

Potential Effect of Dietary Vitamins A, C, and E, their Levels in Serum within Asthmatic Children

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SUMMARIZED

The respiratory allergic ailment is an inflammatory condition joined by oxidative stress. Extra elements of anti-inflammatory factors such as antioxidants may have a curative effect. This study planned the status of vitamins (A, E & C) in food and sera of young some Egyptian children with allergic asthma coming to the National Nutrition Institute (NNI). The study inclusive 104 children who attended the pediatric outpatient clinic of NNI during August and September 2014. The subjects in the study, both boys and girls, were randomly selected within the age range from 7-10 years. Asthma signs were assessed by a Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Data on nutritional status had been collected using specially designed questionnaires to cover required information on food intake (24-hour recall) and dietary pattern (food frequency) for chosen items. Body mass index was calculated based on the bodyweight within kilograms divided by the square of the body height in meters. After an overnight fast of 12 hours, blood samples of 5ml were collected from the children to determine serum levels of vitamin A, E, and C. The outcome revealed decreased daily intake and serum content from vitamin A, E, and C within asthmatic children parallel to normal children. **Conclusion** Despite the low level of intake antioxidants or there in serum within asthmatic children with no significant differences, they had signs of asthma, which confirms that the decrease in these vitamins, even a small amount, leads to asthma sensitivity.

Key words: Asthma- Antioxidant – Children

INTRODUCTION

Asthma is defined as a morbidness of the airways. Inveterate inflammation is expounded to airway hyper-responsiveness that ends up in repeated episodes of breathlessness, chest tightness, sound within the chest, or coughing, which is able to vary over time and in adversity. Symptom episodes either are generally associated with widespread, but variable, airflow obstruction within the lungs that is usually reversible spontaneously or with appropriate asthma treatment sort of a fast-acting bronchodilator (GINA, 2017). Asthma diseases have increased prevalence. Despite decades of research on risk factors, the causes of those disorders are poorly understood. They are thought to develop through complex interactions between genetic and environmental factors (Moreno-Macias and Romieu 2014). Asthma could be a common and potentially serious chronic disease that imposes a considerable burden on patients, their families, and therefore the community. It causes respiratory symptoms, limitation of activity, and flare-ups (attacks) that sometimes require urgent health care and perhaps fatal (Pedersen et al., 2018). Asthma is characterized by recurrent attacks of dyspnea, cough,

expectoration of tenacious mucoid sputum, and frequently wheezing. Symptoms could also be mild and will occur only in association with a respiratory tract infection, or they will occur in various degrees of severity to the purpose of being life threatening. Classic asthma usually begins in childhood and becomes progressively more severe throughout life. The acute attack is characterized by dyspnea usually related to expiratory wheezing that will be heard without a stethoscope. Cough is also present but is sometimes not the predominant symptom (Federico et al., 2016). Asthma could also be a chronic disease requiring ongoing and comprehensive treatment goals to chop back the symptom burden (i.e. good symptom control while maintaining normal activity levels) and minimize the possibility of adverse events like exacerbations, fixed airflow limitation, and treatment side effects (GINA, 2019).

Vitamin A is a group of chemical substances – retinoid, fat-soluble compounds essential for the human body. It cannot be produced and have to be provided as a part of the diet. In animal origin food, it is present in ester form as retinyl palmitate, which is converted in the human body to alcohol – retinol. In a plant-based diet,

it is present in form of β -carotene, β -cryptoxanthin, and other carotenoids (Shmarakov et al., 2013). The function of vitamin A is its role in the vision cycle (Kiser et al., 2014), regulatory and promoting effects on the immune system, a valuable enhancer of immunity against numerous infectious diseases and pathologies (Huang et al., 2018). Both the T cell-mediated and antibody-dependent immune responses are affected by this vitamin, which is relevant in the process of synthesis of immunoglobulins A and E (Pantazi et al., 2015). Retinoid also has repressive activity on IgE; therefore, they may ameliorate allergic diseases mediated by IgE (Heine et al., 2018, Seo et al., 2017). Vitamin A has to a certain degree, a therapeutic effect in diseases transmitted through the respiratory system, e.g. measles, infantile diarrhea, or pneumonia in children (Hu et al., 2018).

Vitamin C can act as a hydrogen donor to reverse oxidation and therefore functions as an antioxidant that reacts with free radicals (FRs) and deactivates them before they cause damage to proteins or lipids (Hacışevki, 2009). Vitamin C (ascorbic acid) is an important antioxidant and thus works in aqueous environments of the body. Vitamin C

cooperates with Vitamin E to regenerate α -tocopherol from α tocopherol radicals in membranes and raises glutathione levels that is playing a role in the thiol group protection versus oxidation (Kojo, 2004). Oxygen metabolites may play direct and indirect roles in the modulation of airway inflammation (Shanmugasundaram et al., 2001). Vitamin C works in enzyme activation, oxidative stress decrease, and immune tasks. There is considerable evidence that vitamin C may protect against respiratory tract infections and reduce the risk for cardiovascular disease and some cancers (Schlueter and Johnston, 2011).

