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ORIGINAL ARTICLE

Tracing of Local Atopy Among Apparently Non-atopic Asthmatics with Nasal Polyps

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Abstract

Background: **Asthma is still a main etiology of complaining all over the world. Much indirect evidence recommends that immunoglobulin E (IgE) and Eosinophil could have an essential role in asthma irrespective of conventional atopic condition.**

Objective: **To trace the expression of local Eosinophil (%) and local IgE in the absence of systemic IgE in asthmatic cases with nasal polyps.**

Subjects and methods: **90 subjects were included and were divided into 3 groups: Group A: consists of 30 patients had non-atopic bronchial asthma and nasal polyps. Group B: consists of 30 patients with nasal polyps only. Group C: consists of 30 healthy normal candidates as controls.**

Results: **The mean levels of local Eosinophil (%) count and local IgE were significantly increased in group A and B in comparison with group C ($P < 0.001$ for both). There was a statistically significant positive correlation between local IgE ($r = 0.89$, $P < 0.001$) and VAS for symptoms severity. There was a statistically significant positive correlation between local Eosinophil (%) ($r = 0.89$, $P < 0.001$) and VAS for symptoms severity.**

Conclusion: **Local Eosinophil (%) and local IgE showed significant elevation in patients with bronchial asthma and nasal polyps and cases with nasal polyps in comparison to controls. Moreover, Local IgE and local Eosinophil (%) were found to be positively correlated with symptoms severity.**

Keywords: Asthma, Eosinophil, IgE, Nasal polyps, Non-atopic

1. Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disease of the nose and para-nasal sinuses, present in 3% of the adults. In addition, approximately 40% of cases with CRSwNP complain from asthma[1]; with the classic manifestations of cases with chronic rhinosinusitis with nasal polyps and comorbid asthma featured by advanced age, greater possibility of allergic rhinitis and prolonged onset of nasal manifestations as well as bronchial obstruction.[2] In fact, in cases with non-atopic asthma and late-onset asthma, CRSwNP was occasionally demonstrated[3]

Essentially, asthma course in cases with CRSwNP is often severe and is of great difficulty to be managed compared to CRSwNP free asthmatic cases.[3]

Another research has revealed non-asthmatic CRSwNP cases might have minor airway dysfunction, accompanied by type II inflammation[4] and is indicative of an asthmatic phenotype in CRSwNP cases.[4]

It was demonstrated that asthma is still not diagnosed in twenty five percent of case with CRSwNP;

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and on assessment of bronchial hyper-responsiveness 34% of adults with CRSwNP were displayed to have formerly undiagnosed asthma.[5]

We aimed to trace the expression of local Eosinophil (%) and local IgE in the absence of systemic IgE in asthmatic patients with nasal polyps.

2. Subjects and methods

In the current study, 90 subjects were included and were divided into 3 groups:

Group A: 30 patients with nasal polyps and asthma by pulmonary function test & history.

Group B: 30 patients with nasal polyps and no asthma by pulmonary function test & history.

Group C: 30 healthy normal candidates with no nasal polyps and no asthma by pulmonary function test and history as a control group.

Inclusion criteria: Patients with nasal polyps, Normal IgE level in serum and Apparently non-atopic by history.

Exclusion criteria: High serum IgE level, History of any atopy, Positive skin test, Extensive disorders which include cystic fibrosis, Malignancy, Pregnant and lactating women.

2.1. Methodology

The present prospective cohort study was conducted, throughout September 2021 and December 2022, according to the ethical issues of the Ethics Unit, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

All the included patients were subjected to the next: an appropriate history taking which include the complete present history, allergic history, medication history, and history of different systemic diseases; social history which include (housing state, presence or absence of pets) family history and past history; and clinical examination.

