

## Epidemiological and immunological study of nasal polyposis among allergic patients in Babylon province: Cross-sectional study

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### Abstract

**Objective:** To determine the prevalence of nasal polyposis among allergic patients, and to investigate the impact of polyposis on allergic inflammatory markers.

**Method:** The cross-sectional study was conducted from January 2018 to January 2019 at the Asthma and Allergy Centre, Babylon, Iraq, and comprised patients aged 15-71 years with allergic asthma and or allergic rhinitis. The patients were divided into two groups; A with nasal polyposis, and B without nasal polyposis. Other than demographical data, total serum immunoglobulin E, and blood eosinophil percentage were collected. Data was analysed using SPSS 22.

**Results:** Of the 240 patients, 81 (33.8%) were in group A, and 159 (66.2%) were in group B. The overall mean age of the sample was 35.9±13.8 years. The overall mean immunoglobulin E level was 221±141 and the mean peripheral eosinophil percentage was 4±1.68. Prevalence of nasal polyposis increased with age ( $p<0.05$ ), but was not affected by gender or residency ( $p>0.05$ ). The markers increased significantly in the presence of polyposis in patients with respiratory allergy ( $p<0.05$ ).

**Conclusion:** Nasal polyposis was found to be highly prevalent in patients with respiratory allergy and the combined presence of these two diseases caused additional increment in allergic markers.

**Keywords:** Nasal polyposis, Allergy, Asthma, Allergic rhinitis.

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### Introduction

Respiratory allergy is an immunoglobulin E (IgE)-mediated hypersensitivity reaction of the respiratory mucosal lining for inhaled allergens, with prevalence ranging 10-20%. The annual incidence of respiratory allergy was reported in the United States to be 20-40 million,<sup>1</sup> while in the middle east, including Iraq, it has been found to have increased from 9% to 38% which is because of modern lifestyle that is more urbanised.<sup>2</sup>

Clinical manifestations of respiratory allergy are the results of series of events that involve both immunological and biochemical aspects that are triggered by the inhalation of respiratory allergy involving type 1 IgE-mediated hypersensitivity reaction. Development of respiratory allergy is influenced by different factors, like genetic makeup of the individual and environmental exposure to respiratory allergens and other environmental irritants.<sup>3</sup>

Nasal polyposis (NP) arises from mucosal lining of the nose and paranasal sinuses. NP is characterised histologically by epithelial layer proliferation, hyperplasia of the mucus secreting glands, increased basement membrane

thickness, oedema, and foci of fibrosis with stromal cellular infiltration. Paucity of the epidemiological studies and variation in the methods of identification and recording of NP, including case history, simple rhinoscopic examination, nasal endoscopic assessment and/ or advanced imaging studies like computed tomography (CT) scanning, make it difficult to have an assessment of the accurate NP prevalence in the general population. NP is a disease with overall prevalence of about 2-4%, and this figure is affected by the age of the participants in a study. The exact aetiology of NP is still unknown and there are different theories that have tried to explain the formation of NP, like allergy, role of infection, abnormality of nasal autonomic nervous system, polysaccharide abnormality and enzyme abnormality.<sup>4</sup>

Although NP is not a fatal disease, it can adversely affect the quality of life of the sufferers. NP is a clinical condition that can be treated by both medical and surgical means, and, commonly, both modalities of treatments are required for optimum outcome. NP is characterised by high rate of recurrence even after endoscopic sinus surgery, with the recurrence rate reaching 40% within six months following surgery.<sup>5</sup>

There is a controversy about the association between allergy and NP. The current study was planned to assess the prevalence of NP in allergic patients, and to evaluate the impact of NP on inflammatory allergy markers, including peripheral eosinophil count and total serum IgE.

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## Patients and Methods

The cross-sectional study was conducted from January 2018 to January 2019 at the Asthma and Allergy Centre (AAC), Babylon, Iraq. After approval from the ethics review committee of the Faculty of Medicine, University of Kufa, Iraq, the sample size was calculated using the equation:  $N = Z_{1-\alpha/2}^2 P(1-p)/d^2$ . In the equation, N was the sample size,  $Z_{1-\alpha/2}$  was the standard normal variate (at 5% type 1 error  $p < 0.05$ ), P was the expected proportion in population based on previous studies, and d was precision.<sup>6</sup> The prevalence was assumed to be 10% according to the findings reported earlier<sup>7</sup> and the power of study was kept at 80%.

