Zinc status among children with bronchial asthma in central child's teaching hospital/Baghdad

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Abstract

Background:Pediatric asthma is a syndrome of lung dysfunction with an imbalance between the forces that maintain airway patency and those forces that operate to narrow or close the pediatric airway. Zinc has been supposed to have anti-oxidant, anti- apoptotic, anti-inflammatory and anti-allergic effects in the organism . Zinc deficiency is suspected to play a role in the pathogenesis, control, and severity of allergic, skin and airway diseases.

Objectives: To evaluate the relationship between zinc serum level and bronchial asthma(its duration and severity).

Patients and methods: A prospective case –control study was conducted at the central Child teaching hospital in Baghdad in a period extended for six months from 15th March to 15th September , 2016. 47 children from ages 2 to 12 years (mean age 5.6year) of both gender who were known cases of asthma were enrolled in the study, matched in age and gender with the control group of 47 healthy children without history of chronic disease. The zinc concentrations in serum were measured in both cases and controls.

Results:A total of 94 children were included, 47 patients who were asthmatic (22 males& 25 females). Mean age of children with asthma and control group children was 5.6 year . Body mass index percentile was higher in asthmatic patients (p 0.001). The study shows that asthmatic children significantly more likely to have family history of asthma compared to control group ($p<0.001$). in this study the meanconcentrations of zinc are lower in asthmatic children(67.4µg/dl) incomparison tocontrols(86.1µg/dl). And a significant correlation between serum zinc level with each of asthma severity and use of steroids and bronchodilator , ($p < 0.001$) for each.There was no significant association between age , gender, Body mass index(BMI) family history and duration of asthma with the low serum zinc level . (p 0.923, 0.478, 0.343 and 0.138 respectively).

Conclusion: Serum zinc level is lower in patients with bronchial asthma regardless their age and gender, and serum zinc level has significant relation to the severity of asthma and the use of steroid.

Introduction

asthma is a severe pediatric disease, affecting a great number of infants during their very first years of life which requires early and specific cures. Pediatric asthma should be viewed as a syndrome of lung dysfunction with an imbalance between the forces that maintain airway patency and those forces that operate to narrow or close the pediatric airway[(1)]

Although asthma is the most prevalent chronic disease in children and starts in the majority of the cases before the age of 5 years , it is still one of the most difficult disorders for physicians to diagnose in infant/preschoolers. This is due in part because in this age group, the clinical symptoms of asthma are variable and non specific because other wheezing disorders coexist , and neither airflow limitation nor airway inflammation, the main pathologic hallmarks of the condition, can be assessed routinely in this age group [(2)].

Relationship between asthma and zinc deficiency

Zinc is one of the essential dietary factor and of the most widely distributed biometals present in all organs, living tissues, and secretions. The total body Zinc content of human subjects is 1.5-3 grams and it is the second most abundant trace element in the body after iron(4grams) [3].Zinc is an important antioxidant element in the airway epithelium as well as skin. [4]

Zinc protects respiratory tract epithelial integrity by both preventing caspase 3 activation and the lysis of proteins that provide intercellular connection [5].Zinc supplementation significantly decreased the number of eosinophils and other inflammatory cells , resulting in a less severe inflammatory response. [6,7].Both asthma and Zinc deficiency are known to favor the Th2 inflammatory cytokine profile. Of particular interest was diminished functional activity of the Th1 cells but unaffected activity of Th2 cells, by this means causing a relative Th1 deficiency[8].