Entire cases were undergone allergy testing: total IgE, skin prick testing for popular inhalant allergens. Bronchial asthma was diagnosed by a clinician according to a history of repeated dyspnea, wheezes or cough attacks or positive airway responsiveness testing, according to the current international guidelines.[6,7]

Subjective manifestations which include nasal obstructions, nasal secretion, loss of sense of smell, and facial pain, were assessed utilizing a VAS.[8] The diagnosis of nasal polyps was confirmed according to medical history, nasal endoscopy, or CT of the para-nasal cavities, based on the European Position Paper on rhino-sinusitis as well as on nasal polyps.[9]

Conventional spirometry was used to evaluate the pulmonary function for each participant via portable dry rolling SpiroBank spirometer (Company nSpire Health™, Medics MGA USB, Germany). The reference values were calculated based on the guidelines of the American Thoracic Society.

Following proper inspection of the nasal cavity by using a nasal speculum, a cotton swab (caliber of one centimeter). Following acquisition of the nasal discharge, the swabs were wrapped in a Salivette and centrifuged at 3000 revolutions for 10 min.

After that, transported into Eppendorf tubes and frozen at 80C till additional assessment. Local IgE levels in the nasal discharges were assessed by ELISA. After that, 3 ml of blood specimens were withdrawn from cases to evaluate eosinophilic numbers and serum IgE levels. In addition, specimens were removed from the discharge and stained. After that, one hundred cells were measured, and the numbers and percentages of eosinophil were measured. The total IgE antibodies level in all samples were evaluated by utilizing the AlaSTAT-3g Allergy assay and expressed as IU/mL/Gm ($IUmL^{-1}$ g^{-1}).

Five milliliters of blood were taken following a fast of 12 h under sterilized situations. The CBC and differential WBCs counts were measured with a hemocyte analyzer.

2.2. Statistical analysis

The significance is established when $P < 0.05$. Statistical analysis was conducted by using SPSS software version 25 for Windows. The figures were renewed by utilizing GraphPad Prism software version 8.

3. Results

Baseline socio demographic features of the comprised patients are illustrated in Table 1 and Fig. 1. The mean FEV1% predicted, PEFR% and FEV1/FVC were significantly decreased in group A compared to with group B and C ($P < 0.001$ for all). (Figs. 2–4), (Table 2). The mean levels of local Eosinophil (%) count and local IgE were significantly elevated in group A and B compared to group C ($P < 0.001$ for both), while no significant differences were recorded among the 3 studied groups in the context of total Eosinophil (%) in blood, total serum level of IgE, mean Hb (g/dl) level or WBCs (Figs. 5–7), (Table 3).

Among patients within group A, six (20%) patients had intermittent bronchial asthma. Whereas nine

Table 1. Baseline demographic features of the comprised cases.

Variables	Group A Mean (SD)/*N* (%)	Group B Mean (SD)/*N* (%)	Control Mean (SD)/*N* (%)	*P* value
Variables	30	30	30	
Age	38.31 ± 7.23	37.78 ± 5.8	40.1 ± 3.89	0.578
Sex				
Male	12 (40%)	9 (30%)	11 (36.66%)	0.32
Female	18 (60%)	21 (70%)	19 (63.33%)	
BMI(kg/m^2)	21.4 ± 4.9	20.7 ± 3.8	22 ± 2.7	0.78
Obese Patients	8 (26.66%)	10 (33.33%)	9 (30%)	0.98
Smoking behavior				
Current smokers	6 (20%)	8 (26.66%)	5 (16.66%)	0.45
Previous smokers	1 (3.33%)	3 (10%)	2 (6.66%)	
Never smoking	23 (76.66%	19 (63.33%)	19 (63.33%)	
Comorbidities	5 (16.66%)	3 (10%)	0 (0%)	0.09

Abbreviations: BMI, Body mass index; SD, Standard deviation, P=Probability Value.