The study population was selected by simple random sampling from allergic patients attending the AAC. Their names were arranged in a list and chosen by using random digit table. The sample was raised from among patients aged 15-71 years with bronchial asthma, allergic rhinitis, or both. After taking informed consent from the patients, allergic rhinitis was diagnosed according to the guidelines provided by the Allergic Rhinitis and its Impact on Asthma (ARIA) initiative,<sup>8</sup> while asthma was diagnosed according to the Global Initiative for Asthma (GINA) using history and pulmonary function tests.<sup>9</sup>

History and clinical examination by physician was undertaken for all the participants and all had sensitivity to at least one of the common allergens that are routinely tested at AAC, like pollens, including five grasses, bermuda, plantain, tree I, tree II, tree III, chenopodium and mugwort, moulds, including mould I alternaria, mould II cladosporium, mould III penicillium, mould IV aspergillus, and candida, mites, including dermatophagoides pteronyssinus and dermatophagoides farina. These were tested using percutaneous skin tests with glycerine preservative extracts (Staller Genes SA-France). Other inhalant allergens such, as house dust mites (HDM) genus glycyphagus and date pollen were also tested with intradermal skin tests (Allergy Vaccine Lab., Iraq).

Patients treated by antihistamines and systemic oral steroids over the preceding two weeks and those with other inflammatory diseases and helminths infestation were excluded.

Nasal endoscopy was done by an ear nose, throat (ENT) specialist to confirm the presence or absence of NP. The patients were divided into two groups; A with NP, and B without NP.

Total serum IgE was measured using enzyme-linked immunosorbent assay (ELISA) kit (Call biotech, US) and, according to the instructions of the manufacturer, IgE level

was considered to be elevated at  $>100$  IU/ml.

Eosinophil count in peripheral blood was detected by CELL-DYN Ruby System (Abbott Diagnostics, US). Reference ranges for eosinophil percentage in normal adults is 1–6% of the total peripheral blood white blood cell count (WBC), according to the Australasian Society of Clinical Immunology and Allergy (ASCI) 2010 guidelines.<sup>10</sup>

Data was analysed using SPSS 22. Descriptive statistics were done, using frequencies and percentages for qualitative data, and mean  $\pm$  standard deviation (SD) for quantitative variables. Chi-square test was used to compare demographic information between the groups while t test was used to compare the mean values.  $P \leq 0.05$  was considered significant.

## Results

Of the 240 patients, 81(33.8%) were in group A, and 159(66.2%) were in group B. The overall mean age of the sample was  $35.9 \pm 13.8$  years. Of the total, 117(48.8%) were with allergic rhinitis, 42(17.5%) with allergic asthma and 81(33.8%) with both asthma and rhinitis. The mean IgE level was  $221 \pm 141$  and the mean peripheral eosinophil count was  $4 \pm 1.68$ .

NP was present in 24(29.6%) cases each of asthma and allergic rhinitis, and in 33(40.7%) patients who had both asthma and rhinitis (Table 1).

There was significant difference between age and the presence of NP ( $p=0.046$ ), while no significant difference was found with respect to gender and patient residency ( $p > 0.05$ ) (Table 2).

**Table-1:** Prevalence of nasal polyposis (NP) in allergic patient.

Study groups	NP ( n (%))	No NP (n(%))	Total
Asthma (n=42)	24 (29.6)	18 (11.3)	42 (17.5)
Rhinitis (n=117)	24 (29.6)	93 (58.5)	117(48.8)
Both (n=81)	33 (40.7)	48 (30.2)	81(33.8)
Total	81(100)	159(100)	240
p- value	$<0.001$		

**Table-2:** Relationship between nasal polyposis (NP) and some epidemiological variables.

Parameter	Number	NP (n (%))	No NP (n(%))	p- value
<b>Age (years)</b>				
<20	30	4 (4.9)	26 (16.4)	0.046
20-40	126	43 (53.1)	83 (52.2)	
41-60	70	27 (33.3)	43 (27.0)	
>60	14	7 (8.6)	7 (4.4)	
<b>Gender</b>				
Male	132	42 (51.9)	90 (56.6)	0.483
Female	108	39 (48.1)	69 (43.4)	
<b>Residency</b>				
Urban	168	60 (74.1%)	108 (67.9%)	0.325
Rural	72	21 (25.9%)	51 (32.1%)	

**Table-3:** Impact of nasal polyposis (NP) on inflammatory allergic markers (total immunoglobulin E [IgE] and eosinophil count).

