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Association of Hemoglobin Level with Clinical Severity and other Disease Markers in Patients with Allergic Rhinitis

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ABSTRACT

Background: Allergic rhinitis is a common disorder of immune origin. It has a significant effect on the quality of life of patients with subsequent social, occupational, economic, and psychological effects. It is characterized by a local and systemic inflammatory process mediated by immunoglobulin E (IgE) after exposure to various types of allergens. The associated systemic inflammation is evident by raised levels of several inflammatory markers, as well as by the effect of this inflammation on various other body systems.
This study aims to characterize the prevalence of anemia in patients with allergic rhinitis and evaluate the relationship of hemoglobin level to some inflammatory biomarkers of the disease.
Methods: The study population consist of 150 patients with allergic rhinitis randomly selected from patients visiting the department of otolaryngology clinic in Al-Sadder teaching hospital in Annajaf, Iraq during the period from April 1st, 2016 to March 30th 2017. The mean age of participants was 30.7(±10.95) years with a mean duration of allergic rhinitis of 5.4(±4.7) years. In this study, several serum and nasal markers were measured which include total serum immunoglobulin-E, inflammatory cytokines (interlukine-6, interlukine-18), leptin hormone and eosinophil count in nasal smear. Suitable Statistical tests were used to evaluate different possible associations among various measured parameters of interest and $P<0.05$ was considered as significant.
Results: The study findings showed a significant negative correlation between hemoglobin levels and the serum level of IL-6, leptin, IgE and blood eosinophil count. The prevalence of anemia was significantly higher in patients with more severe nasal eosinophilia than those with mild nasal eosinophilia. Similarly, the prevalence was significantly higher in patients with perennial type of allergic rhinitis than those with seasonal type.
Conclusions: Some markers of systemic inflammation in allergic rhinitis correlate significantly with hemoglobin levels and may have etiologic contribution to the anemia in these patients specially in the perennial type of the disease .

Keywords: Allergic rhinitis, anemia, hemoglobin, Interleukin 6, interleukin 18, leptin, immunoglobulin E.

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INTRODUCTION

Allergic rhinitis is one of the most common disorder of immune origin. It is characterized by a local and systemic inflammatory process mediated by immunoglobulin E (IgE) after exposure to various types of allergen [1].
Allergic rhinitis is now looked at as primarily a Th2 inflammation with a central rule for Th2-dericevd cytokines in the pathogenesis of the disease and its clinical manifestation. A plethora of cytokines have been shown to induce, maintain and amplify the inflammatory allergic inflammation and promote IgE synthesis and release, as well their action to upregulate adhesion molecule specially for eosinophil recruiting them to the nasal mucosa and also increasing the production of mucus and increasing airway hyperreactivity. On the other hand, evidence are emerging in the literature that Th1-related cytokines play a balancing rule keeping the Th2 pathway under some control through various cytokines like IFN-gamma and IL-12 creating a functional dichotomy [1] . Allergic rhinitis is a common respiratory disease affecting 40% of children and 30% of adults in developed countries .In the united states , the prevalence of AR the prevalence of clinically diagnosed disease ranges from 14% in adults to 7% in children while in Europe the prevalence is estimated at 13% [2] [3] [4]. Data on the true prevalence of AR in Iraq is lacking , although it is estimated that the prevalence of AR across the middle east ranges from 9-38% [5]. Anemia ,defined as hemoglobin level less than 12gm/dl for adult non-pregnant female and less than 13 gm/dl for adult male[6], is known to complicate many chronic inflammatory diseases [7]
The association of anemia with asthma , AR and other atopic disorders have been reported in many studies worldwide [8] [9] [10]. Bener et al suggested that hemoglobin level and anemia may strongly contribute to the development of asthma and allergic disorders in children [11].
Anemia has been shown to be an independent risk factor for developing lower respiratory tract infections in childhood by impairing sufficient tissue oxygenation [12] which may cause some degree of immune derangements promoting development of allergic disease later in life [13] .
Several cytokines and other inflammatory markers have been shown to be elevated and corelated with the severity of AR and many of those may at the same time be implicated in the development of anemia on the long term [14] [15] [16].
The present study aims to estimate hemoglobin concentration across various degree of symptom severity in patient with AR and evaluates its relationship to

various markers in the disease like eosinophils count in blood, leptin hormone , IL-6 , IL-18 , IgE and also its relationship with types of allergic rhinitis and nasal smear eosinophils count.

PATIENTS AND METHODS

This is a cross-sectional study that enrolled 150 patients with allergic rhinitis. Sixty-eight were female (45.3%) and 82 were male (54.7%). their age ranges from 15-60 years. The participants were randomly selected during their attendance in the otolaryngology clinic in Al-Sadder teaching hospital in Annajaf, Iraq during the period from April 1st, 2016 to March 30th, 2017.