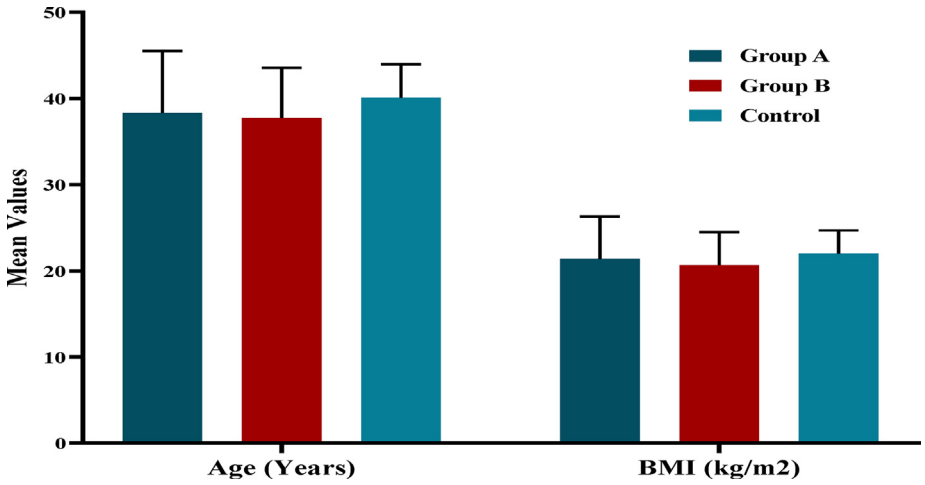

Fig. 1. Mean age (years) and BMI among studied groups.

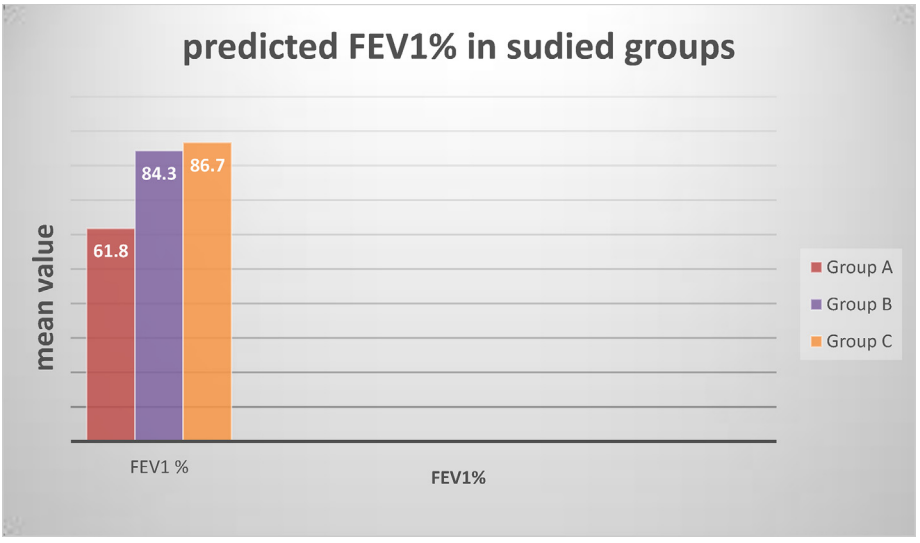

Fig. 2. Mean FEV1% predicted among studied groups.

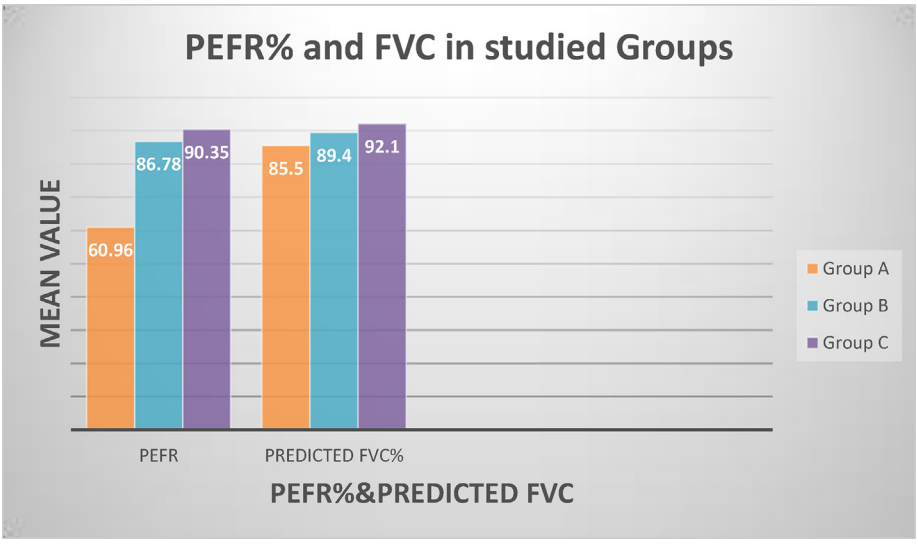

Fig. 3. Mean PEFR% and predicted Vital Capacity among studied groups.