Nasal polyposis	IgE (Mean±SD*)	Eosinophil percent (Mean±SD*)
Present (n=81)	260.36±131.505	4.64±1.726
Absent (n=159)	200.95±142.968	3.78±1.589
p-value	0.002	0.001

The mean IgE level and mean peripheral eosinophil count in allergic patients with NP were significantly greater than those in allergic patients without NP (Table 3).

## Discussion

The current study showed high prevalence of NP among allergic patients and the findings are similar to those reported earlier.<sup>11-13</sup>

In contrast, a study<sup>14</sup> in Greece recorded prevalence of about 4%, while another<sup>7</sup> reported 10% prevalence of NP in asthmatic patients.

The high prevalence of NP in our patients may be explained by environmental factors<sup>2</sup> like the dusty climate of the country that helps to transport airborne allergens, especially fungi, which aggravate allergic attacks accompanied by irritation to nasal mucosa and release more allergic inflammatory mediators participating in polyps formation. Additionally, frequent upper respiratory tract infections may be another aggravating factor.

Results showed no significant difference between the genders in terms of NP, which is line with some studies<sup>12</sup> and in contrast with others<sup>15</sup> which demonstrated male domination.

Prevalence of NP increased with age in the current study which was also reported earlier.<sup>12,13,16</sup> Also, there was no difference in the prevalence of NP according to patient's dwelling in either urban or rural areas, and this was in agreement with an earlier study.<sup>17</sup>

The current study found higher levels of peripheral eosinophilia to be the most important allergic inflammatory marker in the presence of polyposis, and this finding matched the results reported earlier.<sup>18,19</sup> Some studies found that eosinophil count was high not just in the blood of allergic patients with polyps, but they were also significantly higher in nasal mucosal tissues of atopic patients with polyps.<sup>20</sup>

In the current study the mean total serum IgE was significantly higher in patients with polyposis than those suffering from allergy alone. Similar result was reported by a study.<sup>21</sup> Another study<sup>22</sup> found that serum levels of IgE and eosinophil were significantly higher in patients with allergy and NP, and a more recent study<sup>23</sup> demonstrated

that atopic chronic sinusitis with nasal polyps (CRSwNP) patients were characterised by increased eosinophil accumulation which leads to eosinophilic inflammation characterised by elevated interleukin-5 (IL-5), eosinophil cationic protein (ECP) and total IgE. However, in contrast to the above results, one study<sup>19</sup> demonstrated no correlation between total IgE levels and mucosal disease based on computed tomography (CT).

Results of the current study confirmed the eosinophil-mediated inflammatory nature of NP that has been demonstrated by earlier studies<sup>23,24</sup> as eosinophils constitute the hallmark of polyps as a result of granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-5 action, which function to prolong eosinophil life. Also, polyps contain adhesion molecules that cause eosinophil extravasation.<sup>23,24</sup>

Elevation in eosinophil and total IgE could be explained by the supposition of many researchers who illustrated that proteins derived from different pathogens like bacteria and viruses are implicated to act as super-antigen that cause stimulation of B cells, mast cells and basophils, leading to activation of antibody-mediated immune response, with class-switching to IgE. The most important super-antigen is staphylococcus aureus enterotoxin B (SEB) and the way anti-staphylococcus aureus enterotoxins IgE present nearly in half of polyposis epithelial tissue sections.<sup>25</sup>

The local inflammatory disease of upper airways, like NP, influences systemically on inflammatory mediators and add to the burden on allergic patients by increasing the coexisting inflammatory processes as they already suffer from high level of eosinophil and IgE owing to mast cell triggering and degranulation and T-helper cell-2 (Th2) lymphocytes activation,<sup>21,25</sup> therefore the synergic effect of these two diseases will tend to worsen one another as concomitant occurrence of NP in allergic patients cause longer and severe nasal symptoms and prominent sinus radiological changes.<sup>22</sup> Equally, degree of severity in patients with allergic asthma is associated with radiological severity of nasal mucosal disease like polyposis.<sup>26</sup>

In the light of the findings, we recommend that nasal polyposis should be considered a common comorbid disease in allergic patients. Besides, patients with respiratory allergy, weather allergic rhinitis and or allergic asthma, should be routinely screened by endoscopic nasal examination for the presence of polyps to ensure appropriate management in those patients.

## Conclusion

Nasal polyposis was found to be highly prevalent in patients with respiratory allergy and the combined

presence of these two diseases caused increment in levels of allergic markers.

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**Conflict of Interest:** None.

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