Patients with allergic diseases other than allergic rhinitis, chronic inflammatory diseases or chronic respiratory disease were excluded from the study. Written consent was obtained from each participants and ethical approval of the study was documented according to effective local regulations.

For each patient, a nasal swab was performed to obtain a nasal smear to detect and grade the degree of nasal eosinophilia. nasal eosinophilia was categorized as either normal, mild, moderate and marked or sever according to Sood (2005) [17]:

- Normal (1 +): when the eosinophilia (< 5%) or (cells >10/ HPF).
- Mild (2 +): when the eosinophilia (> 5%) or (cells 10 – 30/ HPF).
- Moderate (3 +): when the eosinophilia (50%) or numerous cells but not completely covered all microscope field.
- Marked or Severe (4 +): when the eosinophilia (50%) or numerous cells but completely covered all microscope field.

Each patient was asked to fill in a questionnaire regarding basic demographical information as well as a record of the main clinical symptoms. The latter was used to calculate a clinical severity score based on the reported severity of symptoms [18] [19].

Measurements of serum levels of IL-6, IL-18 and IgE were done using Enzyme Linked Immunosorbent Assay (ELISA) techniques. Hematological parameters were measured by automated hematological analyzer system (SYSMEX KX 21N, Japan).

Statistical analysis of data was performed by using IBM SPSS® Statistics software version 25. The data was presented as mean (± standard deviation) as descriptive statistics. Independent sample T-test was used to test for differences in non-categorical data while Chi square test was used for categorical variables. Correlation tests were used to test for some association among variables of interest. P-value of ≤0.05 was regarded as significant.

RESULTS

The mean and standard deviation of the main parameters measured during this study are shown in table 1.

Table 1 main measurements values for the some serological, hematological and other clinical parameters.

Variable	Mean ± SD	Range
Age(years)	30.733±10.95	13-60
BMI (Kg/m^2)	27.383±5.213	14-40.2
d.A.R. (years)	5.350±4.664	1-20
IGE (IU/ml)	205.6±164.8	21.3-548
IL6 (pg/ml)	15.345±8.27	3.3-40.9
IL18 (pg/ml)	72.411±46.42	12-210
Leptin (ng/ml)	10.858±13.05	3.9-90.2
Eosinophil percentage	5.223±2.868	0.81-14.1
Clinical symptoms score	3.738±1.022	1.6-9.8
Hemoglobin concentration (gm/dl)	12.84 (± 2.1)	8.2- 18.1

The study results reveal a significant negative correlation of various degrees between hemoglobin concentration and mean serum level of IL6, Leptin, IgE. On the other hand, no significant correlation was found with serum IL-18 level. A significant correlation was also found relating hemoglobin level with the eosinophil counts in the peripheral blood of the participants, these relations are summarized in table 2. However, it was found that

generally there was no significant correlation between the level of hemoglobin and the clinical severity score derived from the severity of the patient's symptoms. Similarly, no significant correlation was found between the hemoglobin level and the disease duration of the allergic rhinitis, nor with the BMI for patients.

Table 2. Summary of significant correlation between some inflammatory biomarkers and hemoglobin levels in patients with allergic rhinitis

Parameter	r	P value
IL-6	-0.30	<0.01
Leptin	-0.23	<0.01
IgE	-0.34	<0.01
Eosinophile count	-0.20	<0.05

Using Qi-square statistics , There were significant differences in the prevalence of anemia in patients subgroups based on nasal eosinophil grades ($p<0.05$) .For the normal , mild , moderate and severe group the ratios of anemic patients were 6.67%, 8.6%,31.4%, 33.3% respectively as shown in figure 1 .

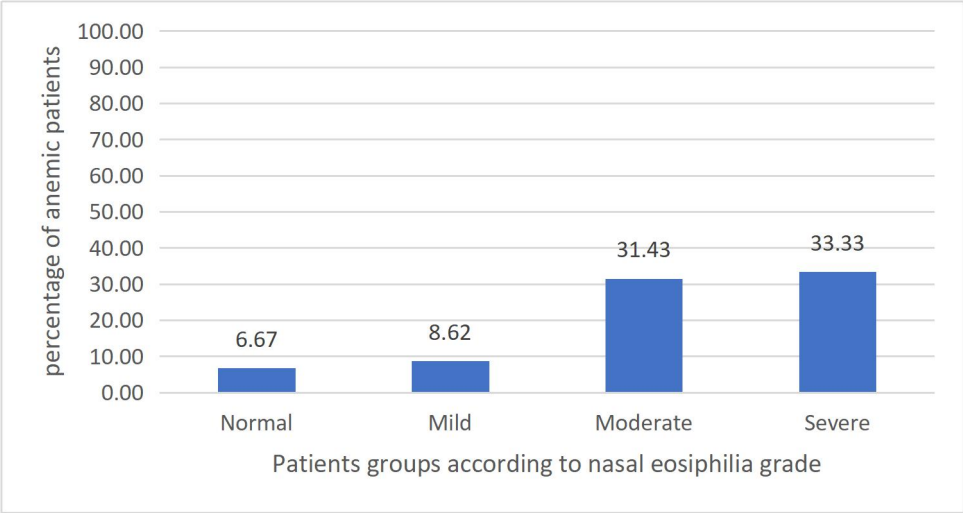

Figure 1 Prevalence of anemia in patients with allergic rhinitis and different grades of nasal eosinophilia