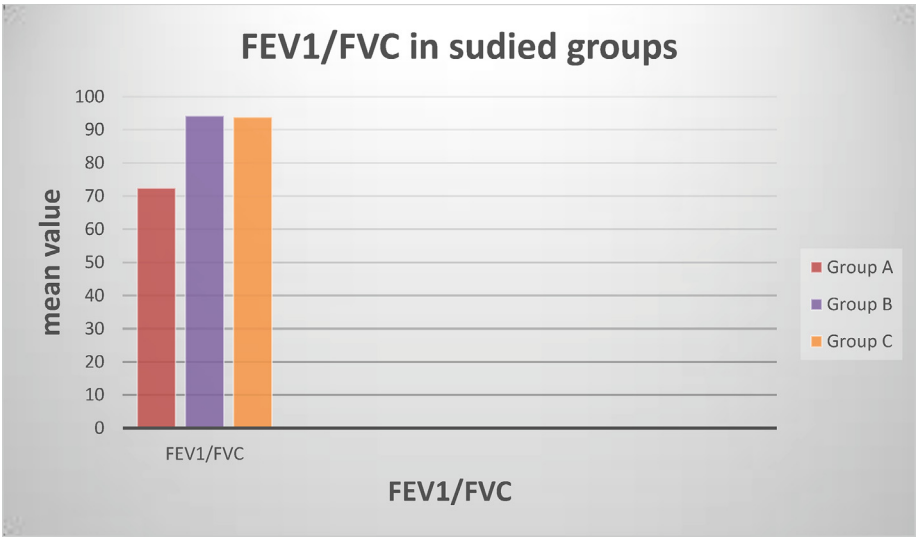

Fig. 4. Mean FEV1/FVC among studied groups.

Table 2. Pulmonary function tests.

Variables	Group A	Group B	Control	*P* value
	Mean (SD)/*N* (%)	Mean (SD)/*N* (%)	Mean (SD)/*N* (%)	
Number	30	30	30	
FEV1% predicted	61.88 ± 5.3	84.3 ± 2.7	86.7 ± 5.6	<0.001
PEFR%	60.96 ± 3.5	86.78 ± 4.7	90.35 ± 5.2	<0.001
Vital Capacity	85.58 ± 2.6	89.4 ± 2.4	92.1 ± 6.8	0.068
FEV1/FVC	72.48 ± 4.08	94.21 ± 5.14	93.81 ± 9.45	<0.001

Abbreviations: FEV1, forced expiratory volume in the first second; FEV1, Forced vital capacity; P, Probability Value; PEFR, peak expiratory flow rate; SD, Standard deviation.

(30%) patients had moderate persistent bronchial asthma, 12 (40%) patients had severe persistent asthma. The mean VAS for assessment the severity of symptoms was 35 ± 12. (Fig. 8), (Table 4)

There was a statistically significant positive correlation among local IgE (r = 0.89, $P < 0.001$) and VAS for symptoms severity. There was a statistically significant positive correlation between