These might be due to an imbalance between Th1 and Th2 cell functions — a switch from the Th1-dependent cellular immune response to a Th2-dependent humoral immune response. Because both asthma and Zn deficiency are associated with a skewing toward an upregulation of the production and release of various proinflammatory cytokines through the Th2 response, asthmatics who are also Zinc deficient are probably to have amplified inflammation . Considering the previous findings that Zn deficiency worsens allergic inflammation, and Th2 dependent response is a feature of allergic inflammation.[9]

Observational studies have shown that diets low in antioxidants, such as zinc , selenium , magnesium ,vitamin C ,vitamin A, omega-3 polyunsaturated fats (fish oil), are associated with an increased risk of asthma [10 ,11]

The immune system is extremely dependent on the availability of Zn for maintaining its homeostasis. Inflammatory diseases can cause an increase in the demand for Zn. As a result, greater demand for Zn by the immune system could be a contributing factor to the Zn deficiency noted in inflammatory diseases [12]

Aim of the study

This study was performed to assess status of zinc in serum of patients with bronchial asthma a is a risk factor for asthmatic symptoms **,**to study the relation between serum zinc level and the duration and severity of asthma and to study the relation between serum zinc level and steroid medications used by asthmatic children.

Patient and methods

A prospective case –control study was conducted at the central Child teaching hospital in Baghdad in a period extended for six months from March 15th to September 15th , 2016. Forty seven children from ages 2 to 12 (mean age 5.6) of both gender who were known cases of asthma (more than one attack of airway obstruction which was reversible on bronchodilators and/or steroid) under no zinc supplements in drug history , and had visited the Emergency department, the outpatient clinic and the Respiratory ward in the hospital during the study period were enrolled in the study, matched in age , gender and with the control group of 47 healthy children without history of chronic disease , they had no history and evidence of asthma and zinc deficiency , they had never any episode of shortness of breath and/or wheezing and had never used asthma medications, Coming with their parents who bring another ill child to hospital or attending for scheduled dental outpatient clinic during the study period were taken as a control group.

The parents gave their written consent after receiving detailed and specific information about the risks and benefits of the study.

A questionnaire was completed through interview with the patients and their parents included details concerning:

Age, gender, medical history, drug intake, date of onset of asthma, frequency of admission per year, duration of asthma, classification of asthma as (mild, moderate, severe), depending on clinical base i.e. day and night symptoms, family history of asthma and drugs taken for control.

Weight and height were measured using a regularly calibrated a balance beam scale and the height rod attached to the balanced beam scale, respectively, with light clothes and no

shoes. Data were recorded on paper forms, and the anthropometric measurements were used to calculate BMI.

BMI was calculated by dividing weight and height squared (kg/m2) . after BMI is calculated, the BMI number is plotted on the Center for Disease Control and Prevention (CDC) BMI –for- age growth charts to obtain a percentile ranking.

BMI -for –age weight status categories and the corresponding percentiles are listed according to the following table :

Table 1:

Weight Status Category	Percentile Range
Underweight	Less than the 5th percentile
Healthy weight	5^{th} percentile to less than the 85^{th} percentile
Overweight	85^{th} to less than the 95^{th} percentile
Obese	Equal to or greater than the 95^{th} percentile

Sample preparation and analytic method: For zinc determination,1.5 ml of blood was collected in biochemical tube then the sample was centrifuged for 4-5 minutes at 3000-4000 rpm then collected in plain tube and stored at -20℃ till the time of assay.The zinc concentration in serum was measured by means of spectrophotometer UV/VIS with thermostatation of wave length wavelength 578nm.Normal value of serum zinc level were from 70-120 µg/dl in pediatric age group. [13]

Limitation of the study: zinc level measurement is not available in the hospital lab, so we compelled to send blood samples outside the hospital and time limitations after sample aspiration like holiday days .

Statistical analysis : Statistical package for social sciences version 22 was used for data analysis . Discrete variables presented as numbers and percentages and continuous variables presented as mean with standard deviation. Chi square test for independence used to test the significance of associations between discrete variables. T test for two independent variables and ANOVA were used to test the significance of the observed variation in means between independent samples.

