

Assessment of Immunoglobulin E in Asthmatic Pediatric Patients

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ABSTRACT

Background: Recurrent reversible symptoms of hyperresponsiveness of bronchi and obstruction of air flow occur in bronchial asthma which is a chronic airway disease with pathologic inflammation. **Objective:** To assess the IgE level among asthmatic patients in children.

Patients and Methods: our research was conducted on 116 children (87 asthmatic cases and 29 non-asthmatic healthy age and sex matched as control group). This were recruited from Pediatric Department and Outpatient Clinic at Zagazig University Hospital. The cases were subdivided to three groups according to the GINA guide line. They were assessed for the pulmonary functions with assessment of IgE.

Results: In terms of IgE levels, statistically significant differences were found between the four groups tested with all asthmatic groups were significantly higher than control group ($p < 0.001$). Well controlled group had higher values of FEV1% and FVC% with statistically significant difference between asthmatic patients groups. Sensitivity; specificity, PVP and PVN of IgE level were 100.0%, 96.6%, 98.9% and 100% respectively.

Conclusion: IgE level can be considered a good predictor for severity of bronchial asthma.

Keywords: Bronchial asthma, Immunoglobulin E (IgE).

INTRODUCTION

Asthma is a diverse illness defined by persistent airway inflammation. Cough, chest tightness, shortness of breath and wheezes are the main respiratory symptoms of bronchial asthma, which differs in severity, with diminished expiratory airflow. Airway inflammation is linked to airway hyperreactivity, also known as bronchial hyperresponsiveness (BHR), which is described as the airways' natural inclination to constriction due to various stimuli (like irritants and environmental allergens) ⁽¹⁾.

According to family and twin research, genetics has a major influence in the development of asthma and allergies, most likely via multiple genes of moderate impact (i.e., genes linked with relative e risks in the range of 1.2–2) ⁽²⁾. Asthma in humans may be initiated due to oxidative stress processes, which contributed due to gene polymorphism ⁽³⁾.

Estimation of the total IgE level supports the existence of atopy. Atopy, or the tendency to create excessive amounts of immunoglobulin (Ig) E antibodies in response to allergens, is almost always found in children with asthma ⁽⁴⁾. Asthma patients often have more sensitive airways, making them more sensitive to allergens, irritants, exercise, cold air, and virus infection ⁽⁵⁾.

A child's serum IgE concentration varies with age and is typically less than 10 IU/mL in the first year of life for the majority of infants. According to many population researches, prevalence of asthma/BHR and total serum IgE levels are linked, regardless of particular allergy reactivity or allergy symptoms to commonly allergenic substances ⁽⁶⁾.

We aimed at this study to assess the IgE level among asthmatic patients in children.

PATIENTS AND METHODS



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A case-control study conducted on 116 individuals at Pulmonology & Allergy Unit in Pediatric Hospital and Biochemistry Department divided in to 4 groups: A: 29 non-asthmatic participant. B: 29 well controlled asthmatic patient. C: 29 partially controlled asthmatic patient. D: 29 uncontrolled asthmatic patients. Classification of asthmatic children occurred according to the level of asthma control into three groups: controlled, partially controlled or uncontrolled according to GINA recommendation at 2008 considering the following items ⁽⁷⁾: Daytime symptom, limitation of activation, nocturnal symptom, need for relievers, pulmonary function test, and exacerbation.

Ethical approval:

Research Ethics Committee of Zagazig University's Faculty of Medicine approved the study after all participants' parents gave written informed consent (ZU-IRB#6175/14-6-2020). Work was done in accordance with the Declaration of Helsinki, the ethical code of the world medical association for human studies.

Inclusion criteria: Children from both sexes with bronchial asthma aged from 5-15 years after taking approval from their parents.

Exclusion criteria: Children with chronic pulmonary disease, children suffering from liver, kidney and heart disease and parents' refusal of participation.

All patients were subjected to full history taking, general and local chest examination.

Laboratory investigations:

Routine complete blood count, C-reactive protein, liver function tests, kidney function tests, IgE level assessment, and pulmonary function tests.

We used spirometry to assess lung function and volume versus time. It is a simple and quick technique to carry out: Patients were instructed to take a deep

breath and then forcibly evacuate air for as long and as rapidly as possible (a forced vital capacity manoeuvre-). Forced expiratory volume in one second (FEV1), Forced vital capacity (FVC) and the ratio of the two volumes (FEV1/FVC) were assessed.

Blood samples were obtained from all subjects 2 ml of whole blood was collected into EDTA-treated tubes for DNA extraction.