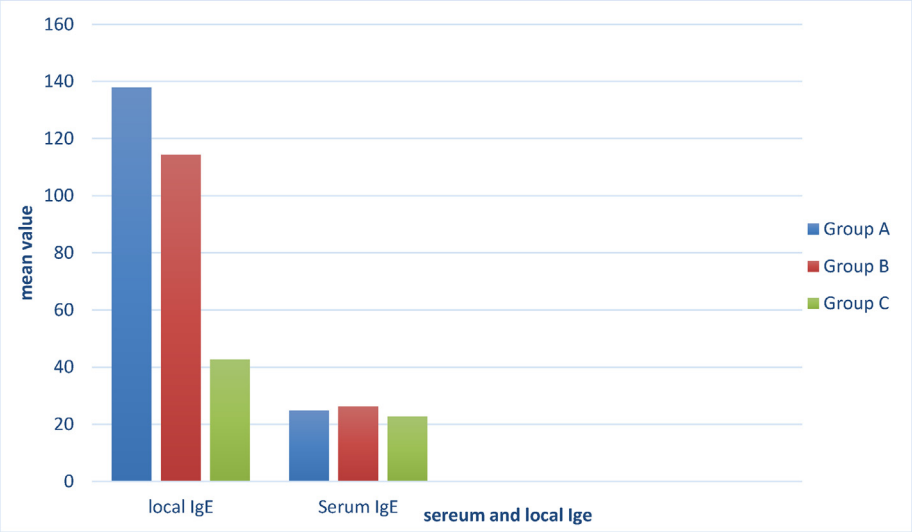

Fig. 5. Mean total serum IgE and local IgE among studied groups.

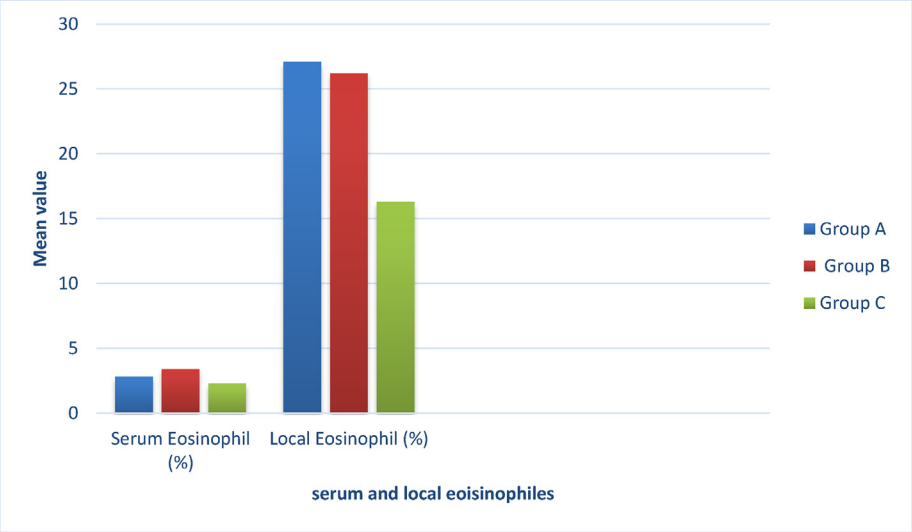

Fig. 6. Mean total serum Eosinophil (%) and local Eosinophil (%) among studied groups.

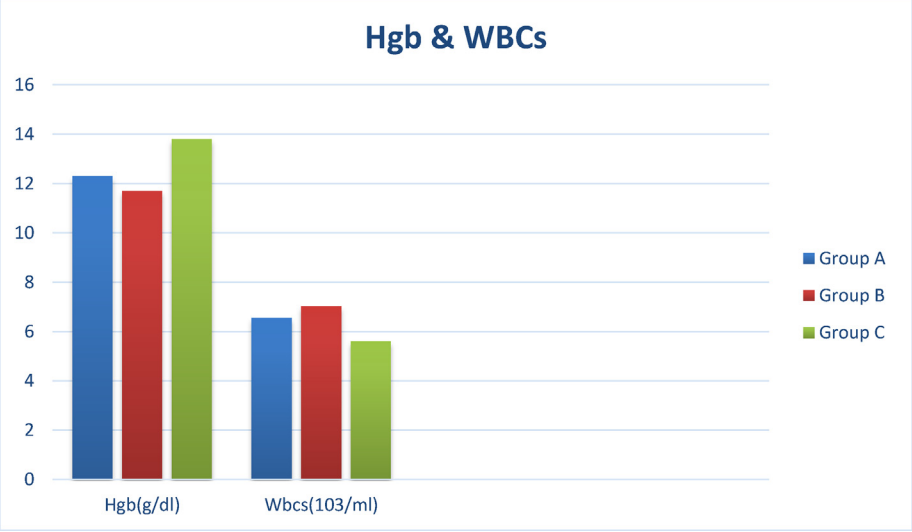

Fig. 7. Mean Hemoglobin and WBCs among studied groups.