Results

In table 2 there was no significant difference in mean age between the two study groups ($P > 0.05$, table 1), Mean BMI was significantly higher in asthmatic patients than in control group ($P < 0.05$)

Table 2: Descriptive statistics of measured variables:

Variable	Study Group	Min	Max	Mean	SD	P value
Age (y)	**Asthmatic**	2	12	5.6	3.1	1.000
	Control	2	12	5.6	3.1	
BMI	**Asthmatic**	14.1	21.3	17.1	1.7	**0.001**
	Control	13.9	19.6	15.9	1.7	
Duration of Asthma (y)	**Asthmatic**	1	8	3.1	2.1	---
	Control	-	-	-	-	
Number of admissions	**Asthmatic**	1	7	3.5	1.8	---
	Control	-	-	-	-	

Table 3: Characteristics of sampled patients:

Variable	Category	Asthmatic Patients		Control Group		P Value
		N=47	100.0%	N=47	100.0%	
Age Group	**2-4 y**	23	48.9%	23	48.9%	1.000
	5-9 y	16	34.0%	16	34.0%	
	10-12 y	8	17.0%	8	17.0%	
Sex	**Male**	22	46.8%	22	46.8%	1.000
	Female	25	53.2%	25	53.2%	
Weight Percentile	**< 5th**	1	2.1%	0	0.0%	0.315
	5th -95th	46	97.9%	47	100.0%	
	> 95th	0	0.0%	0	0.0%	
Height Percentile	**< 5th**	2	4.3%	0	0.0%	0.153
	5th -95th	45	95.7%	47	100.0%	
	> 95th	0	0.0%	0	0.0%	
BMI Percentile	**< 5th**	1	2.1%	0	0.0%	0.071
	5th -95th	42	89.4%	47	100.0%	
	> 95th	4	8.5%	0	0.0%	
Family history of asthma	**Yes**	26	55.3%	0	0.0%	**<0.001**
	No	21	44.7%	47	100.0%	
Serum Zinc Level	**Low**	34	72.3%	0	0.0%	**<0.001**
	Normal	13	27.7%	47	100.0%	
	High	0	0.0%	0	0.0%	

There was no significant association between study group and each of age group, sex/ wt /ht/ BMI centile levels (P > 0.05).

Asthmatic children significantly more likely to have family history of asthma compared to control group (P < 0.05)Low serum zinc level is significantly associated with asthma compared to control group (P < .05).

