



The Role of Interleukin 17 Cytokine in Asthma and Its Relation with Severity of Attack

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دور سايتوكين انترلوكين 17 في مرض الربو وارتباطه بقوة النوبة

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ABSTRACT

Background: Several reviews have shown a pro-inflammatory role of Interleukin-17 (IL-17) level and have an association to numerous inflammatory illnesses, like rheumatoid arthritis, allograft rejection, systemic lupus erythematosus, and asthma. The T helper-17 (Th-17) cellular fraction of CD4+ T-cells that have been involved as the principal pathogenic cells in a variety of illnesses that has an autoimmune base, produce the cytokine interleukin-17A (IL-17A).

Asthma is a chronic inflammatory disease associated with recurrent airways obstruction that is relieved either spontaneously or with medications. Both innate and adaptive immunogenic cells in asthma collaborate with respiratory epithelium to generate "bronchial hyper-reactivity (BHR)". To determine the role of IL-17 in asthmatic patients and the relationship between IL-17 and asthma severity.

Materials and methods : The participants in the study ranged in age from 20 to 50 years old. These individuals were divided into two groups: 50 patients with asthma and 50 people who appeared to be healthy. serum IL-17 was measured in all study participants.

Results: IL-17 revealed a significant (p-0.001) rise in the values of IL-17 among asthmatic cases (mean = 176.6) compared to healthy controls (mean=22.55). The difference in IL-17 levels between severe and mild asthma was also significant, with a p-value of 0.005.

Conclusion: This study suggests that there was a significant difference in the concentrations of IL-17 between asthmatics and healthy control (p-0.001). In severe asthma, IL-17 levels are significantly (p-0.005) higher than in mild/moderate asthma.

Keywords: Severe asthma; IL-17; inflammation; healthy group; mild asthma.

INTRODUCTION

Defining endotypes of asthmatics becomes serious, primarily for asthma management. Henceforward, the necessity for biomarkers in asthma will help to differentiate between these endotypes [1]. Several previous researchers have identified a robust association between asthma and inflammations [1-5].

A well-known subtype of T helper cells (Th17), secretes IL-17 A, which is a pro-inflammatory cytokine newly discovered [6]. IL-17 production has increased in many chronic inflammatory illnesses in humans, including allograft rejection, systemic lupus erythematosus, rheumatoid arthritis, and asthma, which have been linked to IL-17 A expression [7].

In allergic airway inflammation, Th17-mediated neutrophilic airway inflammation is up-regulated, but Th2-mediated eosinophilic airway inflammation is also up-regulated [8]. The cellular axis of IL-23–Th17 stimulates eosinophilic airway inflammatory response mediated by Th2 cells [5-9].

IL-17 mRNA was found linked to CD3 gamma chain mRNA, indicating that the cytokine has a lymphocytic origin (Th17) [10]. Furthermore, it has been demonstrated that IL-17 is found in the air-ways of asthmatic subjects [11-13]. Th17 cells, a unique lineage of CD4+ effector cells, generate IL-17 [14]. Greater secretion of "CXCL1 and CXCL8 (IL-8)" from the bronchial epithelial cells by IL-17 A and IL-17 F is thought to induce the neutrophilic inflammatory response of the respiratory air-ways [15]. In bronchial biopsies from asthma patients, a higher expression of tissue IL-17, can induce bronchial fibroblasts to produce cytokines.

This study was designed to assess the role of IL-17 in asthma and its association with the severity of asthma among Iraqi patients.

PATIENTS AND METHODS:

Sampling and design

Patients at Merjan Teaching Hospital, Hilla city, Babylon, were the subjects of this study. All of the samples were taken between August 2019 and January 2023. This is a case-control study, and the participants in this study ranged in age from 20 to 50 years old. These people were divided into two groups: 50 people with asthma and 50 people who appeared to be in good health. The calculated body mass index (BMI) was utilized to decide whether or not an individual is overweight [BMI=weight (kg) / height (m)²].

Inclusion and exclusion criteria

Criteria for inclusion: Participants are separated into two groups: patients (asthmatic women and men) and healthy controls (apparently healthy non-asthmatic women and



men). Those who were accepted to participate in the current study had an average age of 20-50 years old.

Criteria for exclusion:

Any subject who had one or more of the following: diabetes mellitus, rheumatoid arthritis, pregnancy, hypertension, smokers, inflammatory illnesses of any kind, and autoimmune illnesses of any kind.