Table 3. Laboratory data.

Variables	Group A	Group B	Control	*P* value
	Mean (SD)/*N* (%)	Mean (SD)/*N* (%)	Mean (SD)/*N* (%)	
Number	30	30	30	
Serum Eosinophil (%)	2.8 ± 1.2	3.4 ± 1.1	2.3 ± 1.7	0.45
Local Eosinophil (%)	27.1 ± 1.3	26.2 ± 1	16.3 ± 3.6	<0.001
Serum IgE	24.8 ± 5.9	26.2 ± 2.8	22.7 ± 1.9	0.093
Local IgE	137.83 ± 16.89	114.2 ± 11.5	42.9 ± 5.7	<0.001
Hb (g/dl)	12.3 ± 2.1	11.7 ± 1.8	13.8 ± 2.4	0.089
WBCs (10^3/ml)	6.55 ± 3.4	7.02 ± 1.2	5.6 ± 2.1	0.065

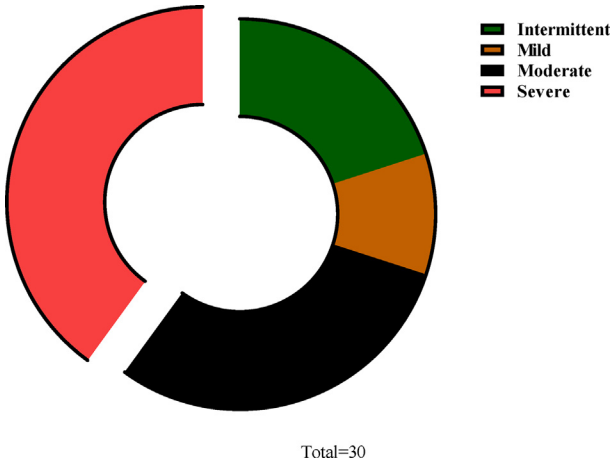

Fig. 8. Distribution of asthma severity among studied groups.

Table 4. Severity of symptoms.

Severity of bronchial asthma	
Intermittent	6 (20%)
Mild persistent	3 (10%)
Moderate persistent	9 (30%)
Severe persistent	12 (40%)
VAS score	35 ± 12

Abbreviations: VAS, Visual Analouge Scale for severity assessment.

local Eosinophil (%) (r = 0.89, $P < 0.001$) and VAS for symptoms severity. (Figs. 9 and 10), (Table 5).

4. Discussion

According to the current study, the mean FEV1% predicted, PEFR% and FEV1/FVC were significantly decreased in group A in comparison with group B and C ($P < 0.001$ for all). Similarly, Li et al.[10] reported that spirometry parameters, including FEV_1/FVC% and FEV_1% predicted were significantly reduced in asthmatic cases (both $P < 0.001$).

Increase in absolute eosinophil count (AEC) develops occasionally in asthmatics as eosinophilic inflammation is a main pathological way as regards airway inflammatory conditions. Therefore, it has been demonstrated that there is a positive correlation between the increase in AEC and asthma degree.[11] As a result, AEC has been regarded as a helpful biomarker in terms of bronchial asthma to determine the eosinophilic phenotypes and is a frequent target with regard to novel therapeutic options.[12] Furthermore, Mummadi et al.[13] found that AEC is helpful indicator to determine the nasal and bronchial allergy as well as its degree. In the current study, no significant differences were reported among the 3 studied groups regarding AEC. In agreement with our finding, Shrestha et al.[14] did not report significant difference in AEC between non-atopic asthma group and control group.

On the contrary, Bai et al.[15] have revealed that an increase in BEC more than 110 cells/μL is a predisposing factor as regards incident asthma. In Li et al.[10] study, blood eosinophilia and IgE have been demonstrated to be main predisposing factors for asthma development in CRSwNP cases.