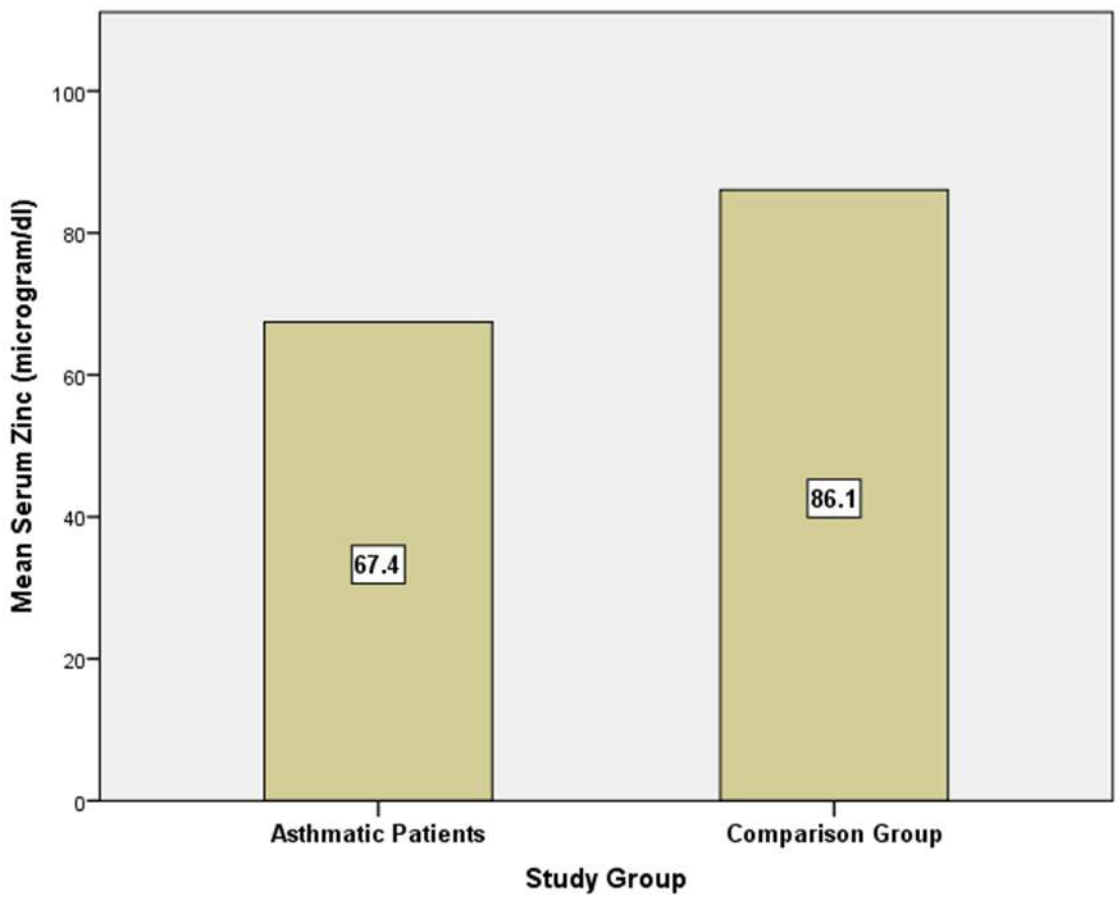

Figure 1: Observed Mean zinc levels in each study group

The mean serum zinc level in asthmatic patients was lower than that of the comparison group (67.4 vs 86.1microgram/dl).

Table 4: Mean serum Zinc levels of sampled asthmatic patients according to studied variables

Variables	N	Serum Zinc (µg/dl) Mean	SD	P value
Age Group				0.603
• 2-4 y	23	66.5	6.7	
• 5-9 y	16	68.9	8.5	
• 10-12 y	8	67.1	7.0	
Sex				0.587
• Male	22	66.8	7.6	
• Female	25	68.0	7.1	
Weight Percentile				0.196
• < 5th	1	58.0	---	
• 5th -95th	46	67.7	1.1	
• > 95th	0	---	---	
Height Percentile				0.207
• < 5th	2	61.0	4.2	
• 5th -95th	45	67.7	7.3	
• > 95th	0	---	---	
BMI Percentile				0.197
• < 5th	1	58.0	---	

• 5th -95th	42	68.1	7.4	
• > 95th	4	63.3	2.5	
Severity of Asthma				**< 0.001**
• Intermittent	6	81.0	3.5	
• Mild persistent	5	74.4	8.0	
• Moderate persistent	14	67.3	2.5	
• Severe persistent	22	62.3	2.5	
Duration of Asthma				0.298
• ≤ 1 y	11	68.1	9.0	
• 2-5 y	28	68.3	7.4	
• > 5 y	8	63.8	2.4	
On steroids				**< 0.001**
• Yes	38	64.5	3.6	
• No	9	79.9	1.9	
Family history of asthma				0.415
• Yes	26	66.7	5.3	
• No	21	68.4	9.3	

According to this study, Mean serum Zinc level did not vary significantly with each of age group, sex, BMI percentiles, or family history and duration of asthma (P >0.05).

Severity of asthma and use of steroids showed significant variation in mean serum zinc levels that the increase in asthma severity is accompanied with lower zinc mean level and those who use bronchodilators are having lower mean serum zinc (P < 0.05)

Table 5: Distribution of sample asthmatic patients according to serum zinc level and to studied variables:

	Serum Zinc Level				
	Low		**Normal**		
Variables	**N=34**	**100%**	**N=13**	**100%**	**P value**
Age Group					0.923
• 2-4 y	17	50.0%	6	46.2%	
• 5-9 y	11	32.4%	5	38.5%	
• 10-12 y	6	17.6%	2	15.4%	
Sex					0.478
• Male	17	50.0%	5	38.5%	
• Female	17	50.0%	8	61.5%	
Weight Percentile					0.532
• < 5th	1	2.9%	0	0.0%	
• 5th -95th	33	97.1%	13	100.0%	
• > 95th	0	0.0%	0	0.0%	
Height Percentile					0.371
• < 5th	2	5.9%	0	0.0%	
• 5th -95th	32	94.1%	13	100.0%	
• > 95th	0	0.0%	0	0.0%	
BMI Percentile					0.343
• < 5th	1	2.9%	0	0.0%	
• 5th -95th	29	85.3%	13	100.0%	
• > 95th	4	11.8%	0	0.0%	
Severity of Asthma					**< 0.001**
• Intermittent	0	0.0%	6	46.2%	
• Mild	1	2.9%	4	30.8%	

• Moderate	11	32.4%	3	23.1%	
• Severe	22	64.7%	0	0.0%	
Duration of Asthma					0.138
• ≤ 1 y	8	23.5%	3	23.1%	
• 2-5 y	18	52.9%	10	76.9%	
• > 5 y	8	23.5%	0	0.0%	
On Steroids					**< 0.001**
• Yes	34	100.0%	4	30.8%	
• No	0	0.0%	9	69.2%	
On Bronchodilator					**< 0.001**
• Yes	34	100.0%	2	15.4%	
• No	0	0.0%	11	84.6%	

There were significant associations for s. Zn level with each of asthma severity, use of steroids, use of bronchodilator that low zinc levels are associated with more severe disease and with the use of bronchodilator ($P < 0.05$)

Other variables showed no significant association with zinc levels according to this study ($P>0.05$)

