Calcium Status in Preschool Asthmatic Children

Prof. Magdy M. Ashmawy Sakr[1]; Prof. Mohammad I. Abdel - Aal[1], Dr. Mahmoud F.M. Salem[2]; Mohammad Y. M. Abdel -Salam[1]

[1]Pediatrics Department, Damietta Faculty of Medicine, Al-Azhar University, Egypt.
[2]Clinical Pathology Department, Damietta Faculty of Medicine, Al-Azhar University Egypt.
mohamedyouness986@gmail.com

Abstract: Background: Asthma is a chronic inflammatory condition of the lung air ways resulting in episodic air flow obstruction and it is a global health problem affecting an estimated 330 million individuals worldwide with a reported prevalence of 5-20% in children aged between 6-15 years. Calcium is the fifth most abundant element in the human body and is essential for life. It has a key role in many physiological processes including skeletal mineralization, muscle contraction, nerve impulse transmission, blood clotting, and hormone secretion. **Objective:** Assess the calcium status in preschool asthmatic children. **Patients and method:** It was a cross sectional study, which conducted at Al-Azhar University Hospital, New Damietta City, in the period from April 2017 to April 2018. **Results:** The prevalence of asthma in our cases was more frequent among rural (60%) than urban (40%) areas. There were no statistically significant difference in total and ionized calcium regarding severity of asthma. There was positive correlation at total calcium regards heart rate and white blood cells. There was positive correlation at ionized calcium regards white blood cells, but there was negative correlation regards potassium. There was positive correlation at eosinophils regards heart rate and white blood cells. **Conclusion:** Hypocalcaemia appears to be a risk factor for development of asthma in children. Severity of asthma was not related to the serum calcium level.
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1. Introduction:

Asthma is a chronic inflammatory condition of the lung air ways resulting in episodic air flow obstruction. Although the cause of childhood asthma has not been determined, a combination of environmental exposures, inherent biologic and genetic susceptibilities has been implicated [(1)]. Asthma is a global health problem affecting around 300 million Individuals of all ages, ethnic groups and countries. It is estimated that around 250 000 people die prematurely each year as a result of asthma [(2)].

Therefore, asthma has a significant social and financial burden on public health [(3)]. Furthermore, asthma in Egypt is a significant health problem among school children and its prevalence in children (2-12 years) is nearly 8,2%[(4)]. Worldwide, childhood asthma appears to be increasing in prevalence, despite considerable improvements in our management and pharmacopeia to treat asthma [(1)]. Calcium is the fifth most abundant element in the human body and is essential for life. It has a key role in many physiological processes including skeletal mineralization, muscle contraction, nerve impulse transmission, blood clotting, and hormone secretion. More than 99% of calcium in the body is stored in the skeleton and less than 1% of calcium is located in the blood, soft tissues and extracellular fluid [(5)].

Potassium is the most abundant cation in the intra cellular fluid and its concentration within the cells is approximately 30 times higher than in the extra cellular fluid [(6)].

In asthmatic children, exposure of the airways to antigen, bacterial infection and environmental pollutants may cause a defect in calcium homeostasis, leading to increased permeability and utilization of calcium in a variety of cells such as mast cells, neutrophils and respiratory smooth muscle cells. The resulting decreased calcium in plasma and increased intracellular calcium concentration, leads to smooth muscle tension [(7)]. Abnormal electrolyte concentrations in asthma patients can be attributed to low intake or secondary to asthma medications. Hypokalemia was the earliest electrolyte disturbance reported in acute asthma and it was related to the use of β2-agonists and aminophylline therapy. Hypocalcemia have also been reported after administration of β2-agonists and in acute asthma treated with intravenous aminophylline due to increase in the urinary excretion of calcium [(8)].

Nagdeote et al., (2011) [(7)] recommended in their work that hypocalcemia associated with asthma should be corrected, not only for its deleterious effect on respiratory muscle power but also for its possible contribution to bronchial hyper-reactivity.

Aim of the work:

The aim of the work was to determine whether there is any change in serum calcium in asthmatic children and the need for correction.

2. Patients and methods:

This study was a cross sectional study which will be carried out at Damietta faculty of medicine, Al-Azhar University Hospital.

Inclusion criteria:

Age at first six years of life, both sexes are included and asthmatic children.

