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Original article

Significance of computerized tomography and nasal cytology in the diagnosis of rhinosinusitis among asthmatic children

Background: *Chronic sinusitis, allergic rhinitis, and asthma are conditions that frequently coexist. Nasal sinus disease may contribute to poor control of asthma; this suggests that sinonasal involvement might be a risk factor for asthma severity and morbidity. Proposed mechanisms of this interaction include the presence of postnasal drip, nasobronchial reflex or systemic effect of mediators released from inflamed paranasal sinus tissue.*
Objective: *In the present study, we sought to investigate the relationship of sinonasal inflammation as assessed by coronal sinus computerized tomography (CT) scanning, nasal cytology score, and asthma severity.*
Methods*: Twenty-five children with asthma were recruited from the Pediatric Respiratory Clinic of Ain Shams University. Their ages ranged from 5-13 years with a mean age of 7.78 years. Twenty healthy children who were age- and sex-matched and who had normal sinus CT scans were selected as the control group. Patients were subjected to asthma severity assessment, nasal cytology, total serum IgE assay, and paranasal CT scanning and scoring.*
Results: *Sinus CT scoring showed abnormalities in 88% of asthmatic children, and sinus CT scores correlated positively to asthma severity. Nasal cytology scores for eosinophils and neutrophils correlated positively with sinus CT scores. The most frequent symptoms associated with sinusitis were rhinorrhea (68%) and nasal obstruction (40%). The maxillary sinus was the most frequently affected one followed by the ethmoid sinus. Pathological features included mucosal thickening, osteomeatal complex occlusion, and polyp formation.*
Conclusion: *Computed tomography scan is a useful diagnostic tool for assessment of sinus disease in asthmatic children. Rhinosinusitis is a common asthma comorbidity. Nasal eosinophil or neutrophil score >0.5 provides a better predictive value for rhinosinusitis compared to total serum IgE.*

Keywords: computerized tomography, nasal sinus, asthma, sinusitis, allergic rhinitis, children.

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INTRODUCTION

The coexistence of asthma and rhinosinusitis has been noted in the medical literature. Up to 80% of patients with asthma have rhinitis and over 50% of patients with sinus disease have asthma[1]. Patients with severe asthma in particular, appear to have the most prominent abnormalities on computed tomography (CT) scanning of the paranasal sinuses[2].

Nasal sinus disease may contribute to poor control of asthma [3] and sinus disease, severe enough to warrant surgical intervention, has been investigated as an independent risk factor associated with frequent severe asthma[4]. Newman et al.[5] showed an association between extensive sinus diseases on CT scanning and relative increase in the peripheral eosinophil count. Although a casual relationship has not been proven, clinical studies indicate that proper medical and surgical management of chronic sinusitis in asthmatic children results in improvement of sinonasal and asthmatic symptoms[6]. The rationale of treating the nose in asthmatic patients follows the concept of "united airways" because nasal inflammation can influence the lower airways and intranasal corticosteroids can relieve symptoms of sinusitis and asthma[7].

Proposed mechanisms of this interaction include the presence of a postnasal drip of infectious or inflammatory mediators and activated T lymphocytes that migrate to the mucous membrane of the adjacent airway mucosa extending the inflammation to the lower airways[7]. Sino-pulmonary reflex activated by cellular

inflammatory products and mouth breathing might also cause increased water and heat loss in the lower airways thereby contributing to asthmatic symptoms[8].

This work is aimed at identifying the significance of computed tomography scanning, nasal cytology examination, and serum total IgE assay in the diagnosis of sinusitis and rhinitis among asthmatic children, and to correlate these findings to asthma severity. This might have therapeutic implications in terms of adequate asthma control.

METHODS

Patients:

Group A: Twenty-five asthmatic children attending the Pediatric Respiratory Clinic of Ain Shams University were recruited as a random sample during the period from November 2001 to March 2002. The patients had history of episodic wheezing and dyspnea, a documented reversibility in FEV_1 >20%, they were treated with inhaled steroids in variable doses according to asthma severity. All patients were symptomatic. They were 20 males and 5 females, their ages ranged from 5-13 years with a mean of 7.78 years.

Patients were assessed for asthma severity according to GINA guidelines 2000[9] and were categorized as mild (8 patients), moderate (9 patients) and severe asthmatics (8 patients). According to history and rhinoscopic examination asthmatic patients were further divided into children with allergic rhinitis (n= 15) and those without allergic rhinitis (n= 10).

