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Assessment of Serum Osteopontin Level in Children with Bronchial Asthma and its Relation to Disease Severity

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Abstract

Background:*Many different mediators have been implicated in asthma and they may have a variety of effects on the airways which could account for all of the pathological features of allergic diseases. we aimed to assess Osteopontin(OPN) level in children with bronchial asthma.****Methods:****Our study done at Pulmonology unit Pediatric department of Zagazig University.Our study carried out on 190 children divided into 2 age groups ≤ 5 years*

*and > 5 years. Each age group divided into 5 subgroups according to different severities of asthma into intermittent, mild, moderate and severe persistantasthma with healthy control group. serum OPN level were done for patients and controls.****Results:****we found that OPN show high significant difference between asthmatic and control group. Also, we reported that there was high significant difference between the control and asthmatic as Osteopontin in <5 age group and in 5-12 age group.At cut off point >14.8, area under the curve was 0.937, sensitivity was 97.8%, specificity 95.7%, PPV 96.4% and NPV 94.3%. **Conclusion:** The present study has shown that asthma patients exhibit higher serum OPN levels than controls.. Serum OPN is a promising biomarker in the diagnosis of bronchial asthma.*

Key words: *Osteopontin- bronchial asthma- Diagnosis.*

I. Introduction:

Bronchial asthma is a serious general health problem. People of different age groups all over the world are affected by this chronic airway disease. The prevalence of asthma reaches an estimated 300 million individuals worldwide, and it is increasing in most countries, especially among children ***(1)*****.**

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role: in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells ***(2)*****.** OPN is expressed in a wide range from these inflammatory cells.

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Osteopontin (OPN) is an extracellular matrix protein and immune modulator with a wide range of functions; it is recognized as a key cytokine in Th1 immune responses, OPN also play a role in early T lymphocyte activation which is implicated in several physiological and pathological events [(3)].

It has chemotactic properties, which promote cell recruitment to inflammatory sites. It also functions as an adhesion protein involved in cell attachment [(4)].

Many different mediators have been implicated in asthma and they may have a variety of effects on the airways which could account for all of the pathological features of allergic diseases [(5)].

The study aimed toassess OPN level in children with bronchial asthma and to determine the relation between OPN and severity of bronchial asthma in Pulmonology unit Pediatric Department of Zagazig University Hospitals.

II. Patients and Methods

Technical design:

1. Study design:

This study is a prospective case-control study.

2. Setting:

This study was carried out in in the Pediatric Department of Zagazig

University Hospitals from May 2019 till December 2019.

3. Target population:

Children with bronchial asthma admitted to Pediatric Department of

Zagazig University.

4. Inclusion criteria

Cases: all patients presented by wheezy chest and diagnosed as bronchial asthma by history, clinical picture and investigations in preschool and school age children.

Healthy control: age and sex comparable healthy children.

5. Sample size:

Our study carried out on 190 children divided into 2 age groups ≤ 5 years and > 5 years. Each age group divided into 5 subgroups according to different

severities of asthma into intermittent, mild, moderate and severe persistent

asthma with healthy control group.

Methods:

All patients were subjected to the following:

A- Full history taking including:

B- Laboratory investigations.:

C- c-reactive protein (CRP)

Human Osteopontin (OPN) test

Principle of the test:

The kit uses a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to assay the level of Human Osteopontin (OPN)in samples.

Statistical analysis

Analysis of data was done using Statistical Program for Social Science version 20 (SPSSInc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. In order to compare parametric quantitative variables between two groups, Student t test was performed. Qualitative variables were compared using chi-square (X2) test or Fisher's exact test when frequencies were below five. ROC curve was done. When a variable was not normally distributed, A P value < 0.05 is considered significant

III. Results:

- This table shows that there is high significant difference between the studied groups as regard consanguinity, family history and family history of allergy **(Table 1).**
- This table shows that there is high significant difference between the studied groups as regard consanguinity, family history and family history of allergy **(Table 2).**
- This table show there is significant differences between studied groups as regard CRP **(Table 3).**
- This table show there is significant differences between studied groups as regard CRP **(Table 4).**
- This figure shows that there is high significant difference between the studied groups as regard OPNin (<5 years) group **(Figure 1).**
- This figure shows that there is high significant difference between the studied groups as regard OPNin (5-12 years) group **(Figure 2).**
- This figure shows that at cut off point >14.8, area under the curve was 0.937, sensitivity was 97.8%, specificity 95.7%, PPV 96.4% and NPV 94.3% **(Figure 3).**
- This figure shows that at cut off point >15.15, area under the curve was 0.961, sensitivity was 98.3%, specificity 92.7%, PPV 95.4% and NPV 94.7% **(Figure 4).**