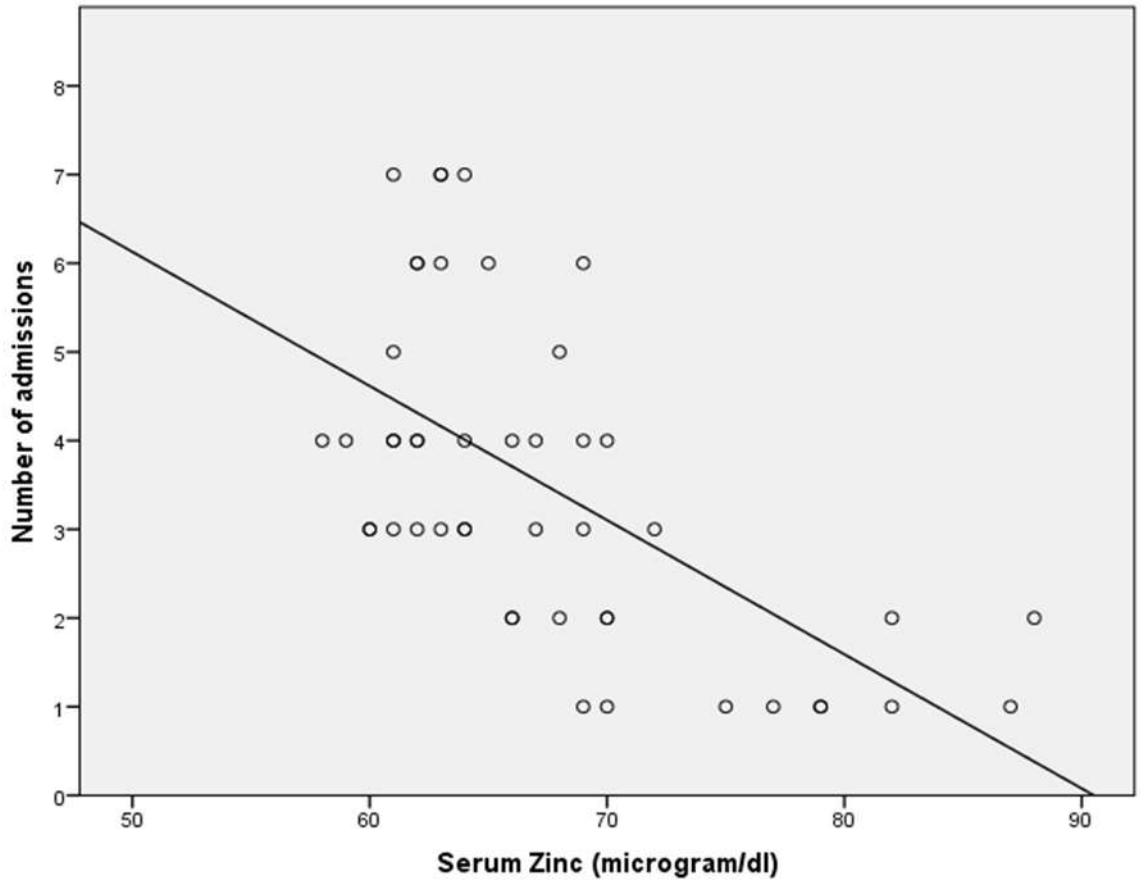

Figure 2: Distribution of sampled asthmatic patients according to serum zinc level and number of admissions to hospital due to asthma.

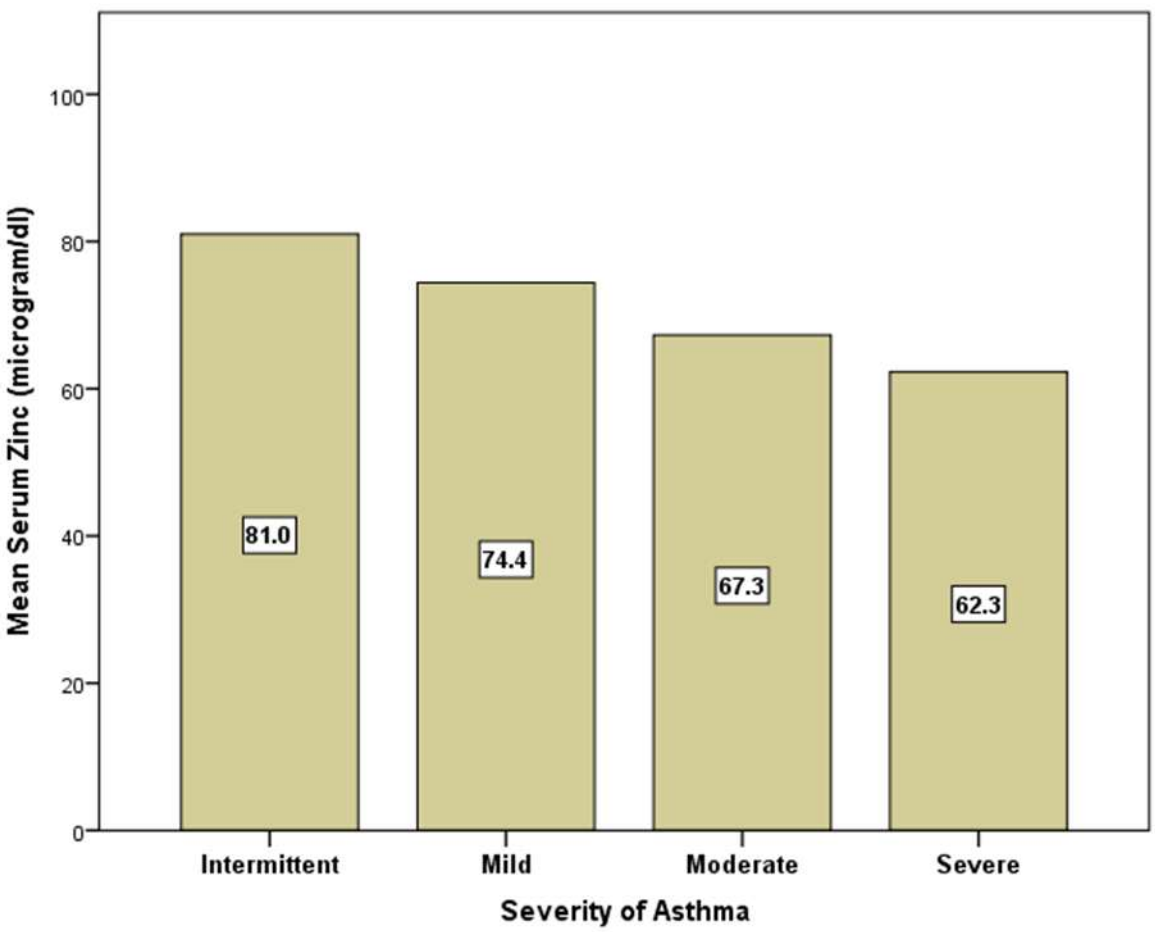

Figure 3: Mean serum Zinc level in asthmatic patients according to the severity of asthma.

