

# CORRELATION OF SERUM IMMUNOGLOBULIN E LEVELS WITH ASTHMA SEVERITY IN CHILDREN (2-12 YEARS) PRESENTING TO A TERTIARY CARE HOSPITAL

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## ABSTRACT

**OBJECTIVE:** To determine the correlation of serum immunoglobulin E (IgE) levels with asthma severity in children (2-12 years) presenting to Pediatric Outpatient Department, Liaquat National Hospital, Karachi.

**METHODS:** A descriptive cross-sectional study was done at Department of Pediatric Medicine, Liaquat National Hospital, Karachi from June 2016 to December 2016. A total of 106 children with symptoms of airflow obstruction characterized by recurrent cough, difficulty in breathing and wheeze were included in this study. The severity of asthma were classified as intermittent, mild, moderate or severe persistent asthma based on subjective experience of the patients. Blood samples for serum IgE levels were taken and serum IgE levels were estimated by automated chemiluminescence system.

**RESULTS:** The average age of the children was  $6.38 \pm 6.0$  years. In this study, intermittent asthma was observed in 24 (22.64%) cases. There were 30 (28.6%) children with mild asthma, 40 (37.74%) children with moderate asthma and severe asthma was found in 12 (11.32%) children. The mean IgE concentration was lowest in children with intermittent asthma ( $277.92 \pm 45.87$  IU/ml), higher in children with mild persistent asthma ( $487.47 \pm 58.47$  IU/ml) and highest in children with moderate and severe persistent asthma ( $688.75 \pm 52.08$  and  $1078.83 \pm 64.10$  IU/ml), respectively. .

**CONCLUSION:** Our results support the hypothesis that severity of asthma is reflected by serum IgE levels in children. We found that the mean IgE concentration correlates with the severity of asthma, being highest in the patients with severe asthma and dropping down as the symptoms wane.

**KEY WORDS:** Asthma (MeSH); Immunoglobulin E (MeSH); IgE concentration (Non-MeSH); Bronchoconstriction (MeSH); Allergy (MeSH); Hypersensitivity (MeSH); Child (MeSH); Child, Preschool (MeSH).

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## INTRODUCTION

Asthma is the most important risk factor for asthma in children. In this condition allergen exposure causes excessive production of IgE antibodies.<sup>1</sup> IgE cause bronchoconstriction by releasing various inflammatory mediators.<sup>2</sup>

High serum IgE level is an indicator of allergen exposure in genetically predisposed individuals.<sup>3</sup> There is a strong relationship between total IgE and asthma prevalence.<sup>4</sup> It is also used to determine

the severity and persistence of asthma in later adulthood.<sup>5,6</sup> Serum IgE level can provide useful information regarding the severity of asthma and persistence of bronchial hyper responsiveness.

Pulmonary function test is the most accurate method of determining air flow obstruction,<sup>7</sup> but it is difficult to perform in children. There is an association between serum IgE levels and the degree of airflow obstruction, hence the severity of asthma can be determined by it.<sup>8</sup> There is no

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consensus on level of serum IgE in relation to asthma severity; different studies have reported varied levels of IgE. The usually accepted range is from 1.5-100 IU/ml.<sup>9</sup> A strong relationship is found between total serum IgE and asthma severity.<sup>10-12</sup>

Our hypothesis is that the severity of asthma in children can be reflected by serum IgE levels. The study is intended to estimate the current magnitude of asthma severity and IgE level in our local population. The rationale behind it is that there is no consensus on mean IgE level and it varies from study to study.<sup>9-11</sup>

The outcome of this study can be used for risk stratification and will help in counselling of patients and attendants. The patients with raised serum IgE levels can then be advised to avoid/minimize allergen exposure for better asthma control.

## METHODS

This cross sectional study was done at Department of Pediatric Medicine, Liaquat National Hospital Karachi from June to December 2016. Total 106 study subjects were included in the study with non probability consecutive sampling technique. WHO software for sample size determination was used considering  $P=13.33\%$ <sup>12</sup>,  $d=6.5\%$ , with 95% confidence level. Inclusion criteria were age between 2 to 12 years of either sex with symptoms of airflow obstruction characterized by recurrent cough, difficulty in breathing and wheeze.