Statistical analysis

The acquired data were coded, entered, presented, and analyzed by computer using the Statistical Package for Social Science (SPSS) version 26 data base software application. Frequencies and percentages were used to depict qualitative data. Mean, standard deviation (SD), and (minimum-maximum) values were determined for quantitative variables. ANOVA was used to compare more than two groups of normally distributed variables, while the Kruskal Wallis test was used to compare more than two independent groups of non-normally distributed variables. The Chi square (X²) test was performed to determine the relationship between several qualitative factors. To analyse the link between various study variables, the person correlation coefficient was determined, with (+) indicating direct association and (-) indicating inverse correlation. In addition, numbers close to 1 suggest significant connection, whereas

values close to 0 indicate weak correlation. The results were considered statistically significant and highly statistical significant when the significant probability (P value) was ≤ 0.05* and < 0.001** respectively. The validity, sensitivity, specificity, predictive value for positive (PVP), and predictive value for negative (PVN) were determined.

RESULTS

There were no statistically significant differences between the four studied groups as regards age (years) and sex. However, there was statistically significant difference between the studied groups as regards the family history as the majority of asthmatic patients had positive family history while none of controls had positive family history (Table 1).

There were statistically significant differences between the four studied groups regarding IgE level where all asthmatic groups were significantly higher than control group (p < 0.001) (Table 2).

Box plot showed that well-controlled group had higher values of FEV1% and FVC% with statistically significant difference between asthmatic patients' groups (Figures 1 & 2). Sensitivity, specificity, PVP and PVN of IgE level were 100.0%, 96.6%, 98.9% and 100% respectively (Table 3 & Figure 3).

Table (1): Basic characteristics of the four studied groups

Variable	Uncontrolled group (n=29)	Partially controlled group (n=29)	Well controlled group (n=29)	Control group (n=29)	Tests	
					f	P value
Age (years)						
Mean ± SD	7.96 ± 3.6	7.9 ± 2.8	8.4 ± 2.8	8.83 ± 2.82	0.6	0.6
Range	(5-14)	(5-14)	(5-15)	(5-14)		(NS)
Weight (kg)						
Mean ± SD	33.8 ± 14.6	28.7 ± 10.4	33.2 ± 9.2	31.2 ± 12.86	1.1	0.3
Range	(18-60)	(17-50)	(20-66)	(19-66)		(NS)
Height (m)						
Mean ± SD	1.35 ± 0.22	1.26 ± 0.15	1.31 ± 0.13	1.35 ± 0.17	1.6	0.2
						(NS)
BMI (kg/m²)						
Mean ± SD	17.89 ± 3.73	17.54 ± 3.23	18.36 ± 2.56	16.51 ± 2.74	3.2	0.075
						(NS)
Variable	No (%)	No (%)	No (%)	No (%)	X²	P value
Sex						
Female	13 (44.8)	12 (41.4)	15 (51.7)	13 (44.8)	0.66	0.9
Male	16 (55.2)	17 (58.6)	14 (48.3)	16 (55.2)		(NS)
Family history						
Negative	1 (3.4)	4 (13.8)	8 (27.6)	29 (100)	130.1	<0.001*
Positive	28 (96.6)	25 (86.2)	21 (72.4)	0 (0)		

(X²) chi-square test. (f) one way ANOVA (NS) non-significant

Table (2): IgE results of the four studied groups

Variable	Uncontrolled (TT) group (n=29)	Partially controlled (CT) group (n=29)	Well controlled (CC) group (n=29)	Control group (n=29)	Tests		
					F	P	Post hoc test
IgE level (IU/ml) Mean ± SD	163.44 ± 9.62	154.58 ± 16.55	150.0 ± 15.5	41.37 ± 9.27	178.9	<0.001	P1<0.001* P2<0.001* P3<0.001* P4=0.468 P5=0.127 P6=0.875

(f) one way ANOVA (NS) non-significant (S) Significant @ kruskal wallis ANOVA
 P1=uncontrolled group vs. control group. P2=partially controlled group vs. control group. P3= well controlled group vs. control group. P4 =uncontrolled vs. partially controlled group. P5 =uncontrolled group vs. well-controlled group. P6 = partially controlled group vs. well controlled group.