Exclusion criteria:

Children with chronic disease as tuberculosis, diabetes mellitus, chronic renal disease, malnutrition, etc.

Children with congenital heart disease.

Children with history of prematurity and admitted at neonatal intensive care unit for long period.

Children with acute severe illness as diarrhea with severe dehydration and pneumonia.

Classification of cases:

Patients will be classified according to ***(NAEPP classification of asthma severity)*** guidelines.

Each child involved this study will undergo the following:

Complete history taking; age, sex, residence and nutritional history.

Family history of asthma or other allergic diseases as allergic rhinitis, and history of atopy. History of frequency of attacks of asthma, medications used in and between attacks of asthma & frequency of nebulization.

Triggering factors for asthma as viral infections, dust mites, pollens, air pollutants and some drugs, e.g. beta-blockers.

History of tetany, convulsions, irritability, sweating, weakness and abdominal distension.

Clinical examination:

- Vital signs (RR, HR, BP, body temperature).
- Weight, height and head circumference.
- Complete medical examination including chest, cardiac, abdominal and neurological examination.

Investigations:

Complete blood count, Serum calcium (total & Ionized) and Serum sodium & potassium.

3. Results:

The patients characteristic and demographic data show that 47.5% of children were female, mean of age were 3.8±1.32 with range from 1 to 6 years, 45% having smoking father and 60% were living in rural, patients with positive family history of asthma was 70.0%. Mean of HR were 112.13±13.07 with range from 90 to 140 and mean of RR were 41.05±5.92 with range from 30 to 52.

Regarding asthma grade it was found that 40% of children were mild intermittent, 38.8% were mild persistent, 18.8 were moderate persistent and 2.4% were sever persistent.

The total and ionized calcium shows that 16.2% of children were low total calcium. Mean of that were 9.23 ± 0.71 with range from 8.2 to 11and 16.2% of children were low ionized calcium. Mean of that were 1.23 ± 0.08 with range from 1.04 to 1.37.

The level of sodium and calcium show that the mean of Na^+ were 138.18 with range from 125 to 153 and mean of K^+ were 4.27 with range from 3.3 to 5.6.

The blood picture in our study patients was as follows, WBCS were 12.69 with range from 7 to 21 and mean of Hb 10.94 with range from 9 to 12.1 and 45% of children were high eosinophil. Mean of that were 5.33 with range from 2 to 9.

Table (1), shows that there was no statistically significant difference in total and ionized calcium regarding asthma grade. **Also this table** shows that there was no statistically significant difference in eosinophil level regarding asthma grade.

Table (1): Comparison between Asthma grade as regards total and ionized calcium

	Intermittent (n=32)		**Mild persistent (n=31)**		**Moderate persistent (n=15)**		**Sever persistent (n=2)**		**X^2 ANOVA**	**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**		
Total Ca Low	6	18.8	5	16.1	2	13.3	0	0.0	**X^2** 0.629	0.890
Normal	26	81.2	26	83.9	13	86.7	2	10.,0		
Mean±S.D	9.10±0.62		9.18±0.70		9.50±0.81		10.22±0.03		F 2.614	0.06
Ionized Ca Low	6	18.8	5	16.1	2	13.3	0	0.0	**X^2** 0.629	0.889
Normal	26	81.2	26	83.9	13	86.7	2	100.0		
Mean±S.D	1.22±0.08		1.23±0.07		1.26±0.09		1.26±0.02		F 1.398	0.250
Eosinophil Normal	17	53.1	18	58.1	9	60.0	0	0.0	**X^2** 2.76	0.430
High	15	46.9	13	41.9	6	40.0	2	100.0		
Mean±S.D	5.00±2.26		5.42±2.59		5.40±2.41		8.50±0.71		F 1.371	0.258

Table (2), showed that total calcium had significant positive correlation with WBCS and heart rate but had significant negative correlation with height and K, also this table showed that ionized calcium had significant positive correlation with WBCS and but had significant negative correlation with K. Also showed that eosinophil had significant positive correlation with WBCS and heart rate.

Showed that no significant correlation between asthma grade and total ca, ionized ca and eosinophil.

Table (2): Correlation between all parameters and total and ionized ca and eosinophil.