The prevalence of anemia was higher in the patients with perennial allergic rhinitis than in patients with seasonal allergic rhinitis ($P<0.05$), as shown in figure 2.

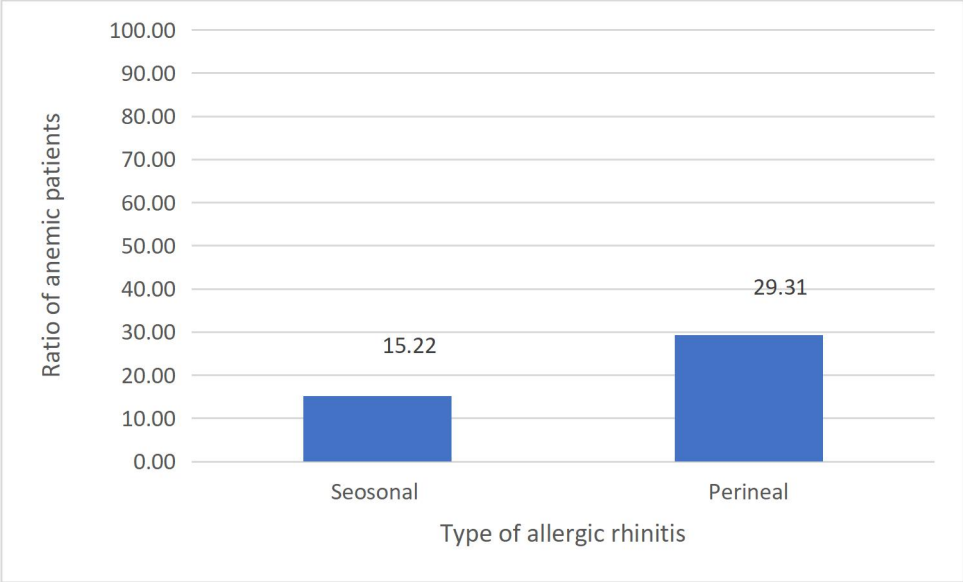

Figure 2 Prevalence of anemia in patients with different types of allergic rhinitis

DISCUSSION

Previous studies have shown that allergic diseases usually accompanied by reduction in hemoglobin levels with increased prevalence of anemia in patients with these diseases [12] [11] [9] . Studies regarding characterization of hemoglobin levels and anemia in allergic patients in Iraq are lacking and this study aimed to study this profile in these patients. This study clearly demonstrate a similar pattern of significant negative correlation between hemoglobin level and two important parameters of allergic status in allergic rhinitis , namely the serum IgE level and the blood eosinophil count , in addition the prevalence of anemia was significantly higher in patients with higher degree of nasal eosinophilia further linking hemoglobin level to the severity of allergic status.

The results of this study show a significant relationship between hemoglobin level and some inflammatory and markers in allergic rhinitis. Most prominent of these finding is the significant negative correlation between hemoglobin level and serum level of IL-6, while the association of serum IL-18 with hemoglobin level was not significant. Interlukin-6 has well established rule in inflammation , immune response and haematopoiesis [20] so its negative correlation with hemoglobin may indicate a causal effect of the systemic inflammatory state that accompany allergic rhinitis in the reduced hemoglobin level documents in the studied patients . As there was no significant relation between hemoglobin level and the severity of clinical symptoms presented as the clinical severity score so this indicates that the inflammatory status rather than the clinical presentation that dictate the severity of the associated decrease in hemoglobin level and the probability of precipitating anemia in patients with allergic rhinitis.

The negative correlation between hemoglobin level and serum level of leptin may reflect the pleotropic nature of this hormone contributing to inflammation and having a possible promoting effect on hematopoiesis [21], the presence of a negative relation may further support the presence of systemic inflammatory response in patients with allergic rhinitis .

Another finding of this study is the presence of higher prevalence of anemia in patients with perennial allergic rhinitis than patients with seasonal type of the disease possibly reflecting the effect of sustained exposure to above mentions cytokines and inflammatory biomarkers in the perennial type which further suppress the hemopoietic process and may predispose to anemia that commonly present in chronic diseases of various etiology.

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