Table (1): Comparison between cases and control as regard family history in **(<5 years) group:**

Variable	Control group (n=19)		Intermittent (n=22)		Mild (n=21)		Moderate (n=21)		Severe (n=12)		χ^2	P value
	No.	%	No.	%	No.	%	No.	%	No.	%		
Consanguinity:												
Negative	19	100	5	22.7	5	23.8	4	19.0	2	16.7	40.94	**<0.001**
Positive	0	0	17	77.3	16	76.2	17	81.0	10	83.3		
Family hx of allergy:												
Negative	19	100	6	27.3	5	23.8	5	23.8	2	16.7	37.6	**<0.001**
Positive	0	0	16	72.7	16	76.2	16	76.2	10	83.3		
Family hx of asthma:												
Negative	19	100	4	18.2	6	28.6	4	19.0	2	16.7	41.44	**<0.001**
Positive	0	0	18	81.8	15	71.4	17	81.0	10	83.3		

Table (2): Comparison between cases and control as regard family history in (5-12 years) group:

Variable	Control group (n=19)		Intermittent (n=22)		Mild (n=21)		Moderate (n=21)		Severe (n=12)		χ^2	P value
	No.	%	No.	%	No.	%	No.	%	No.	%		
Consanguinity:												
Negative	19	100.0	7	31.8	7	33.3	6	28.6	1	8.3	34.94	**<0.001**
Positive	0	0.0	15	68.2	14	66.7	15	71.4	11	91.7		
Family hx of allergy:												
Negative	19	100.0	5	22.7	5	23.8	5	23.8	1	8.3	41.71	**<0.001**

Positive	0	0.0	17	77.3	16	76.2	16	76.2	11	91.7		
Family hx of asthma:												
Negative	19	100.0	10	45.5	10	47.6	10	47.6	7	58.3	17.12	**0.001**
Positive	0	0.0	12	54.5	11	52.4	11	52.4	5	41.7		

Table (3): Comparison between cases and control as regard CRP in (<5- years) group:

Variable	Control group (n=19)	Intermittent (n=22)	Mild (n=21)	Moderate (n=21)	Severe (n=12)	F	P value
CRP,mg/L							
Median Range	0.8 (0.5-4.3)	18.5 (5.0-24.0)	13.1 (11.0-28.1)	18.4 (3.3-32.9)	35.3 (20.6-68.8)	35.01	**<0.001**

Table (4): Comparison between cases and control as regard CRP in (5-12 years) group:

Variable	Control group (n=19)	Intermittent (n=22)	Mild (n=21)	Moderate (n=21)	Severe (n=12)	F	P value
CRP mg/L							
Median Range	0.9 (0.7-4.0)	20.9 (6.0-27.0)	12.6 (12.0-27.0)	18.7 (3.0-32.1)	34.3 (18.0-69.7)	33.02	**<0.001**