Group B: Ten normal age and sex-matched children were selected. Their ages ranged between 5-12 years with a mean of 6.8 years. Sinus CT was done for another cause and proved to be normal. They formed the control group.

Study measurements:

All patients and controls were subjected to history taking using a detailed structured questionnaire, clinical examination including assessment of nasal symptoms, anterior rhinoscopy, and ENT examination. Investigations included complete blood counting (CBC), chest X-ray postero-anterior view and pulmonary function tests. Total serum IgE was measured using the ELISA technique.

CT scans:

Standardized computed tomography scans of paranasal sinuses using Hi-speed GE machine were performed in the CT Unit of Ain Shams University Hospital. Direct Coronal CT scanning through the paranasal sinuses was performed while the patient is lying prone or supine with hyperextended neck. Serial 3-4 mm contiguous sections perpendicular to the hard palate were taken. Sections were imaged with wide window settings to reveal bone details (window width=1500, and window level =250 HU).

Although complete CT examination of the paranasal sinuses and nasal fossae is obtained by a combination of coronal and axial studies; only direct coronal imaging was performed in this study because: (1) coronal CT scans afford the best display of the osteomeatal complexes -resembling the endoscopic view most closely; (2) its validity in assessment of sinus mucosal abnormalities has been advocated by many authors[10,11], and we preferred to save the patients excessive radiation exposure.

All patients were scanned after intranasal administration of decongestant and cleaning of the nose, so that any findings on CT scans will not be attributable to acute mucosal disease as was advised by Crater et al., and Phillips and Platts-Mills[11,12]. Scans were analyzed for mucosal thickening in the sinuses, osteomeatal complexes and nasal cavities. Maximal single-wall mucosal thickening was measured in millimeters. Patients were classified regarding sinusitis into mild (limited sinusitis), or moderate to severe (extensive sinusitis) according to a previously published sinus CT scoring system[10,13] (Table 1). A total of 30 points were allowed (21 from the sinuses, 6 from the osteomeatal complexes and 3 from the nasal passages). The total CT scan score was used to classify the patients as having limited disease (CT score 0-12) or extensive disease (CT score > 12). The sinus scans were reviewed by one of the authors, experienced in interpreting sinus CT and blinded regarding the patient's history and clinical examination. Maximal score for mucosal thickening is 30 points; values in tables are measured in mm. Because of the smaller size of the ethmoidal sinuses relative to other sinuses the same number of points were given to lesser degrees of thickening.

Osteomeatal complex is defined as the area between the middle and inferior turbinates. It is the confluence of drainage of frontal, ethmoid, and maxillary sinuses. Mucosal inflammation might cause osteomeatal complex obstruction leading to sinusitis.

Nasal cytology:

Mucosal specimens were scraped from the surfaces of the middle third of the inferior turbinate with rhinoprobes, transferred onto glass slides fixed in 95% ethyl alcohol and stained with modified Wright-Giemsa stain. Nasal basophilic

metachromatic cells and eosinophils were enumerated at x1000 magnification under a light microscope. At least 10 well spread epithelial sheets were examined. The quantitative score was rated according to a scale previously described by Meltzer[14] (Table 2). The grading was on the scale 0-4+; the ratio of eosinophils to neutrophils in the nasal secretion that exceeds 0.1 is considered specific for seasonal and perennial rhinosinusitis. The presence of nasal eosinophil to neutrophil ratio of >0.5 provided the best specificity and sensitivity and positive predictive value for this condition.

Table (1): CT scoring system of the paranasal sinuses.

Site of Mucosal thickening	Score points			
	0	1	2	3
Frontal (n=2)	0-1	2-5	6-9	>10
Maxillary (n=2)	0-1	2-5	6-9	≥10
Sphenoid (n=1)	0-1	2-5	6-9	≥10
Ethmoid (n=2)	0	1	2-3	≥4
Osteomeatal Complex (n=2)	none	mild	mod	severe
Nasal Passages (n=1)	none	mild	mod	severe

mod= moderate.

Table (2) Semi-quantitative nasal cytology grading score

Quantitative scoring	Grade
Eosinophils/neutrophils	
0.1-1.0*	0
1.1-5.0*	1+
6.0-15.0	2+
16.0-20.0*	3+
>20.0*	4+
Basophilic cells	
0.1-0.3*	0
0.4-1.0*	1+
1.1-3*	2+
3.1-6*	3+
>6*	4+

Mean number of cells per 10 high power fields (X1000) After Meltzer [14].