Essentially, targeting sputum and AEC have been considered as the backbone of novel advancement in the context of allergic eosinophilic asthma.[16]

Local Eosinophil (%) in the current study revealed significant elevation in patients with bronchial asthma and nasal polyps and cases with nasal polyps in comparison with the controls ($P < 0.001$). The notion that the differences in the severity of eosinophilic inflammatory condition is principally noticed in the airway not in plasma might be partially owing to the influences of oral steroids occasionally administrated in IgE-low non-atopic cases giving significant effects in terms of circulating eosinophil compared to airway eosinophil. Of note, airway hyper-responsiveness is an identified adverse event of eosinophil infiltrations.[17]

Shrestha et al.[14] recorded that the levels of total IgE was significantly higher non-atopic asthma group in comparison to the controls ($P < 0.05$). Additionally, Cruse et al.[18] demonstrated the capability of monomeric IgE to stimulate lung mast cells regardless of all allergen binding. As a result, IgE could probably be regarded as an inflammatory

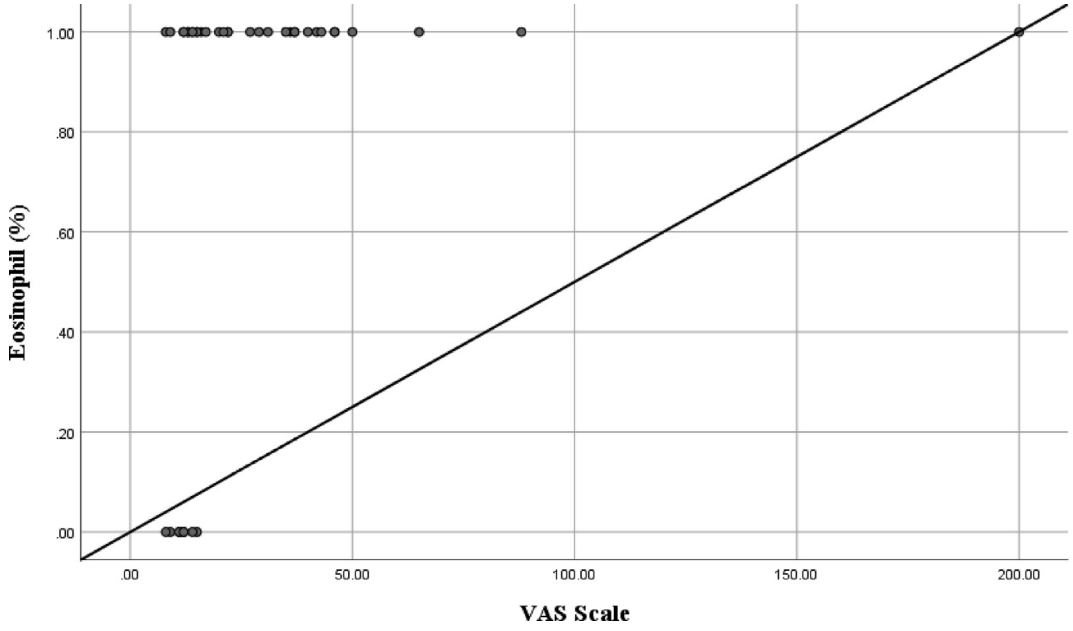

Fig. 9. Correlation between Total Eosinophil (%) levels and VAS.