	Total Ca		**Ionized Ca**		**Eosinophil**	
	r	**P value**	**r**	**P value**	**r**	**P value**
age	-0.186	0.098	-0.056	0.619	-0.082	0.467
Weight	-0.203	0.071	-0.070	0.535	-0.076	0.500
Height	-0.232	0.038*	-0.097	0.393	-0.136	0.227
Heart rate	0.3	0.007*	0.205	0.068	0.393	0.001*
Respiratory rate	0.176	0.118	0.087	0.443	0.057	0.615
Asthma grade	2.614	0.057	1.398	0.250	1.371	0.258
Hb	0.134	0.236	0.179	0.112	0.044	0.700
WBCS	0.274	0.014*	0.243	0.030*	0.388	0.001*
Platelets	-0.167	0.139	-0.055	0.626	0.046	0.684
K	-0.235	0.036*	-0.27	0.016*	-0.016	0.891
Na	0.006	0.961	-0.041	0.717	-0.086	0.446
Total Ca	-	-	-	-	0.185	0.100
Ionized ca	-	-	-	-	0.215	0.056

4. Discussion

In the present study, demographic characteristics of studied children demonstrated that the male sex was more frequent among cases (42 male child = 52.5%) than female (38 female child = 47.5%).

This finding is supported by study done by Beuther, (2007) [9] who stated that the increased risk of childhood asthma in males is probably related to young males airway size is smaller when compared to the females airway, which may contribute to increased risk of wheezing after a cold or other viral infection.

Also, asthmatic males are expected to have more asthma and atopy than females during childhood, which may be explained by gender-dependent effects, including linkage of thymic stromal lymphopoien to lower IgE levels of girls [10].

In addition, GINA, (2011) [11] reported that male six is a risk factor of asthma in children.

Furthermore, these results were in agreement with the percentages reported by several studies as those done by Hassan et al., (2017) [12], Joseph et al., (2005) [13], Abdallah et al., (2012) [14] and Al-Dawood, (2001) [15] in Egypt, United States, Egypt and Saudi Arabia where asthmatic boys were 53.6%, 52%, 55.4% and 60% respectively.

Also, we found that the presence of smoking fathers were more frequent among cases (44 child = 55%). This could be explained by that the passive exposure to tobacco smoke, particularly at very young age might be significantly related to the incidence of asthma due to affection of airway growth [16].

This percentage was in agreement with those reported by El- Mazahy et al., (2014) [17], Wang et al., (2002) [18] and Al-Dawood, (2001) [15] in Egypt, China and Saudi Arabia, where smoking fathers among asthmatic children were 52.8%, 65% and 70% respectively.

On the contrary, Zedan et al., (2009) [4] and Abdallah et al., (2012) [14] they found no significant association between asthma and smoking fathers.

As regard to residence distribution in our study, there was increase in prevalence of asthma among rural (48 child = 60%) than urban (32 child = 40%) areas.

These results were in agreement with the percentages reported by several studies as those done by Ekici et al., (2012) [19] and El-Mazahy et al., (2014) [17] in Turkey and Egypt respectively.

On the contrary, Zedan et al., (2009) [4] and Abdallah et al., (2012) [14] stated that there was no statistically difference between prevalence of childhood asthma in urban and rural areas that may be explained by similarity in environmental conditions in both areas due to close proximity to each other and relatively low levels of air pollutions.

Regarding the family history of bronchial asthma, we found that the presence of positive family history among cases was (56 child = 70%). This

finding could be expected as genetics play an important role in the causation of asthma and allergy, with identification of putative susceptibility genes for asthma in several populations [20].

This finding is supported by study done by Abdallah et al., (2012) [14] who stated that a positive family history of asthma was significantly associated with asthma in the studied children. He explained that by the fact that asthma is a syndrome influenced by genetic and environmental factors and also, that the hereditary component has been demonstrated by familial studies. In addition, these results were in agreement with the percentages reported by several studies as those done by Baldaçara et al., (2013) [21] and Davoodi et al., (2013) [22] in Brazil and India, where positive family history of asthma among asthmatic children were 67% and 74% respectively.

As regard to degree of asthma severity, there was predominance of mild asthma (63 child = 78.8%) followed by moderate asthma (15 child = 18.8%) then severe asthma (2 child = 2.4%).

