

## Association between Interleukin-5 & Body Mass Index among Iraqi Asthmatic Patients

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### Summery:

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**Background:** Asthma is an allergic hypersensitivity disease in which many mediators play a role in its pathogenesis. One of these etiological agents is the mediators such as Interleukin-5 (IL-5). The aim of this study to demonstrate the association between IL-5 and obesity in asthma development.

**Materials & Methods:** One hundred and four sera samples for asthma cases have been studied in comparison with 41 non-asthmatic bronchitis as a patient controls beside 30 apparently healthy controls. Cytokine has been estimated using ELISA method in correlation with Body Mass Index (BMI).

**Results:** This study revealed a significant correlation between IL-5 concentration and BMI ( $P < 0.05$ ), particularly among females.

**Conclusion:** There is certain correlation between obesity and asthma accompanied by IL-5. **Key Words:** Asthma, IL-5, ELISA, BMI.

### Introduction:

It was proposed that asthma is a hypersensitivity reaction occurring due to exposure to certain allergen and leading in class switch to IgE isotype, which eventually results in liberation of mediators after the interaction between cytophilic IgE and allergen [1-3]. Some of these mediators promote cellular accumulation. These cells release pro-inflammatory and subsequently inflammatory cytokines such as IL-4, IL-5 & GM-CSF. It was denoted that these mediators play a major role in asthma pathogenesis and finally the disease severity [4-5]. Furthermore it was reported that there are many factors which enhance the disease development. One of these factors is obesity which is referred to by the term of Body Mass Index [6]. This study is a trial to estimate the BMI and its correlation with IL-5 which was proved to be elevated in sera of asthma patients [7].

### Materials & Methods:

Sera samples were collected from 94 volunteers [i.e. there is an oral permission of these patients to perform these tests] of Iraqi asthmatic patients in addition to 41 non-asthmatic bronchitis patients as patient controls and 30 apparently

healthy controls. All the patients have been diagnosed under the supervision of consultant committee in Al-Zahra'a Center for Asthma & Allergy. The main criteria for asthma are nocturnal coughing [often in children], wheezing and shortness of breath besides IgE elevation and Eosinophilia [8]. The level of IL-5 have been estimated in all sera samples according to [Diacclone Fleming Com. Kit Instructions] by using ELISA method. The patients' body weight & the length have been estimated as well as for the controls.

All the data have been analyzed statistically using Simirnov-Kolmogrov Test to show the statistically significant departure from normality and ANOVA (Kruskal-Wallis) Test for serum IL-5. The validity of these test has been determined by Resiever Operative Curve (ROC) [9].

### Results:

#### **I- Clinical and Demographic picture of the Asthmatic Patients:**

The demographic picture was listed in table 1 in comparison with control groups. The table below showed the demographic characteristics of asthmatic patients. The mean of patients' age was 27 years while the mean age for disease onset was 7 years; in comparison with patient controls the mean of age of the disease onset was 2 years.

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**Table 1. Clinical & demographic picture of Asthmatic patients in comparison with controls:**

Disease in years	Asthmatic patients	Healthy Controls	Patient Controls
Age (Mean $\pm$ SD)	27.1 $\pm$ 17.9 *	28 $\pm$ 17.9	27.7 $\pm$ 13.8
Age of onset (mean)	7	-	2
BMI (Kg/m <sup>2</sup> )	28.8 $\pm$ 11.7	21 $\pm$ 3.9	22.9 $\pm$ 3.1
No. of Females	59 (62.8%)	16 (51%)	23 (56.1%)
No. of males	35 (37.2%)	14 (49%)	18 (43.9%)
Total Number	94	30	41

\* = [P value (ANOVA) = 0.94]

It is clearly from table 1 that the mean of BMI for asthmatic patients is higher than that for control groups and all the asthmatic patients are considered as overweight individuals [up to 25 Kg / m is normal].

**II- Interleukin-5 Level in the sera of the study groups:**

Cytokines play a role in the asthma pathogenesis. One of these cytokines is IL-5. The concentrations of IL-5 in the sera of asthma cases, bronchitis cases and the healthy controls has been listed in the table below:

**Table 2. Cytokines sera levels of asthmatic patients in comparison with patients and healthy controls groups:**

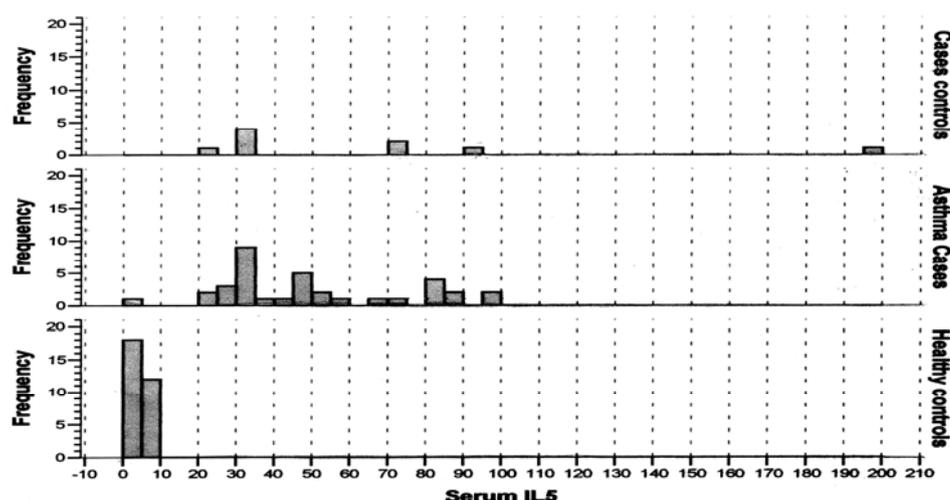
Cytokines Concentration	Asthma Cases	Healthy Controls	Patient Controls	P value
IL-5 Level in pg/ml	45 $\pm$ 24.7*	4.5 $\pm$ 1.5	33 $\pm$ 56.3	< 0.001
Number	35	30	9	
<b>P value for difference in median between:</b>				
Asthma cases Vs Healthy Controls < 0.001,				
Patient Controls Vs Healthy Controls < 0.001,				
Asthma cases Vs Patient Controls = 0.98 NS				

\* = Median  $\pm$  SD

The above table shows that there are a highly significant differences between the IL-5 concentration in the sera of apparent healthy control group [ mean con. is 4.6 with a median of 4.5 pg /ml], asthmatic patients [ mean conc. is 49 pg / ml with a median of 45 pg /ml ] ; and patient controls [ mean conc. is 46.3 with a median of 33 pg / ml ](P < 0.001) . On the other hand there is no significant difference between the IL-5 conc. in the sera of

asthmatic patients and non-asthmatic bronchitis patient controls (P = 0.98).

The next figure [Figure 1] reveals the frequency of IL-5 level among the patients' sera in addition to controls. It is clear that the majority of healthy control's values are within low level in comparison with the asthma cases. While the patient controls values accumulate at middle region between the previous other groups.

**Figure 1. The frequency of IL-5 levels in the sera of Asthma patients in comparison with control groups.**

**III- Asthma & BMI:**

The mean of BMI was measured to be 29 Kg / m<sup>2</sup> for asthmatic patients in comparison with 22.9 Kg / m<sup>2</sup> for patient controls. While BMI for apparent healthy individuals was 20.8 Kg / m<sup>2</sup>. It is clear that

there is a significant difference between asthmatic cases and the healthy control group (P = 0.007). On the other hand there is no significant difference between the mean of BMI for patient controls and asthma cases (P = 0.06).

**Table 3. Mean of Body Mass Index (BMI) in Kg/m2 in Asthma patients and the Control groups:**

BMI (Kg/m2)	Asthma Cases	Healthy Controls	Patient Controls	P value
Mean ± SD	29 ± 11.1	20.8 ± 4.6	22.9 ± 3.1	0.001
Number	88	30	41	
P value	Asthma cases Vs. Healthy Controls = 0.007 Asthma cases Vs. Patient Controls = 0.06 NS			

**IV- The Correlation between BMI & IL-5 according to gender:****Table 4. The Relationship between BMI in Female Asthmatic patients & IL-5**

Body weight groups in ( BMI Kg/m2:	Number	BMI (Kg / m2)	IL-5 (Pg / ml)
Normal < 25	22 (40)	20.1 ± 1.1	46 ± 12
Over weight (25-29.9)	14 (25.5)	27.8 ± 10	59 ± 9
Obese ≥ 30	19 (34.6)	35.1 ± 11*	88.7 ± 8.1
Total Number	55 (100)	33.7	64.6

\* = Mean ± SD , P value < 0.05

The association between BMI and IL-5 have been studied. The results are listed in the above tables 4 and 5. according to the gender. Table 4 reveals the distribution of patients according to their body weight. It shows that the higher No. of

patients are considered as over-weight or obese [33 (60%) from 55 asthma cases]. This table shows also the significant association between [ IL-5] and increasing in BMI [P < 0.05].