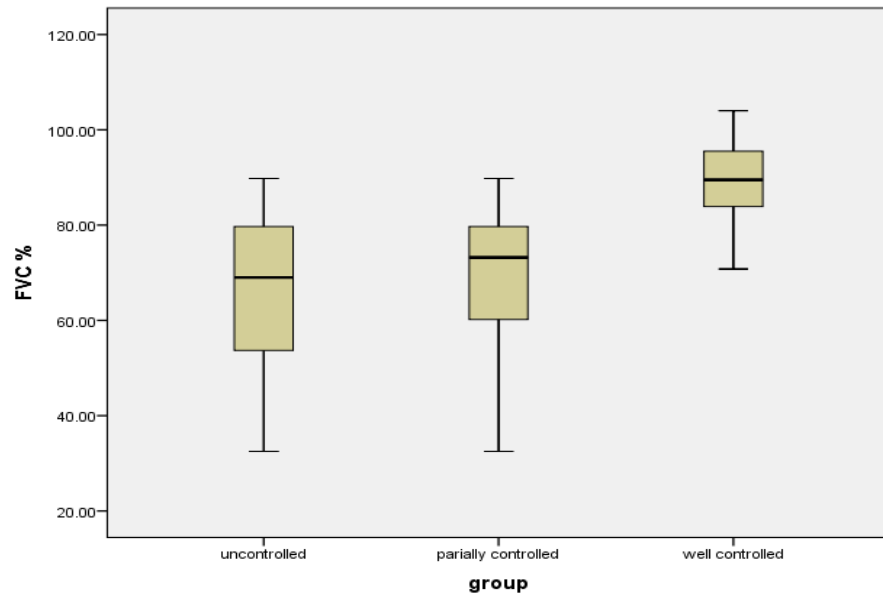


Figure (1): Comparison of FVC% between asthmatic patients.

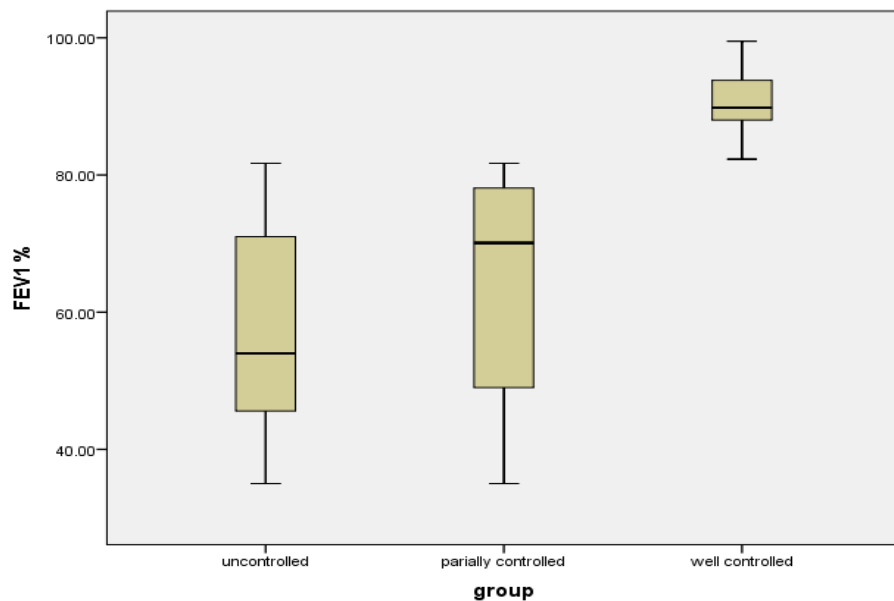


Figure (2): Comparison of FEV1% between asthmatic patients.

Table (4): Sensitivity, specificity, PVP and PVN of IgE level as a predictor for asthma

IgE level			Groups			
			Asthmatic (n=87)		Control (n=29)	
Positive ≥ 111 (n=88)			87		1	
Negative <111 (n =28)			0		28	
AUC	CI	CUT off	Sensitivity	Specificity	PPV	NPV
0.995	0.984-1.0	111	100.0%	96.6%	98.9%	100.0%

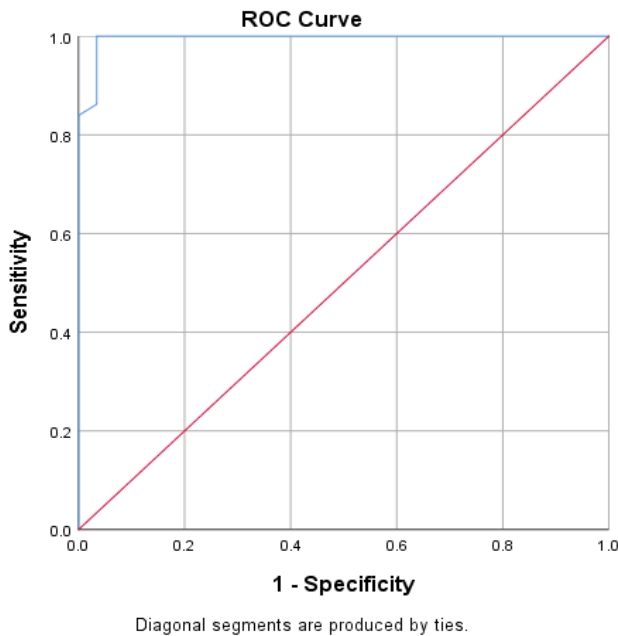


Figure (3): Roc curve of IgE level as a predictor for asthma.