Statistical methods

Student's t test was used to compare the mean values of parametric data, Spearman's rank correlation test was employed for measuring the association between values assuming they were not normally distributed, and Chi-square to test the association between variables. In addition, Fisher exact testing tables containing values less than 5, ANOVA for evaluating quality of several group means and Kruskal test as the non-parametric equivalent to ANOVA were used. p values of <0.05 are considered significant. The computer software used for statistical analysis was SPSS 7.4 for windows.

RESULTS

In the present study, patients and controls were age and sex matched (p > 0.05), cases had significantly higher serum eosinophil count, eosinophil, basophil and neutrophil cytology scores, and sinus CT score (p<0.05). They also had significantly higher total serum IgE compared to controls (Table 3). Blood eosinophil count, eosinophil cytology score, neutrophil cytology score, sinus CT score, and total serum IgE correlated positively with severity of asthma (Table 4).

Table (3) Nasal cytology score, sinus CT score and total serum IgE of patients with compared to controls.

Variable		Mean Rank	Mann-Whitney U	p
Basophil cytology score	Controls	6.25	7.500	0.00001
	Patients	22.70		
Eosinophil cytology score	Controls	6.80	13.00	0.00003
	Patients	22.48		
Neutrophil cytology score	Controls	6.50	10.000	0.00002
	Patients	22.60		
CT score	Controls	7.00	15.000	0.00004
	Patients	22.40		
		Mean ±SD	**t**	**p**
Serum IgE (IU/ml)	Controls	14.20 ±5.03	3.49	0.001
	Patients	117.04 ±92.23		

Patients with allergic rhinitis (AR+) had significantly higher eosinophil cytology score, neutrophil cytology score and sinus CT score (p=0.026) compared to those without allergic rhinitis (AR-), but there was no significant difference in serum IgE between AR+ and AR- patients (Table 5).

Table (4) Correlation between CT score, nasal cytology score, serum total IgE and severity of asthma

Variable	Severity of asthma	
	Spearman's (rho)	p
Eosinophil cytology	0.76	0.00001
Basophil cytology	-0.27	0.19
Neutrophil cytology	0.55	0.004
CT score	0.83	0.000001
IgE	0.41	0.04

Table (5) Nasal cytology score, sinus CT score and IgE in relation to allergic rhinitis (AR)

Variables	AR	Mean Rank	Mann Whitney U	p
Basophil cytology	-	13.50	35	0.026
	+	12.67		
Eosinophil cytology	-	9.95	34	0.04
	+	15.03		
Neutrophil cytology	-	10.00	33	0.03
	+	15.00		
CT score	-	9.00	35	0.026
	+	15.67		
Variable	**AR**	**Mean ± SD**	**t**	**p**
IgE	-	130.0±94.9	0.57	0.58
	+	108.0±92.7		

-: absent; +: present

Symptoms and signs associated with sinusitis were rhinorrhea for more than 10 days 68%, nasal obstruction 40%, headache 15%, fever 20%, facial tenderness 10%, fetor oris 20%, and cervical lymphadenopathy 12%. Sinusitis was confirmed by sinus CT score in 82% of patients with rhinorrhea and in 100% of patients with rhinorrhea, fever, headache, nasal obstruction and night cough. All patients with severe and moderate asthma had sinusitis while only 62.2% of mild asthmatics had sinusitis.

The right maxillary sinus was the most frequently affected, while the least affected was the frontal sinus (Table 6). The right osteomeatal complex was totally occluded in 60% of asthmatic children and partially occluded in 12%. The total and partial occlusion of the left osteomeatal complex was found in 48% and 8% respectively. Mucosal thickening was the most common pathological feature in asthmatic children with sinusitis (Table 7, Figures 1 and 2).

Table (6) The frequency of involvement of the different paranasal sinuses and nasal structures in asthmatic children as shown by coronal CT scan

Variable	Right		Left		Bilateral		Free	
	N	%	N	%	N	%	N	%
Maxillary	22	88	13	52	13	52	3	12
Ethmoid	11	44	9	36	9	36	14	56
Sphenoid	2	8	4	16	2	8	21	84
Frontal	3	12	3	12	3	12	22	88
Hypertrophy of nasal turbinate	15	60	13	52	13	52	10	40
Deviated nasal septum	3	12	1	4	1	4	22	88

N: number.

