, while no correlation was shown by Hughesetal.[7,12]

The association between reflux symptoms and nocturnal symptoms were significant statistically. Out of 31 children who had nocturnal exacerbation of wheeze or nocturnal cough, 17 also experienced reflux symptoms while only 2 children had reflux symptoms, out of 19 with no nocturnal symptoms. This is may be inferred that in asthmatic patient's presence of both reflux symptoms and nocturnal symptoms in the history would predict reflux related asthma.

Chest X-ray at the time of admission showed hyperinflation changes in majority of patients, but presence of infiltrates significantly correlated with reflux related asthma. In reflux, positive patients 7 showed infiltrate while 3 patients showed similar picture in reflux negative patients.

Absolute eosinophilic count had no correlation with reflux. Mean count in reflux positive was 296.5 cells while in reflux negative patients were 519.07 cells.

CONCLUSION

Evaluating the association between morbidity of asthma and GER showed that asthmatic children with GER suffered significantly greater morbidity than asthmatic children without GER, in terms of recurrent attacks, chronic persistent asthma, greater sleep disturbance and no. of missed school days.

At the present time, the children should be aware of high prevalence of GER reflux in asthmatic children. It should especially be considered in children with;

- Poorly controlled asthma with recurrent attacks of acute exacerbations.
- Appreciable nocturnal symptoms.
- Requiring long term aggressive management with high doses of steroids.
- Recurrent changes on radiography.
- Worsening of asthma with the use of bronchodilators.
- Appearance for duration of time before onset of asthma.

Therefore, once reflux is detected, medical therapy is warranted in the hope that respiratory symptoms will subside but in particularly severe cause it may be worth trying anti reflux treatment even for 'Normal' amounts of GER.

The most important corollary of our observation is that GER should be considered as a potentially important contributing factor in any patients with poorly controlled asthma. Although there is a high incidence of GER in asthmatic children, only a minority of patients will have significant GER symptoms.

The asthmatic patients most likely to experience measurable benefit from anti-reflux therapy is the patients with significant nocturnal asthma and who have symptoms of both asthma and of reflux.

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