Our study was supported by El-Mazahy et al., (2014) [17] who stated that mild asthma (65.7%) followed by moderate asthma (30%) then severe asthma (4.3%), and Hassan et al., (2017) [12] who stated that severity of asthma among studied children was mild asthma (52.4%), moderate asthma in (40.5%) and severe form of asthma in (7.1%).

Also, matched with Tunon et al., (2007) [23] who stated that mild asthma includes intermittent and persistent affects between 50%-75% of asthmatic patients and is more frequent, more symptomatic and less well controlled in children than adults.

On the contrary, Leonard et al., (2004) [24] stated that mild asthma in (34.8%), moderate asthma in (22.4%) and severe form of asthma in (42.8%) of cases.

Regarding total and ionized calcium in our study we found that in 16.2% of children the values were low for total and ionized calcium and mean of that were (9.23 ± 0.71 mg/dL) and (1.23 ± 0.08 mmol/L) respectively, but there was no statistically significant difference in total and ionized calcium regarding severity of asthma.

Our results supported by Nagteode et al., (2011) [7] who stated that, there was significant decrease in the levels of serum ionized and total calcium irrespective with the severity of asthma with mean of that were (1.15 ± 0.01 mmol/L) and (8.93 ± 0.96 mg/dL) respectively and this significant lowering of serum total and ionized calcium in asthmatic children may be due to the increased infiltration of calcium ions into the tissue cells.

Also, Hala et al., (2014) [8] reported that 22% of asthmatic patients during acute exacerbation had hypocalcaemia and might be due to increase in the urinary excretion of calcium in asthmatic patients treated with intravenous aminophylline. Another explanation is related to magnesium when it is deficient, the action of calcium is enhanced and an excess of magnesium blocks calcium. These interactions are important to the patient with respiratory diseases because the intracellular influx of calcium causes bronchial smooth muscle contraction.

As regard to serum sodium and potassium in our study there were no abnormalities in serum sodium and potassium in our cases, which is supported by Nagteode et al., (2011) [7] who stated that the levels of serum sodium and potassium were not significantly different in asthmatic children from that of normal controls.

Also, our study supported by Potter and Klein, (1991) [25] who stated that no abnormalities in serum sodium during asthmatic attack.

On the contrary, Hala et al., (2014) [8] and Omer, (2001) [26] reported that hyponatraemia occurred in asthmatic patients in 4% and 4.3% respectively. In addition, Robert et al., (2002) [27] and Hala et al., (2014) [8] reported hypokalemia in 64% and 54% of children with asthmatic status respectively.

As regard to eosinophil level in our study there were 45% of children had eosinophilia but there was no statistically significant difference in eosinophil level regarding severity of asthma. Eosinophilia is a prominent feature of asthma, and it is related to severity of asthma, whereas, on a laboratory or natural exposure to antigen, eosinophilic chemotactic factors are released. On the other hand, eosinophil's function as an effectors cell in the development of asthma and allergic disease. Eotaxins are cytokines that promote pulmonary eosinophilia via the receptor CCR3. Single-nucleotide polymorphisms (SNPs) in CCR3 and eotaxin genes are associated with asthma (Lee et al., 2014) [28].

Our study supported by El- Mazahy et al., (2014) [17] who stated that 57% of asthmatic patients had eosinophilia.

In our study, we found a positive correlation at total calcium regards heart rate and white blood cells, but there was negative correlation regards height and potassium. In addition, we found a positive correlation at ionized calcium regards white blood cells, but there was negative correlation regards potassium.

Also, we found a positive correlation between white blood cells and heart rate with eosinophils, but there is no significant correlation between asthma grade and total calcium, ionized calcium and eosinophils.

Conclusions

Hypocalcaemia appears to be a risk factor for development of asthma in children.

Severity of asthma was not related to the serum calcium level. No abnormalities in serum level of sodium and potassium in asthmatic children. Smoking fathers play an important role in developing asthma among their siblings.

Recommendations

Hypocalcaemia in asthmatic children must be anticipated and corrected, not only for its deleterious effect on respiratory muscle power but also for its possible contribution to bronchial hyper-reactivity.

Withholding parental smoking is recommended as it may precipitate asthma in their children.

Further studies are needed to study the mechanisms by which the asthma induces hypocalcaemia on a large scale.

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