Table (7) Pathologic features of maxillary sinusitis

Variable	Rt		Lt		Bilateral		Free		Total	
	N	%	N	%	N	%	N	%	N	%
Mucosal thickening	22	88	13	52	13	52	3	12	25	100
Air fluid level	-	-	-	-	-	-	-	-	-	-
Polypi	1	4	1	4	1	4	-	-	1	4
Adjacent Bony wall changes	-	-	-	-	-	-	-	-	-	-

N: number; -: absent.

Severe sinusitis was diagnosed in 17(68%)of children with asthma {sinus CT score >12}, while mild sinus disease was diagnosed in 5(20%)of children with asthma {sinus CT score <12}. Normal sinus CT was diagnosed in 3(12%)of children with asthma (sinus CT score < 3).

Patients with sinusitis had significantly higher peripheral blood eosinophil count (5.92 ± 1.78 vs 4.08 ± 1.78; $p<0.05$), eosinophil cytology score, neutrophil cytology score compared to those without sinusitis. However, no difference was statistically detected in total serum IgE score (Table 8). Sinus CT score correlated positively to eosinophil and neutrophil scores but not to the basophil score or serum total IgE (Table 9).

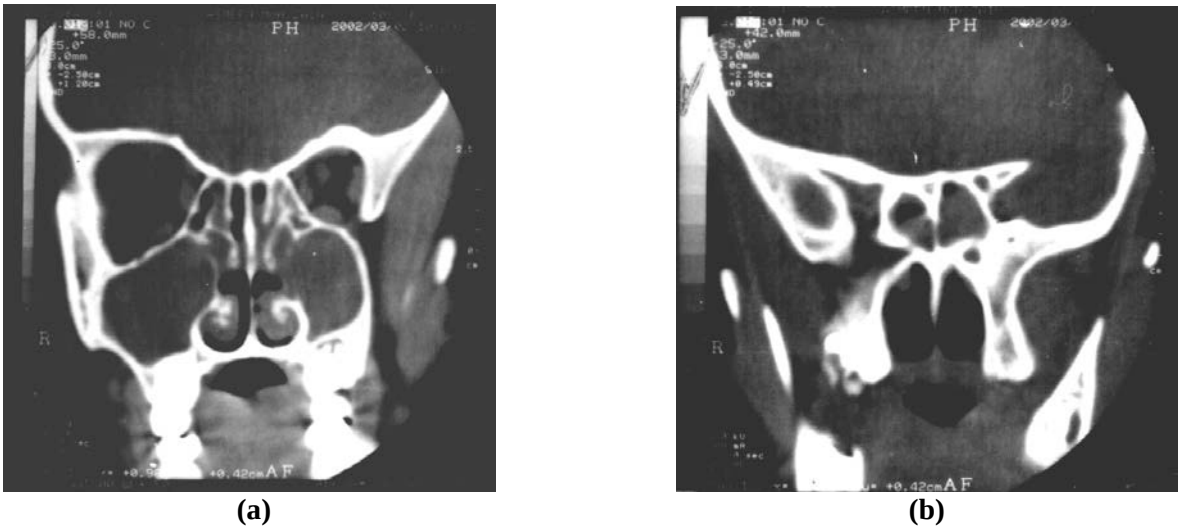
Table (8) Relation between sinusitis, nasal cytology, and serum total IgE.

Scores	Sinusitis	Mean rank	Mann Whitney U	p
Eosinophil cytology	-	9.77	36.00	0.02
	+	16.50		
Basophil cytology	-	13.38	73.00	0.78
	+	12.58		
Neutrophil cytology	-	8.42	18.500	0.0007
	+	17.96		
Variable		**Mean ±SD**	**t**	**p**
IgE	-	85.00 ±71.33	-1.904	0.069
	+	151.75 ±102.38		