Children having known or suspected immunodeficiency, congenital heart disease, neurologically impaired children (as they are at risk for recurrent aspiration), lung diseases like tuberculosis, bronchiectasis, cystic adenomatoid malformation of lung and cystic fibrosis were excluded from study. Children having the history of allergic rhinitis, allergic dermatitis, autoimmune diseases and parasitic infections were also

excluded from the study.

Children fulfilling the inclusion criteria were included in the study after taking informed consent from the parents/care takers. All the study subjects were asked about clinical symptoms and on the basis of their responses, severity of asthma (as per operational definition) was classified as intermittent, mild, moderate or severe persistent asthma. Blood samples for serum IgE levels was drawn by a trained pediatric nurse and sent to the laboratory of Liaquat National Hospital. Serum IgE levels were estimated by automated chemiluminescence system (The Chiron Diagnostics ACS: 180). All data about patients' demographics, history, physical examination, severity of asthma and serum IgE level was recorded by principal investigator on a predesigned performa.

Data was entered and analyzed in SPSS version 19. Mean $\pm$ SD was calculated for quantitative variables i.e. age, weight, and height, duration of disease and serum IgE level. Frequency and percentage was calculated for qualitative variables i.e. gender and severity of asthma. Stratification was done for gender, age, weight, height and duration of asthma to see the effect of these on severity of asthma and IgE levels, chi square test and one way ANOVA were applied respectively, at 95% CI and p value  $\leq 0.05$  was considered as significant.

### Operational Definitions:

**Asthma:** Presence of any two or more of the following symptoms of airflow obstruction more than 4 times in a year characterized by: cough, shortness of breath/fast breathing or presence of wheeze.

**Severe Persistent Asthma:** Patient with continuous day time symptoms (as stated above) and frequent night symptoms ( $> 3$  times per week).<sup>8</sup>

**Moderate Persistent Asthma:** Patient with daily day time symptoms and night symptoms  $> 1$  per week.

**Mild Persistent Asthma:** Patient with day time symptoms  $> 2$  times per week and night symptoms  $> 2$  times per month.

**Intermittent Asthma:** Patient with day time symptoms  $\leq 2$  times per week

**TABLE I: DEMOGRAPHIC PROFILE OF THE ASTHMATIC PATIENTS (n=106)**

Variables	Number (Percentage)
<b>Age (years)</b>	
2-5	47 (44.34%)
6-10	44 (41.51%)
> 10	15 (14.15%)
<b>Gender</b>	
Male	63 (59.43%)
Female	43 (40.57%)
<b>Weight (kg)</b>	
$\leq 16$	53 (50%)
$> 16$	53 (50%)
<b>Height (cm)</b>	
$\leq 116$	52 (49.06%)
$> 116$	54 (50.94%)
<b>Duration of Asthma (months)</b>	
$< 24$	49 (46.23%)
$> 24$	57 (53.77%)
<b>Severity of Asthma</b>	
Intermittent Asthma	24 (22.64%)
Mild Persistent Asthma	30 (28.30%)
Moderate Persistent Asthma	40 (37.74%)
Severe Persistent Asthma	12 (11.32%)

**TABLE II: MEAN SERUM IGE LEVELS IN ASTHMATIC PATIENTS WITH RESPECT TO ASTHMA SEVERITY**

IgE Level (IU/ml)	Intermittent Asthma	Mild Persistent Asthma	Moderate Persistent Asthma	Severe Persistent Asthma	
Mean	277.92	487.47	688.75	1078.83	
Std. Deviation	45.87	58.47	52.08	64.10	
95% CI for Mean	Lower Bound	258.55	465.63	672.09	1038.10
	Upper Bound	297.29	509.30	705.41	1119.56