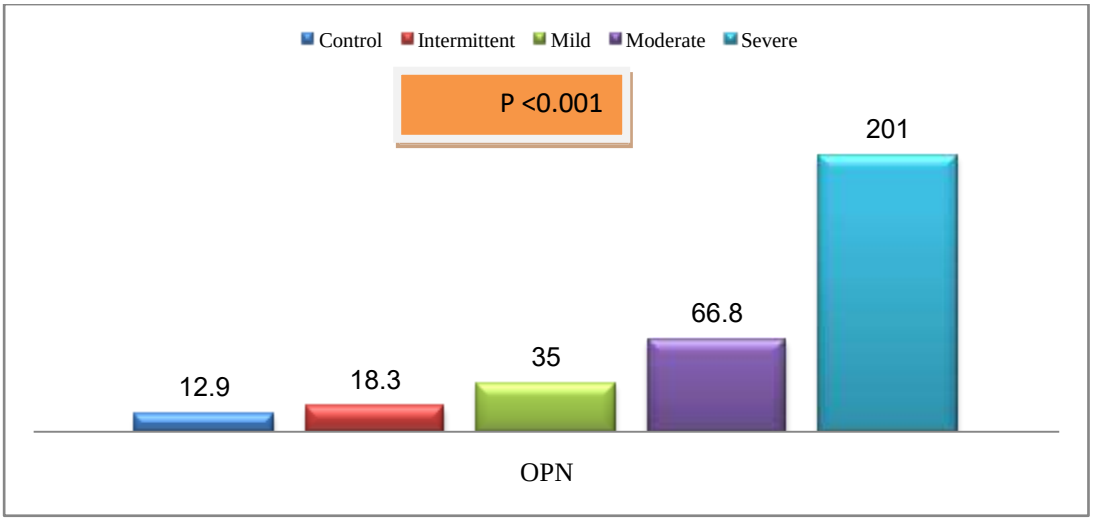

Fig. (1): Osteopontin in between cases and controls in (<5 years) group

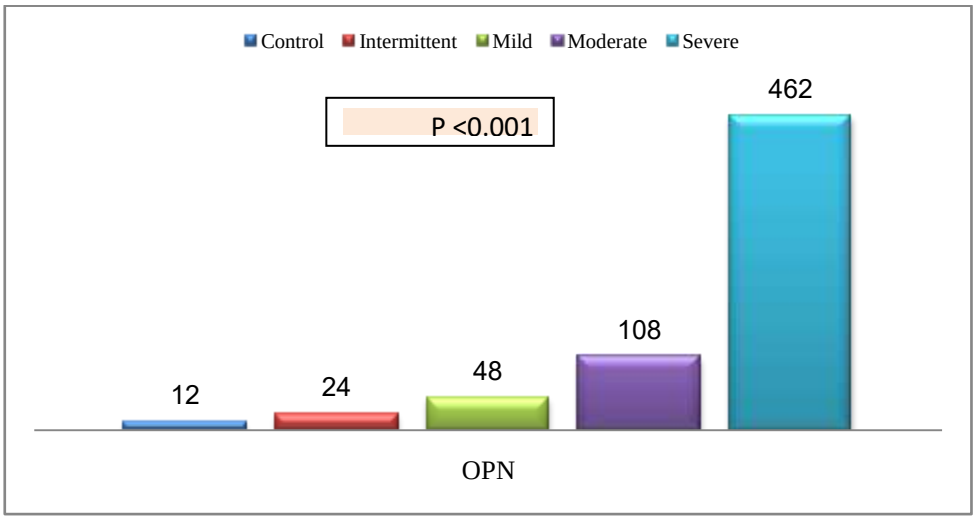

Fig. (2): Osteopontin in between cases and controls in (5-12 years) group

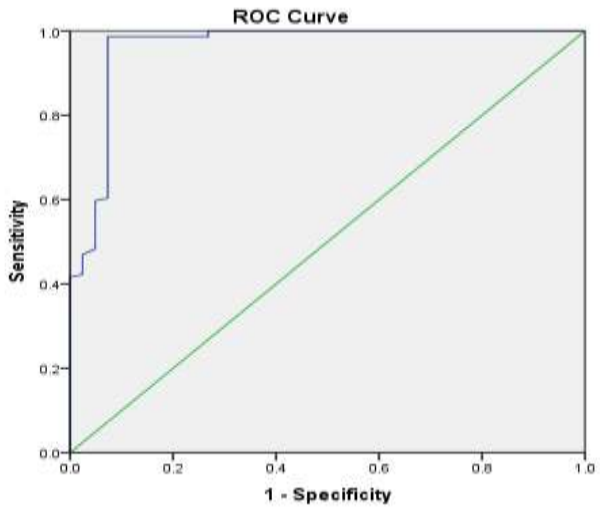

Fig. (3): ROC curve Analysis for Predictive ability of OPN in detection of brochial asthma (< 5 years)