-: absent; +: present

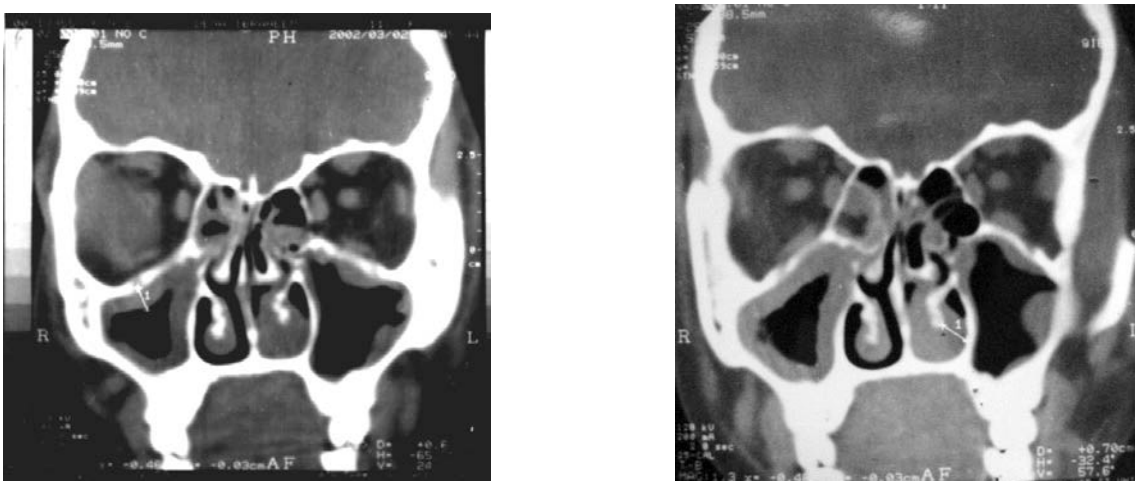
Table (9) Correlation between nasal cytology scores, serum total IgE and sinus CT score.

Variables	Sinus CT score Spearman's (rho)	p
Basophil Cytology score	-0.06	0.788
Eosinophil Cytology score	0.48	0.015
Neutrophil Cytology score	0.89	0.0001
IgE	0.35	0.086



(a) **(b)**

Figure (1). Coronal CT scans of paranasal sinus of a 10-year-old asthmatic girl. (a) Both maxillary sinuses are occupied by high-density inflammatory material, with subsequent occlusion of both OMC. Most of the ethmoid air cells are also involved. (b) Mucosal thickening of both sphenoid sinuses is evident. Picture of extensive pansinusitis (CT score = 26).



(a) **(b)**

Figure (2). Coronal sinus CT scans of an 11-year-old asthmatic girl. Marked circumferential mucosal thickening is noted at the frontal sinuses (a) and maxillary sinuses (= 6.3 mm) on the right side. Tendency to polyp formation (suggesting allergic sinusitis) on the left side is also evident, leading to bilateral complete occlusion of OMC. Hypertrophy of both inferior nasal turbinates (more on the left side =7 mm). Nasal septum is deviated with convexity to the right side. (CT score = 21).

DISCUSSION

Chronic sinusitis has been shown to be associated with asthma, both in children and in adults[2]. Chronic sinusitis and persistent asthma are both characterized by an eosinophilic tissue response, an important pathophysiologic link[15]. The present study showed a high frequency of sinus disease in asthmatic children. This supports the increasing evidence of a close relation between upper and lower airway disease. Moreover, the highly significant correlation found between asthma severity and sinus CT score in mild, moderate and severe asthma further supports the validity of the CT score results. This came in contrast to the results of a previous study[16] showing no correlation between asthma severity and morphologic abnormalities of the airways. The lack of correlation in this previous study may be due to the use of x-ray rather than CT scan in the evaluation of sinus disease.

Coronal sinus CT scan is well known to have dramatically improved the imaging of nasal cavity and paranasal sinuses, to the point that x-ray imaging is no more performed owing to its inability to assess sinus mucosal abnormalities[17]. Brescani et al.[2] have shown that sinus disease is a major problem in patients with severe asthma and that the extent of the abnormalities on CT scanning is related to the degree of eosinophils in the peripheral blood.

In the present study, nasal cytology scores were also higher in patients compared to controls. Elevated levels of eosinophils, basophils and neutrophils in nasal cytology of asthmatic children compared to normal children were found by Baroody et al.[18], Makalkin et al.[19], and Jirapongsananuruk and Vichhyanond[20]. Tissue eosinophilia is the result of expression of cytokines, chemokines, and adhesion molecules; these interact with late antigen 4, expressed on lymphocytes, monocytes, eosinophils, and basophils, increasing their cytological score[21].

A positive linear correlation existed between asthma severity and both nasal eosinophil (strong correlation) and neutrophil score (moderate correlation), while there was no correlation with that of basophils. It is recognized that chemokines such as RANTES or eotaxin are selectively active on eosinophils whereas platelet activating factor (PAF) and leukotriene B4 are chemotactic for both eosinophils and neutrophils[22].