**TABLE III: COMPARISON OF MEAN SERUM IGE LEVELS IN ASTHMA SEVERITY WITH RESPECT TO AGE GROUPS**

Age Group (years)	Severity of Asthma	n	IgE Levels (IU/ml)		P-Values
			Mean	Std. Deviation	
2-5 (n=47)	Intermittent Asthma	11	280.91	33	0.0005
	Mild Persistent Asthma	22	481.05	50.15	
	Moderate Persistent Asthma	11	668.27	39.64	
	Severe Persistent Asthma	3	1094	102.67	
6-10 (n=44)	Intermittent Asthma	13	275.38	55.77	0.0005
	Mild Persistent Asthma	7	516.57	77.01	
	Moderate Persistent Asthma	22	681.59	51.09	
	Severe Persistent Asthma	2	1015.5	14.84	
> 10 (n=15)	Mild Persistent Asthma	1	425	-	0.0005
	Moderate Persistent Asthma	7	743.43	37.85	
	Severe Persistent Asthma	7	1090.43	48.72	

**TABLE IV: COMPARISON OF MEAN SERUM IGE LEVELS IN ASTHMA SEVERITY WITH RESPECT TO GENDER**

Gender	Severity of Asthma	n	IgE Levels (IU/ml)		P-Value
			Mean	Std. Deviation	
Male (n=63)	Intermittent Asthma	13	273.85	48.741	0.0005
	Mild Persistent Asthma	18	490.17	55.730	
	Moderate Persistent Asthma	26	688.46	51.603	
	Severe Persistent Asthma	6	1082.00	70.529	
Female (n=43)	Intermittent Asthma	11	282.73	44.066	0.0005
	Mild Persistent Asthma	12	483.42	64.679	
	Moderate Persistent Asthma	14	689.29	54.937	
	Severe Persistent Asthma	6	1075.67	63.579	

**TABLE V: COMPARISON OF MEAN SERUM IGE LEVELS IN ASTHMA SEVERITY WITH RESPECT TO WEIGHT**

Weight (kg)	Severity of Asthma	n	IgE Levels (IU/ml)		P-Value
			Mean	Std. Deviation	
≤ 16 (n=53)	Intermittent Asthma	14	284.29	35.020	0.0005
	Mild Persistent Asthma	21	490.62	57.630	
	Moderate Persistent Asthma	15	661.53	37.960	
	Severe Persistent Asthma	3	1094.00	102.679	
> 16 (n=53)	Intermittent Asthma	10	269.00	58.775	0.0005
	Mild Persistent Asthma	9	480.11	63.268	
	Moderate Persistent Asthma	25	705.08	53.175	
	Severe Persistent Asthma	9	1073.78	53.849	

and night time symptoms <2 times per month.

## RESULTS

There were total 106 children in this study. Most of the children were below 10 years of age as presented in Table I. The average age of the children was  $6.38 \pm 6.0$  years. Average weight, height, duration of asthma and asthma severity are presented in Table I. Out of 106 patients, 59.43% were male and 40.57% were female (Table I). The mean IgE concentration was lowest in children with intermittent asthma  $277.92 \pm 45.87$  IU/ml, higher in children with mild persistent asthma  $487.47 \pm 58.47$  IU/ml) and highest in children with moderate and severe persistent asthma  $688.75 \pm 52.08$  and  $1078.83 \pm 64.10$  IU/ml, respectively. Comparison of mean serum IgE levels among asthma severity with respect to age groups, gender, height, weight and duration of asthma is shown in Table III to VII. Significant difference of mean serum IgE levels was observed among patients with a range of severity of asthma.

## DISCUSSION

Acute exacerbation of asthma is precipitated by environmental factors, like inhalant allergens.<sup>13</sup> IgE is responsible for inflammation of airways and various allergic reactions. Severity of asthma may be modulated by IgE as the IgE levels are associated with asthma. The combination of reported respiratory symptoms and nonspecific bronchial hyper-responsiveness has been shown to correctly identify patients with severe asthma.<sup>14</sup> Serum

IgE levels is also related to airway hyper-responsiveness in asymptomatic children.<sup>6</sup> Higher IgE levels may be correlated with lower lung function and more severe asthma attacks.<sup>15</sup>