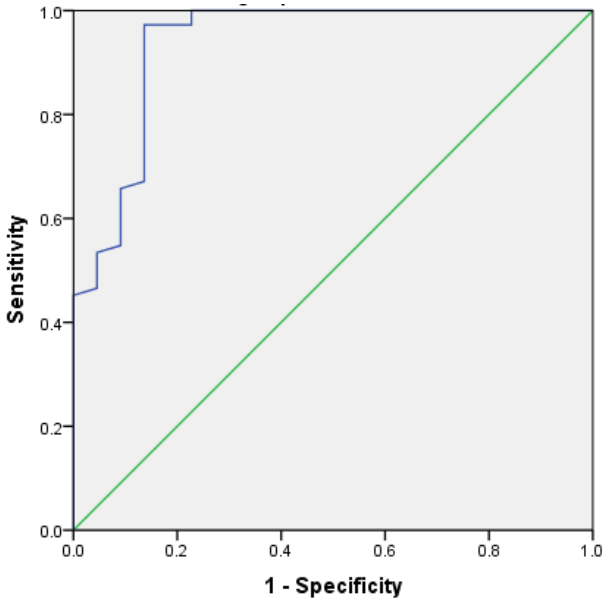

Fig. (4): ROC curve Analysis for Predictive ability of OPN in detection of bronchial asthma (5-12 years)

IV. Discussion

In our study there was high significant difference between the studied groups as regard consanguinity, family history of bronchial asthma and family history of allergy in both age groups as we noticed 118 (62%) of them had history of allergic disorder most of them 99 (83%) had positive history of bronchial asthma.

This was in concordant with**Toema et al.** [(6)]who noticed that Twenty-seven (45%) of them had a history of other allergic disorders. Most of them (70%) had a positive family history of bronchial asthma.

We found that there was high significant difference between the control and different severities of asthma as regard CRP in <5 age group and 5-12 age group.

This was in concordant with **Soferman et al.** [(7)] who measured CRP in 63 asthmatic children aged 2-12 years and found that CRP during exacerbation was significantly higher than the mean level during remission.

In our study we reported that OPN show high significant difference between asthmatic and control group.

This was in agreement with **Toema et al.** [(6)]who carried out a study on 60 asthmatic children aged 6-14 years and found that the OPN levels were higher in the asthma patients than control.

This was also in agreement with**Samitas et al.** [(8)] have demonstrated that the serum and broncho alveolar lavage fluid (BALF) levels of OPN in adult asthma patients in the steady state were higher in comparison to the control group.

Also,**Xanthou et al.** [(9)] who analyzed the distribution of OPN in bronchial tissue using immune histochemical staining revealed that OPN was highly expressed by both bronchial epithelial and sub epithelial

infiltrating inflammatory cells in asthmatic patients, whereas healthy controls either did not express OPN or demonstrated very low OPN expression by some bronchial epithelial cells.

On the contradict, **Kurokawa et al.** [10] showed that allergic reaction are higher in OPN-deficient mice when compared to those of the control group. In addition, allergic reaction decreased after recombinant intra peritoneal OPN application.

Also, this was in concordant with **Konno et al.** [11]who suggested the anti-inflammatory role of OPN in allergic disease, it has previously been shown that OPN has a protective role during secondary pulmonary antigenic challenge, and that therapeutic administration of recombinant OPN.

Also, we reported that there was high significant difference between the control and asthmatic as Osteopontin in <5 age group.

Our study is the first study that report that there is significant difference between the control and asthmatic as regard Osteopontin in this age group.

On the contradict **Akelma et al.** [12] demonstrated that OPN levels of the children with asthma ≤5-years age was similar to the levels in the control group and this can be explained by the presence of mild forms of asthma (only 4 attacks at previous year) as reported by him in this age group.

We also reported that there was high significant difference between the control and asthmatic as Osteopontin in 5-12 age group.

This was in agreement with **Akelma et al.** [12]and **Zhao et al.** [13] who found that serum OPN is significantly higher in asthmatic patients aged 5-12 years.

At the present study at cut off point >14.8, area under the curve was 0.937, sensitivity was 97.8%, specificity 95.7%, PPV 96.4% and NPV 94.3%.

The high validity for Osteopontin can be justified by the high difference in its level between cases and control.

V. Conclusion:

The present study has shown that asthma patients exhibit higher serum OPN levels than controls.. Serum OPN is a promising biomarker in the diagnosis of bronchial asthma.

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