Among our series, 62.5% of mild asthmatics had sinus abnormalities while all moderate and severe asthmatic children had sinus abnormalities, the degree of this abnormality, as assessed by sinus CT score correlated positively to the severity of asthma. These results agree with those of Bresciani et al.[2], who concluded that all severe asthmatics and 88% of mild and moderate asthmatics had sinus abnormalities that correlated positively to asthma severity. Abdelfattah and Elnahas,[23] diagnosed sinusitis in 100% of severe asthmatics, in 75% of moderate and in 66% of mild cases. Virant,[15] reported that sinusitis and asthma occur simultaneously, he found that eosinophilic tissue infiltration, glandular hyperplasia and edema characterize both conditions. Migration of immunologic reaction to adjacent airway mucosa

and postnasal drip of mediators exert a significant effect on bronchial responsiveness and nasobronchial reflex[8].

In the current study, there was a significantly high tissue eosinophil and neutrophil cytology score in patients with allergic rhinitis, and this agrees with Amin et al.[24]. Eosinophils play an important role in late phase response in which T-lymphocytes, cytokines, and adhesion molecules are involved. Cytokines and adhesion molecules are the key factors for increasing nasal cellular infiltrates[25]. Sixty percent of asthmatic children showed signs and symptoms of allergic rhinitis. This might be the result of a neurally mediated pharyngobronchial reflex which when activated in the sinuses triggers bronchial hyperresponsiveness. Aspiration of nasal secretions or increased water and heat loss from lower airways as a result of mouth breathing might also be contributing[8]. There was a significant relationship between existence of allergic rhinitis and sinusitis, in accordance with Jeffrey[26] who found that diseases of nose and paranasal sinuses coexist.

Sixty percent of patients with allergic rhinitis had sinus abnormalities on CT scan, also a positive correlation existed between nasal cytology score and CT score. This agrees with Bresciani et al.[2] and Bhattacharya[17]. Inflammatory process extends from the sinuses to the contagious nasal mucosa, and vice versa, supporting the concept of rhinosinusitis rather than sinusitis alone. The most obvious complaint suggestive of rhinosinusitis was prolonged rhinorrhea more than 10 days (68%) and nasal obstruction (40%). Bresciani et al.[2] observed that the most obvious symptoms were nasal congestion (75%) and rhinorrhea (62.5%).

In the current study, 88% of asthmatic children had sinus disease abnormality denoted by coronal sinus CT scan and scoring system. Nguyen et al.[27] found 63% of asthmatic children affected by chronic sinusitis while Abdelfatah and Elnahas[23] showed that 80% of asthmatic children had sinus disease as diagnosed by CT scan. Rhinosinusitis and asthma share similar cellular and humoral mechanisms; presently sinusitis and asthma are believed to be inflammatory processes in which eosinophils and airway epithelium play a central role; eosinophils would damage the epithelium by releasing cytokines and proinflammatory proteins. The damaged epithelium releases cytokines and further attracts eosinophils, thus starting a vicious cycle of action and reaction that activates sustained inflammation.

In our series, maxillary sinus was the most affected one (88%) with mucosal thickness occurring in 80%; and maxillary polyp in one case bilaterally. This agrees with the findings of Abdelfattah and Elnahas[23]. The extension of sinus involvement as documented by CT scan strongly correlated with the presence of peripheral and tissue eosinophilia as previously shown by other investigators[5,12,28]. According to Jeffery[26] peripheral eosinophilia results from bone marrow stimulation by IL-5 and eotaxin, while tissue eosinophilia is the result of expression of cytokines, chemokines, and adhesion molecules through activation of mast cells and T-lymphocytes. Sinus CT score correlated to nasal neutrophil score and this agreed with Meltzer et al.[29]. On the other hand, Jirapongsananuruk and Vichhyanond[20], observed that neutrophil score did not correlate with sinus disease whereas Jong et al.[30], found that neutrophils more than 5/high power field on rhino probe cytology had 100% sensitivity and 53% specificity.

In conclusion, Severe sinus disease was diagnosed in 68% while mild sinus disease was diagnosed in 20% of asthmatic children using coronal sinus CT. Patients with sinusitis had significantly higher peripheral eosinophil count and eosinophil and neutrophil cytology scores compared to those without sinusitis. Severity of sinusitis as denoted by sinus CT score correlated to asthma severity. Coronal CT scan is a valuable tool for diagnosis of sinusitis in asthmatic children.

Recommendations:

Eosinophil count, eosinophil and neutrophil nasal cytology and sinus CT scanning should be part of the work up of asthmatic children. These are valuable tools for diagnosis of sinusitis and allergic rhinitis in asthmatic children. The treatment of which might improve asthma morbidity.

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