**Table 5. The relationship between BMI in male Asthmatic patients & IL-5:**

Body weight Groups in (BMI) (Kg/m2)	Number	BMI (Kg / m2)	IL-5 (Pg / ml)
Normal < 25	21 (52.5)	22.8 ± 3.8 *	33.8 ± 9.4
Over weight (25-29.9)	3 (7.5)	28.7 ± 12.5	50 ± 7.1
Obese ≥ 30	16 (40)	37.2 ± 12	71 ± 7
Total	40 (100)	29.7	51.6

\* = Mean ± SD , P value < 0.05

The same fact is true for males as shown in table 5. and any alteration in means of IL-5 accompanied by an elevation in BMI values in a significant pattern (P < 0.05).

The effects of BMI on the IL-5 parameters is higher among females rather than males in comparison between the previous tables [Table 4 and 5].

**Discussion:**

Considering the *age of disease onset*, asthma is a hyper-sensitivity reaction with accumulative effect while bronchitis is an infectious acute disease . Most infections occur in extremes of life. Immature immune system predisposes patients to infection in the early childhood, so bronchitis seems to develop during infancy or childhood , [10, 11]

while asthma sign's required more time to be developed. These facts explain why the age of disease onset are significantly varied though the mean of age of patients are comparable [1 & 12]. The current study indicated to the frequency of asthma to occur among *females* (62.8%) rather than *males* (37.2%). This result is compatible to that of Yue Chew and his colleagues [13]. Women seem to be at high risk for developing asthma particularly after menopause [14-15]. On the

contrary the disease is more prevalent among men at teenage than in women [16]. Most studies have reported that women are more likely to be admitted to the emergency units as a cases of acute asthma. [14-15 & 17]. The interpretation for these results may be contributed to the hormonal

differences between male and female & between females themselves before and after menopause [12, 18].

Immunoglobulin E was observed to be correlated with asthma severity which may be related to its role in the induction of a variety of *Cytokines* [19]. These cytokines are proved to play a role in asthma pathogenesis [20]. Among those cytokines was *IL-5* [21]. This study was planned to estimate IL-5 concentration in sera of asthmatic patients besides patients and healthy controls. . Particularly IL-5 gene is called nowadays as "Colony-stimulating factor, Eosinophils" [22]. Interleukin-5 was observed in high level among patients' sera [45 pg /ml] in comparison with 4.3 pg /ml for healthy controls ( $P < 0.001$ ) and [33pg /ml] for patient controls. [Only one value observed to be high and this value is excluded from the statistical analysis and represents abnormal cases and may be due to early allergic case in addition to bronchitis infection].

These findings agree with other works [23-24]. While Park *et al.*, declared that IL-5 level was higher among normal individuals beside those mild acute and severe chronic asthma cases (35.8, 89.9, 178.7 pg /ml respectively) [25]. The interpretation for this variation may be related to race, genetic variation between Iraqi patients and others in addition to the duration of the disease particularly some patients [not all] are undergone corticosteroid treatment.

Obesity was noticed to be as a risk factor in enhancing the chance for developing asthma [13, 17& 26]. This fact was confirmed by measuring the mean of *Body Mass Index* (BMI) as a good indicator for obesity [25].

This marker has been applied for patients and controls groups. The result of the current study has revealed that the mean of BMI was (29, 20.8 and 22.9 kg / m<sup>2</sup>) for asthmatic cases, healthy and patient controls respectively, with a highly significant differences between these groups ( $P < 0.007$ , 0.06 respectively). These results referred to the role of body weight in enhancing the chance for initiation of disease. Besides the role of disease in obesity development. The mechanism for this linkage is unclear. One possible reason for this correlation that people with asthma avoid exercise; so they gain weight [25]. This fact was observed to be correlated with the gender and particularly if we know that most females gain weight after menopause stage due to the hormonal disturbances [24-27]. Moreover it was proposed that asthma is more prevalent among males rather than females [13, 10]. This is true for the infants and children while the incidence noticed to be highly among women rather than men at elderly ages [16].

The link between obesity and asthma during childhood may be explained by the rise in obesity

particularly if we know that the number of obese was doubled in UK during the last decade [28].

This association between obesity and asthma reflects on the other parameters such as IL-5 and subsequently explain the highly correlation between BMI and IL-5. It is well known that there is a relationship between diseases and pathological changes, i.e. post-allergen exposure. As a result of releasing certain mediators as the cytokines, or vaso-active amines, asthmatic clinical signs appear. These events may be enhanced the possibility for decreasing in the exercises; and the rest that most of the asthmatic patients done which subsequently elevating the chance for gaining weight. Moreover corticosteroid treatment of the patients may enhance the likely for weight gain [29].

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