Biochemical analyses of IL 17

All subjects had venous blood samples obtained in the sitting position with a disposable three ml syringe. A venous puncture was used to draw five ml of blood from each individual, which was slowly pumped into two tubes (2.5 mL blood in an EDTA-K3 tube for IL-17 analyses after centrifuging the blood in a gel tube at 14000 RPM for 10-15 minutes. The plasma was split into three portions and kept at -20 C until analysis of IL-17 using the ELISA kit. The plasma levels of IL-17 were divided into three classes: class I (100-130pg/ml), class II (131-170pg/ml), and class III (> 170pg/ml) (11).

Assessment of asthma severity

The asthmatic subjects were evaluated by the pulmonologists at the hospital consultation clinics. The authors used a SPIRO LAB II® instrument to measure "forced expiratory volume in the first second (FEV1)" for both of the study groups in the hospital wards. According to the asthma severity (as detected by spirometric results), asthmatic patients were classified into three classes: mild if the FEV1 was > 80%, moderate if the FEV1 ranged from 50-80%, and severe if the FEV1 > 50% [16].

Statistical Analysis

SPSS version 22 was applied for the statistical investigation. (Means/SD) was utilized to illustrate continuous parameters. To match the means of any double groups, a Student paired-test was operated. A p-value of not exceeding 0.05 was deemed significant.

RESULTS AND DISCUSSIONS

Table (1) shows the demographic features of study subjects. In asthmatic patients, the mean age and SD was (36.8±10.3 years) and that of healthy controls was (36.78±10.3 years). The two groups were similar in age. Likewise, no significant differences in the mean BMI were observed between the groups. This age and BMI matching help to prevent discrepancies in IL 17 results that could be caused by large age and/or BMI differences. The study enrolled an equal number of females and males for both groups. The concentrations of IL-17 in the plasma of asthma patients and a control group were measured as illustrated in table (2). The mean and standard deviation of IL 17 among the

asthma group were ($176.6 \pm 99.3 \text{ pg/ml}$) and among the controls were ($22.6 \pm 32.2 \text{ pg/ml}$). There were significant variations in mean differences of serum IL-17 between study groups at $P=0.001$. Thirty (60%) patients class I levels of IL-17, 4 (8%) patients had class II, and 16 (32%) had class III. Table (3) shows the severity of asthma. Out of the total asthmatics, 19 (38%) revealed severe asthma based on spirometric measures, 15 (30%) showed moderate asthma, and 16 (32%) exhibit mild asthma.

Table-1: Demographic features

Features	Asthma patients	Healthy control	P-value
Ages/years	36.8±10.3	36.78±10.3	> 0.05
BMI (kg/m²)	27.6±5.7	29.8±3.9	> 0.05
Females	25	25	> 0.05
Males	25	25	> 0.05

Table-2: Interleukin 17 (Il-17) and its classes

Features	Asthma patients	Healthy control	P-value
1L-17 (pg/ml)	176.6±99.3	22.6±32.2	0.001
Class I (100-130) No. (%)	4 (8)		
Class II (131-170) No. (%)	30 (60)		
Class III (> 170) No. (%)	16 (32)		

Table (3): Asthma severity based on forced expiratory volume in one second (FEV1)

Level of severity	Number (percentage)
Mild ($\geq 80\%$)	16 (32%)
Moderate (50-80%)	15 (30%)
Severe ($< 50\%$)	19 (38%)

The T helper17 (Th17) cell fraction of "CD4+ T-cells", has been involved as principal pathogenic cells in a variety of autoimmunity illnesses, producing the cytokine interleukin-17A (IL-17A) [17]. In asthma patients, the expression of IL-17 is elevated in the bronchoalveolar lavage fluid, lungs, sputum, and serum. As well, the airways hyperresponsiveness (AHR) severity is linked to the levels of IL-17 expression [18]. The primary role of IL-17 A is to harmonize local tissue inflammatory response by boosting the production of pro-inflammatory and "neutrophil-mobilizing cytokines" and chemokines[19]. A preceding report publicized by [20], revealed there a link between high levels of IL-17 and asthma [20] supporting our outcomes.

Interestingly, transforming growth factor- β (TGF β) is a cellular cytokine with a pleiotropic effect [21-24], synthesized by respiratory epithelia and motivates fibroblast cellular growth, that may enhance pathological fibrosis of lung tissues [5]. The former reviews demonstrated a raised TGF β 1 in "obstructive lung disorders" [1-5]. As well, both TGF β and IL 1B modify Helper-T 17 body cells, which have a serious contribution to the pathogenesis of chronic inflammatory reactions [25]. Furthermore, both TGF β and interleukins can stimulate "platelet derived growth factor (PDG-F)" secretion [26,27]. PDGF is a powerful mitogen released by various body cells including fibroblasts [21,28,29] identified to subsidize an immunogenic consequence in asthma by assisting remodeling of respiratory air passages [30].