Vitamin E is the most abundant lipid-soluble antioxidant present in body tissues (Zingg, 2015). Intake antioxidants have a beneficial effect on the prevention and management of chronic diseases (Cheng, et al., 2018, Amanullah et al., 2019). Vitamin E consists of substances belonging to two closely related groups: tocopherols and tocotrienols, each existing in four isomeric forms, α , β , γ and δ making 8 different group members. The biological potency accounting for 90% of the vitamin activity in tissues is α -tocopherol (Rock et al., 2001). Vitamin E is the major lipid-soluble component in the cell antioxidant

defense and is exclusively obtained from the diet. It has numerous roles within the body because of its antioxidant activity (**Rizvi et al., 2014**).

The present study goal to investigate the relationship between the intake of natural antioxidants and incidence of asthma.

SUBJECTS AND METHODS

The Research Ethics Committee at National Nutrition Institute (NNI) approved this cross-sectional study.

Subjects

The study included 104 children from both sexes who attended the pediatric outpatient clinic of NNI during August and September 2014. They were randomly selected in the age range from 7-10 years. A face-to-face interview was completed with the attending parents. Informed consent was obtained from the parents of the children in the study.

Methods:

Asthma symptoms assessment:

Asthma symptoms were assessed using a Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (**Asher et al, 1995**).

Asthma symptoms were defined in the following cases:

- a) when there were wheezing attacks more than one time during the last 12 months,
- b) when there were ≥ 4 wheezing attacks in the last 12 months,
- c) when sleep was disturbed ≥ 1 night/per week,
- d) when dyslogia occurred due to wheezing in the last 12 months.
- e) if there was dry cough at night, apart from a cough associated with a cold or a chest infection during the last 12 months
- f) if there was wheezing during or after exercise during the last 12 months
- g) if there was a positive answer to the question "Has your child ever had asthma?"

According to (ISAAC) questionnaire the children involved in the study were divided into normal children with no asthmatic symptoms (N=61) and asthmatic children (N=43) showing one or more of the above-mentioned symptoms.

Assessment of non-dietary information:

Information on children's characteristics, age, sex, and parental education level, and parental asthma history, number of siblings, and vigorous exercise (that produces sweating) was obtained from parents

using a demographic questionnaire. Parental asthma history was defined as a reported history of clinically-diagnosed asthma in one or more parents. The vigorous sweat-inducing exercise was defined as performing an exercise that induced sweating more than three times a week.

Dietary assessment:

Data on nutritional status had been collected using specially designed questionnaires to cover required information on food intake (24-hour recall) and dietary pattern (food frequency) for selected items.

a) Food intake:

Using the 24-hour recall method, detailed food intake for each eating event was obtained during the previous day to the interview, starting with the first eating event (breakfast) and continuing with each eating event subsequently until before sleep. Amounts of foods and beverages consumed were determined by using dietitian equipment, utensils of known weights, and volumes.

b) Food frequency method:

This method was used to obtain a profile of food intake for the study group. A questionnaire was designed

to cover the selected food items on daily, weekly and monthly basis.

The chosen nutrient content of the last 24 hour was computed using the compiled food composition tables of the National Nutrition Institute, (NNI, 2006). The nutritional value of foods and beverages consumed was compared to the recommended dietary allowances “RDAs” of WHO.FAO./UNU) (Gibson, 1990) and were considered as cut off points for micronutrients.

Anthropometric Measurements:

Body height was measured to the nearest 0.1 cm. Bodyweight was measured with an electronic scale to the nearest 0.1 kg with participants wearing light clothes and barefooted. Body mass index was calculated based on the body weight in kilograms divided by the square of the body height in meters. Percentiles according to age and sex were defined in the intervals $p \geq 95-98$ and $p \geq 99$ (Wohlfahrt-Veje, et al,2014).

Laboratory Investigation:

Sampling

Five millimeters (5 ml) of venous blood were withdrawn from every participant by complete aseptic procedures. The blood was collected in plain vacutainer tubes then centrifuged at the speed of 3000 rpm for separation

of serum. The separated serum was kept in special aliquots at -20 °C until assaying.

All subjects participating in this study were subjected to the following laboratory measurements:

Measurement of vitamins A& E:

The measurement of these vitamins was done using high-performance liquid chromatography (HPLC) by ultraviolet detector by isocratic separation and C18 columns. Vitamin A (λ max) was detected at 325 nm. Vitamin E (λ max) was detected at 295 nm., (Greaves et al.2010). Reference range for vitamin A in serum for children 7-12 years (12.8-81.2 mcg/dl) according to Ross (2006) and that for vitamin E for children 0-17 years: (3.8-18.4 mg/l) according to Traber (2006)

Measurement of vitamin C:

The concentration of vitamin C in serum was estimated by the phenylhydrazine spectrophotometry method. Absorbance of sample and standard were read against blank at 520 nm with spectrophotometry (Karim et al., 2011). Reference range for vitamin C in serum was (0.6 -2 mg/dl) according to (Ball 2004).