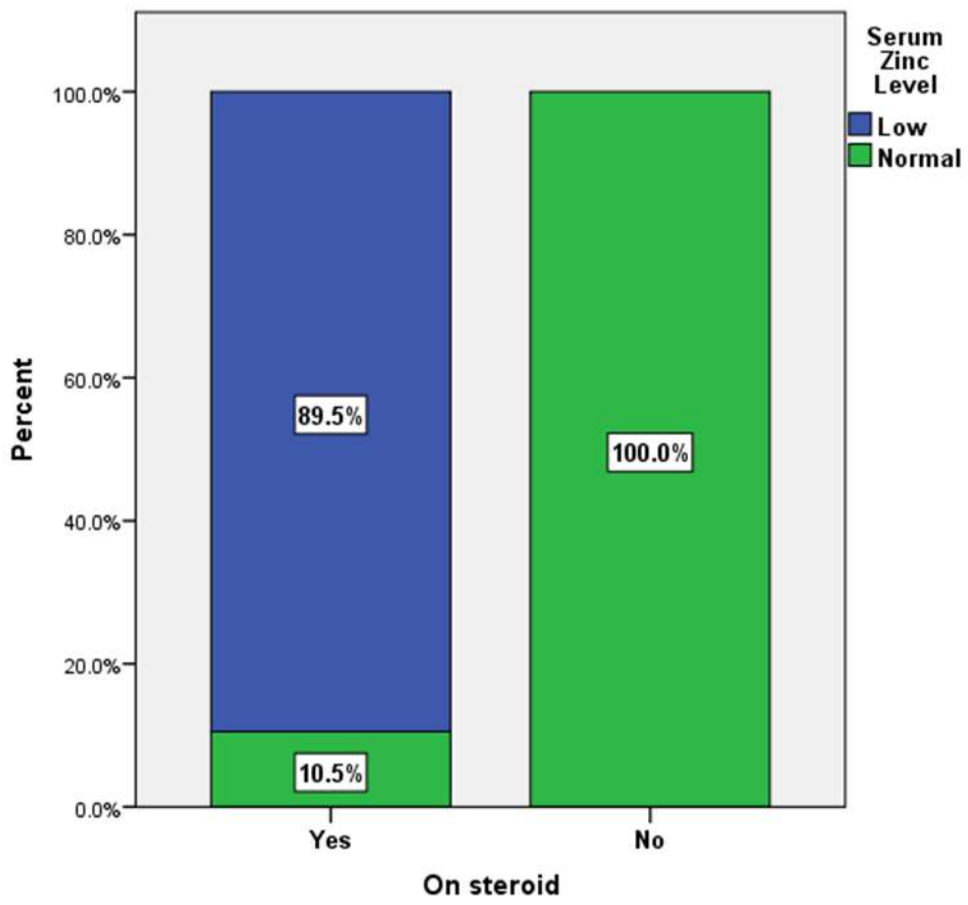

Table 6: Distribution of sampled asthmatic pediatric patients according to use of steroid prophylaxis and the normality of serum zinc levels.