To our knowledge no such kind of study has been previously conducted locally or internationally, that correlate serum IgE level with asthma severity in children. In our study the mean IgE concentration was lowest in children with intermittent asthma, higher in children with mild persistent asthma and highest in children with moderate and severe persistent asthma, while in an study by Rosario CS, et al, there was no correlation between serum IgE level and mild to moderate and severe asthma.<sup>16</sup> This discrepancy may be due to different race and allergens in different countries. Another similar international study showed mean values of forced expiratory volume (FEV<sub>1</sub>), forced vital capacity (FVC) and FEV<sub>1</sub>/FVC% were significantly lower in high IgE level group as compared to low IgE group.<sup>17</sup>

In a local study conducted by Satwani H, et al. there was no significant association

of serum total IgE levels with allergy severity.<sup>18</sup> These results are different from our study because in this study they checked overall allergic symptoms, not the severity of asthma as related to serum IgE level. Another local study also revealed positive correlation between serum IgE level and asthma but they did not compared asthma severity.<sup>19,20</sup> A similar local study showed significant high level of serum IgE level in poorly controlled asthma children<sup>21</sup> but asthma severity categorization was lacking in their study. Other similar international study showed correlation between higher asthma severity and higher serum concentration of total IgE.<sup>12</sup>

In our study there was association of mean serum IgE level with age, gender, weight, height and duration of asthma. In a similar international study there was no association of age with serum IgE level.<sup>6</sup> In a study by Haselkorn T, et al. mean serum IgE levels more in adolescent children.<sup>22</sup> While in another study by Borish L, et al. showed higher mean serum IgE levels in males as compared to females.<sup>23</sup>

Our study had several limitations. It was a tertiary-care based study, so the most of the children were referred from primary care physicians; there may be bias regarding asthma severity. Socioeconomic characteristics may be different than the general asthma population. Furthermore we did not assess the presence of asthma comorbidities such as allergic rhinitis that may also affect the severity of asthma.

## CONCLUSION

Our results support the hypothesis that serum IgE levels reflect the severity of asthma in children. We found that the

**TABLE VI: COMPARISON OF MEAN SERUM IGE LEVELS IN ASTHMA SEVERITY WITH RESPECT TO HEIGHT**

Height (cm)	Severity of Asthma	n	IgE Levels (IU/ml)		P-Value
			Mean	Std. Deviation	
≤ 116 (n=52)	Intermittent Asthma	13	284.62	36.427	0.0005
	Mild Persistent Asthma	24	489.13	55.251	
	Moderate Persistent Asthma	12	667.42	37.917	
	Severe Persistent Asthma	3	1094.00	102.679	
> 116 (n=54)	Intermittent Asthma	11	270.00	55.857	0.0005
	Mild Persistent Asthma	6	480.83	75.634	
	Moderate Persistent Asthma	28	697.89	55.175	
	Severe Persistent Asthma	9	1073.78	53.849	

**TABLE VII: COMPARISON OF MEAN SERUM IGE LEVELS IN ASTHMA SEVERITY WITH RESPECT TO DURATION OF ASTHMA**

Duration	Severity of Asthma	n	IgE Levels (IU/ml)		P-Value
			Mean	Std. Deviation	
≤24 months (n=49)	Intermittent Asthma	8	282.50	36.93	0.0005
	Mild Persistent Asthma	16	498.19	57.05	
	Moderate Persistent Asthma	19	671.89	46.60	
	Severe Persistent Asthma	6	1076	73.72	
>24 months (n=57)	Intermittent Asthma	16	275.63	50.72	0.0005
	Mild Persistent Asthma	14	475.21	59.73	
	Moderate Persistent Asthma	21	704	53.12	
	Severe Persistent Asthma	6	1081.67	59.88	

mean IgE concentration was highest in children with moderate and severe persistent asthma.

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### AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

**MAA:** Concept & study design, acquisition of data, final approval of the version to be published.

**MNC:** Analysis & interpretation of data, final approval of the version to be published.

**KA:** Acquisition of data, drafting the manuscript, final approval of the version to be published.

**SS:** Critical review, final approval of the version to be published.

*Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

### CONFLICT OF INTEREST

Authors declared no conflict of interest

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NIL



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