The mean serum levels of IL17 distributed according to the severity of the asthma were shown in (fig.1). There were significantly higher IL-17 levels with increasing asthma severity ($P = 0.005$).

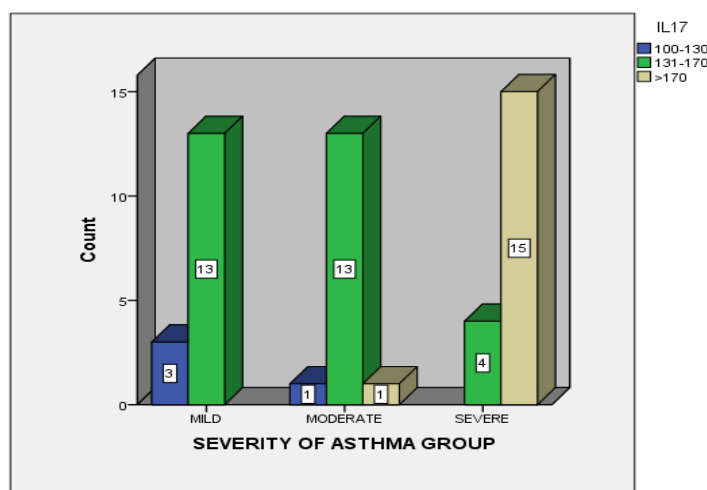


Figure-1: Distribution of IL 17 mean serum levels according to classes of asthma severity.



Similar to our findings, IL-17 levels in severe asthma patients were higher than in with milder forms of asthma, had reported according to Ref. [31]. The expression of IL-17 is amplified and contributes to severe bronchial asthma also reported by another study, in which high sputum IL-17 levels contribute to neutrophilia of respiratory epithelia in obese asthma patients [32].

When compared to healthy controls, the Th17 cellular number in the serum, sputum and bronchoalveolar lavage secretions are higher in allergic asthma patients, and Th17 cell levels are positively correlated with the degree of airway remodeling [11,33]. Along similar studies, other research has established a relation between IL-17 synthesis and the severity of asthma [34].

CONCLUSION

The study suggested that there were significant differences in the levels of IL-17 between asthmatics and healthy control ($p=0.001$). In severe asthma, mean serum IL-17 levels are higher than in mild/moderate asthma ($p=0.005$).

Conflict of interests.

There are non-conflicts of interest.

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الخلاصة

الخلفية

أظهرت العديد من المراجعات دورًا مؤيدًا للالتهابات لمستوى إنترلوكين 17 (IL-17) وله ارتباط بالعديد من الأمراض الالتهابية، مثل التهاب المفاصل الروماتويدي، ورفض الطعم الخيفي، والذئبة الحمامية الجهازية، والربو. الجزء الخلوي T المساعد-17 (Th-17) من الخلايا التائية + CD4 التي شاركت كخلايا ممرضة رئيسية في مجموعة متنوعة من الأمراض التي لها قاعدة مناعية ذاتية، ينتج السيتوكين إنترلوكين-17 (IL-17A). الربو هو مرض التهابي مزمن يرتبط بانسداد الشعب الهوائية المتكرر، ويتم علاجه إما تلقائيًا أو بالأدوية. تتعاون كل من الخلايا المناعية الفطرية والتكيفية في الربو مع ظاهرة الجهاز التنفسي لتوليد "فرط نشاط الشعب الهوائية". (BHR) تحديد دور IL-17 في مرضى الربو والعلاقة بين IL-17 وشدة الربو.

المواد والطرق

تراوحت أعمار المشاركين في الدراسة من 20 إلى 50 سنة. تم تقسيم هؤلاء الأفراد إلى مجموعتين: 50 مريضًا بالربو و50 شخصًا يبدو أنهم يتمتعون بصحة جيدة. تم قياس المصل IL-17 في جميع المشاركين في الدراسة.

النتائج

كشف IL-17 عن ارتفاع معنوي ($P=0.001$) في قيم IL-17 بين حالات الربو (المتوسط = 176.6) مقارنة مع الأصحاء (المتوسط = 22.55). كان الفرق في مستويات IL-17 بين الربو الحاد والخفيف كبيرًا أيضًا، حيث بلغت القيمة الاحتمالية 0.005.

الاستنتاج

تشير هذه الدراسة إلى وجود اختلاف كبير في تراكيز IL-17 بين مرضى الربو والأصحاء ($P=0.001$) في حالات الربو الشديدة، تكون مستويات IL-17 أعلى بشكل ملحوظ ($p=0.005$) منها في حالات الربو الخفيفة/المعتدلة.

الكلمات المفتاحية: الربو الشديد. إيل-17؛ اشتعال؛ مجموعة صحية؛ ربو خفيف.