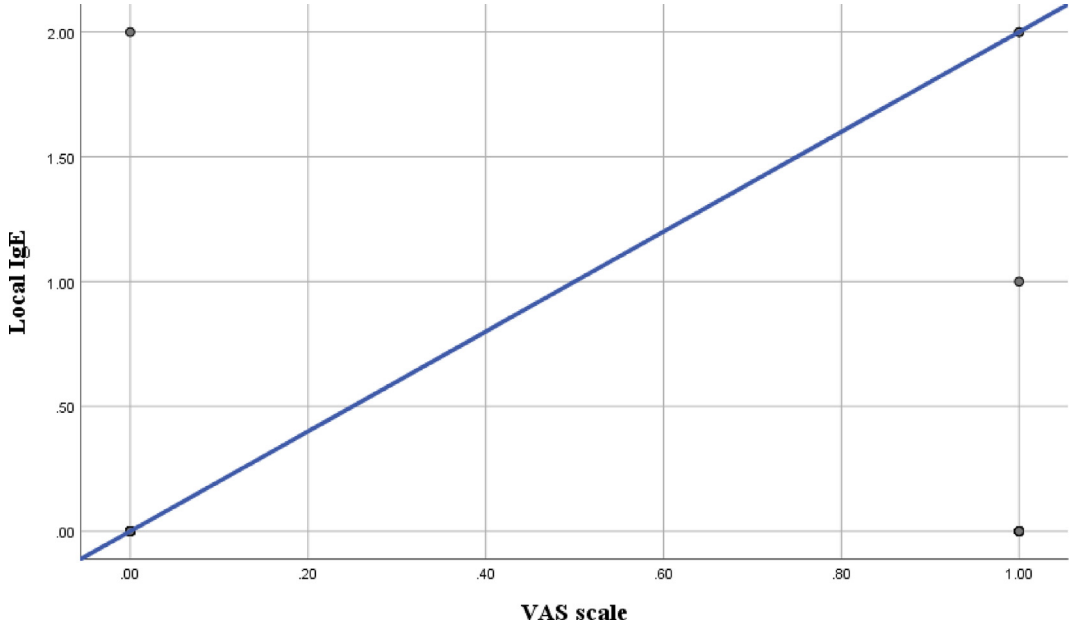

Fig. 10. Correlation between local IgE levels and VAS.

Table 5. Correlation between laboratory parameters and visual analogue scale for bronchial asthma severity.

Variables	Correlation Coefficient(r)	*P* value
Total Eosinophil (%)	0.122	0.45
Local IgE	0.89	<0.001
Local Eosinophil (%)	0.79	<0.001

Abbreviations: *P* value, Probability value.

mediator regardless of atopic condition and a component of non-atopic asthma demonstrating great level of IgE might display resemblances with atopic cases with regard to the molecular degree.,[19] non-atopic asthmatics in our study had no evidence of enhanced production of total serum levels of IgE.

It has been demonstrated that allergen-specific IgE biosynthesis is very predominant in the upper airway mucosa, in which allergens are often

retained.[20] The present study reported significant elevation in local IgE showed between cases with bronchial asthma and nasal polyps and cases with nasal polyps in comparison to controls. ($P < 0.001$). In line with our study, Pillai et al.[21] have revealed that IgE is elevated in the bronchial mucosa among cases with non-atopic asthma.

Among patients within group A, six (20%) patients had intermittent bronchial asthma. Whereas nine (30%) patients had moderate persistent bronchial asthma, 12 (40%) patients had severe persistent asthma. The mean VAS for assessment the severity of symptoms was 35 ± 12.

An increase in the IgE level possibilities of asthma being extensive is greatly probable and greater IgE is identified to be often accompanied by extensive forms of asthma. The great value of IgE, persistence of mucous discharge and cough are recognized as a distinctive phenotype.[22] There was a significant positive correlation between local IgE ($r = 0.89$, $P < 0.001$) and VAS for symptoms severity. In Shrestha et al.[14] study, asthma control status was demonstrated to be associated with significant association with IgE levels. Poorly controlled asthma were demonstrated to be accompanied by greater levels of total IgE. Furthermore, Shrestha et al.[14] reported that steady elevation in IgE level has been demonstrated to be accompanied by the increase in exacerbation rate, greater steps of therapeutic modalities, usage of oral steroids and non-controlled bronchial asthma. In the same line, Pillai et al. [23] reported that omalizumab of non-atopic asthmatics decreases bronchial mucosal IgE + mast cells and enhances lung functions in spite of withdrawal of traditional therapies.

There was a significant positive correlation between local Eosinophil (%) ($r = 0.89$, $P < 0.001$) and VAS for symptoms severity. In accordance with our finding, Manise et al.[24] demonstrated that severe forms of asthma were associated with higher total sputum cell counts in comparison with mild asthmatic individuals. In disagreement with the present study, Gerday et al.[25] reported that bronchial hyperresponsiveness was not significantly correlated with sputum eosinophils (%) in non-atopic group.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

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Conflicts of interest

The authors declared that there were NO conflicts of Interest.

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