DISCUSSION

Bronchial asthma, a common allergic disorder among children, is a chronic airway inflammatory disease. It mainly involves mastocytes, T-lymphocytes and eosinophilic granulocytes. Clinically, it tends to occur with the symptoms of recurrent dyspnea, wheezing, cough and chest distress. According to an epidemiological survey, the current number of asthmatic patients in the world is approximately 0.334 billion. In 2010, the prevalence rate of asthma among Chinese children was about 0.42- 5.73%, the mean of which was 2.32% (8). It is of great significance to foresee the risk of asthma incidence, but there was no sufficient evidence for the identification of asthma susceptibility gene yet both at home and abroad (9).

There have been numerous studies documenting associations between immunoglobulin E level and bronchial asthma in children (10). The main aim of this study was to explore the predictive value of IgE assessment in asthmatic children.

Regarding the basic characteristics of the studied groups, we discovered no statistically significant differences between the four examined groups in terms of age (years), gender, weight (kg), and height (m). Nevertheless, a statistically significant difference was found between the groups investigated in terms of BMI (kg/m²), with well-controlled asthmatic patients having

the highest BMI (19.15 ± 3.3). The majority of asthmatic patients had positive family history while none of controls had positive family history. There was statistically significant difference between the studied groups as regards family history. This agrees with **Li et al.** (11) who found that there was a high statistically significant difference between the studied groups regarding the family history.

The present results showed that there were highly significant differences between the four studied groups as regards FEV1% and FVC where higher values were among control group and well-controlled group. In the study by **Tian et al.** (12) they assessed the pulmonary function via MINAT (Japan) AS-407 pulmonary function instrument, Main indicators included forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), peak expiratory flow (PEF), forced mid-expiratory flow rate (FEF₂₅₋₇₅), mid-expiratory flow rate at 50% vital capacity (MEF₅₀) and mid-expiratory flow rate at 75% vital capacity (MEF₂₅). They found that there was a significant difference between studied groups regarding FVC, FEV1, PEF, FEF₂₅₋₇₅, MEF₅₀ and MEF₂₅ (p<0.05). Therefore, there is an agreement between **Tian et al.** (12) with our results regarding the pulmonary function. In addition, for older aged cases **Sun et al.** (13) also found that there was a highly significant difference between studied groups regarding mean FEV1/FVC ratio and mean FEV1 (p < 0.001).

In bronchial asthma, IgE is thought to play an important role in the development of bronchial hyper-responsiveness. The present study also revealed increased mean serum IgE levels (150.0 ± 15.5, 154.58 ± 16.55, and 163.44 ± 9.62 IU/ml in CC, CT and TT groups respectively) as compared to control group (41.37 ± 9.27) and correlated well with severity of asthma. These finding are consistent with studies done by **Ching et al.** (11), **Chandran et al.** (12) and **Chaudhary et al.** (13).

In **Thirunavukkarasu et al.** (14) study mean IgE levels ranged from 151.95 IU/ml in normal subjects to 1045.32 IU/ml in severe asthmatics and they also observed that IgE levels were increased as the severity of asthma was increased.

Sensitivity, specificity, PVP and PVN of IgE level for prediction of asthma were 100.0%, 96.6%, 98.9% and 100% respectively. The total serum IgE level is increased in children with asthma and wheeze. However, nothing is known about the long-term relationship between total IgE and the onset of

wheezing symptoms and allergy sensitization in children. It is believed that early sensitization and a persistent wheezing phenotype are linked to higher-than-expected total IgE levels in order to examine these long-term relationships. Subjects with high levels of serum IgE at 1 year of age still had high levels of IgE at 6 and 11 years of age, according to the results. High serum IgE levels were shown to be related with both persistent wheeze and early sensitization. This finding led researchers to infer that while total serum IgE levels decrease with age, IgE levels are higher in children who are more likely to develop persistent wheeze and early sensitivity to local aeroallergens⁽¹⁵⁾. In agreement with our results, **Ahmed Al Obaidi et al.**⁽¹⁶⁾ using the ROC curve, showed that it was clear that by selecting the correct cut-off value, it was able to achieve high sensitivity while also having good specificity. At the 200 IU/mL cut-off point in this study, it was shown that 93% of patients tested positive for HIV, but only 90% of controls tested positive. Serum IgE levels were found to be predictive of asthma and may be combined with other indicators to help distinguish between asthmatic and non-asthmatic patients.

CONCLUSION

IgE level can be considered a good predictor for severity of bronchial asthma.

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