Discussion

Asthma is considered a chronic inflammatory disease leading to temporary blockage of air ways, Free oxygen radicals including hydrogen peroxide, superoxide and hydroxyl radicals are involved in the pathogenesis of asthma and Zn is regarded one of the main components of antioxidant enzymes leading to decreased harmful effects of oxygen free radicals. Reduction of zinc may cause diminishing the antioxidants system effects and as a result leads to inflammation and hyper activity in air ways. [14]

When distributing the patients according to the age groups; it has been found that nearly half of patients were in age group 2-4years, which is compatible with Tiran Abdulsttar study[10] in which 60% of the patients were in the age group 1-4 years.In the current study , asthma was slightly more among female, still no significant difference exit between the genders in this study(p 1.000), this is in accordance with Postma DS study[15] show that asthma is more predominant in females. Whereas in C. Almqvist study [16] reported that Boys are consistently have more prevalent wheeze than girls. However in adolescence, the pattern changes and wheeze is more prevalent in females than males. Possible explanations for these gender differences could be linked to hormonal changes during puberty, and gender-specific differences in environmental exposures; i.e. boys have more out door activities than girls.[16] According to the results of this study , asthma was significantly correlated with BMI , this association between high BMI and asthma similar to many studies like Baybeen K [17] and Kim L et al [18] .This could be explained by that Obesity may directly affect the asthma phenotype by direct mechanical effects, by

enhancing the immune response, through related genetic mechanisms, and by sex specific influences (hormones). Alternatively, obesity may be closely linked to other environmental factors such as physical activity, diet, and birth weight. These environmental influences, in combination with genetic susceptibility, may then lead to enhanced susceptibility to asthma [19]

This study revealed the existence of statistically significant association between asthma and positive family history (p <0.001) , Such an association also supported by results of Tiebin Liu et al[20] and Anders Bjerg et al [21] , this may be explained by fact that is more than 100 genetic loci have been linked to asthma.In this prospective study , it has been demonstrated that the serum concentration of zinc in asthmatic patients was significantly lower than that in control group, which is compatible with the previous studies such as Tiran AbdulsttarKakarash[10] , NematBilan et al [14] and BahriErmiset al [22] (p <0.01, 0.009,p<0.01)respectively. This could be explained by, chronic inflammation events cause a characteristic decline in plasma or serum zinc levels, the cause of this hypozincemia is the redistribution of plasma zinc in the body. Activation of the phagocytic cells occurs in IgE-mediated allergic reactions, leading to the release of Leucocyte Endogenous Mediator which increases the movement of zinc from plasma to the hepatocytes, decreasing its serum level . It appears that hypozincemia plays a role in producing, or exacerbating, the allergic diseases .Finally, it is well known that zinc deficiency affects the regulation of T-cell lymphocytes, which may play some part in the development of allergies. [23]

However, the relationship between serum zinc and bronchial asthma still remains controversial as some had reported to have no significant differences like ArikYilmaz et al [24] , and Urushidate S et al [25] .This study showed that severity of asthma was significantly associated with lower serum level(p<0.001), this finding was in concurrence with study done by Khanbabaee G. et al [26] , in which a significant association between the zinc level and severity of asthma (p<0.001**).**In relation between duration of asthma and hypozincemia, this study reported no statistical significant association(p 0.1), that was similar to Tiran abdulsttar study[10] , in which no statistical significance among asthmatic children in relation to the duration of the disease(p 0.69).In this study , the mean serum zinc level was significantly lower in asthmatic children using steroid (p 0.001), which is compatible with AginKh study [27] .The hypothesis may be suggested that pituitary adrenal axis system maintained circulating zinc and mobilizing body zinc[27] .

Conclusion

Serum zinc level is lower in patients with bronchial asthma regardless their age and gender.Children with bronchial asthma have a great risk of zinc deficiency, and serum zinc level has significant relation to the severity of asthma.Corticosteroids(inhalers & /or oral) are a novel in the treatment of asthma, leads to decreased zinc level in the asthmatic patients when used in large doses. Serum zinc level is lower in patients on bronchodilator.

Recommendations

We emphasize that checking zinc levels in children who are hospitalized for an asthma attack may be useful.Zinc supplementation might be suggested in asthmatic patients with hypozincemia, while such a defect could aggregate to the severity of disease.

Supporting the education labs by providing them with sophisticated diagnostic tools to facilitate the investigation.

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