RESULTS AND DISSECTION:

Low socioeconomic status, low birth weight, obesity, urban environment, tobacco smoke exposure, regional or cultural dietary habits in minority subgroups, or dietary modification in families with other members who have asthma or allergy. Table (1) includes these previous parameters plus Maternal and Paternal History of Asthma. The study was included 54 boys (51.9%) and 50 girls (48.1%) aged 7-10 years. There were more parents with “senior high school education” than either those with “college education” or those with “less than senior high school education”. 16.3% of mothers and 7% of fathers of asthmatic cases had a history of asthma, 58.7% of children had one or more siblings. Asthmatic children were overweight, had a significantly higher BMI (20.8±7) than normal children (17.3±5.9), and were more likely to engage in sweating exercise (32.6%) than normal individuals (9.8%). Paternal smoking was significantly higher for asthmatic children parallel normal children.

There is nothing can do about age or family history, there are things can do to reduce risk of asthma, healthy weight and quitting cigarettes are maintained to scale back the severity or frequency of asthma attacks

and, in some cases, erase those (**Garcia-Larsen et al., 2017**). Several prospective studies, both within children and adults, indicate that obesity antedates asthma, which the relative risk of incident asthma increases with body mass index (BMI), also appears to worsen asthma control, (**Saint-Pierre et al., 2006; Lavoie et al., 2006**), some but not all studies indicate that it can increase asthma severity (**Beuther and Sutherl 2007; Taylor et al., 2008**). **Shore, (2007)** observed that either surgical or diet-induced weight loss improves many asthma outcomes, provides additional support for a relationship between obesity and asthma, although, in many of those studies, pulmonary function and airway inflammation outcomes were not assessed. **Das, (2001)** reported that the obesity is also a low-grade systemic inflammatory disease. Overweight and obese of all age have high serum levels of C-reactive protein, interleukin-6, tumor necrosis factor-alpha, and leptin, which are known markers of inflammation. Obesity is both a risk factor and a disease modifier of asthma in both children and adults, the commonly approved incontrovertible fact that asthma is an inflammatory process (**Freedman et al., 2017**). This result of the present

study confirms the findings of previous studies that the elevation BMI is associated with a high prevalence of asthma symptoms in children. **Camargo et al., (1999)** suggested that a rise in BMI of children is associated with a dominance of symptoms that are often attributed to asthma, but not with a higher prevalence of asthma. **Chen et al., (2017)** explained the mechanisms that link obesity and asthma might include obesity-influenced lung physiology, such as reductions in pulmonary compliance and limitations in airflow, systemic inflammation, dysfunctions of the sympathetic nervous system, and common genetic factors. In addition, children with asthma are known to present with reduced levels of physical activity and may potentially suffer from the side effects of corticosteroid medications that increase their risk of obesity.

In recent years, there has been increasing interest in the role of nutrition in the development of asthma, particularly in developing nations. It has been postulated that changes in diet and nutrition may play a role in promoting its onset. In particular, interest has focused on the intake of antioxidant vitamins, especially vitamins A, C, E, and the carotenoids, in the modulation of oxidative lung or airway injury from inflammatory cells.

Table 2 revealed that the daily intake from vitamin A ($\mu\text{g}/\text{day}$) and E (mg/day) within asthmatic individuals were lower than normal children with a percentage from RDAs were 101%, 94%, and 86%, 79% respectively, and there were no significant differences between them. Vitamin C showed a decrease in significant differences ($P=0.022$) of asthmatic children compared to the normal case. These results were in harmony with a study done by **De Luis et al., (2005)**, who concluded that asthmatic patients have a lower intake of vitamins A, C, and E than do non-asthmatic subjects. **Ellwood et al., (2001)** found that diets rich in antioxidant vitamins (Vitamins C, E, and β -carotene) might reduce the susceptibility of the lung to oxidant damage and inflammation. The ways that vitamins C and E may help asthmatics include an increase of histamine, rate of reactive oxygen species removal, decrease in the production of bronchoconstrictor inflammatory markers like prostaglandins, and decrease in a contracture of airway smooth muscle cells (**Han et al., 2013**).

Finding in this study has shown that the risk of childhood asthma increased by fewer levels of serum vitamin C, it was at a beginning of the reference range (**Table 3**). Low

vitamin C serum levels were predictive of asthma. Vitamins A, E, and C in serum of asthmatic cases were lower than normal children were by -5, -2.9, and -11 percent change respectively. The present study was matching with a study done by **Seaton and Devereux (2000)**, who reported that the results were indicated that vitamin C plays a role in the evolution of asthma. Additionally, the study also investigated the temporal relation between vitamin C and asthma by examining the effect of serum ascorbic acid on the existence of current asthma. It is an antioxidant present in the airway and alveolar lining fluid. **Schock et al., (2001)** indicated that vitamin C could modify oxidative insults from inhaled agents, infectious agents, or cellular inflammation. Consistent with this conclusion is the finding by **Romieu et al., (2002)** that supplementation with vitamins C and E in asthmatic children had a protective effect against high levels of ozone. While supplementation, as a treatment for chronic asthma was inconclusive in the literature review by **Kaur et al., (2001)**. **Monteleone and Sherman (1997)** have concluded that vitamin C supplementation provides a short-term benefit in treating asthma. Vitamin E is a peroxy-radical scavenger that can protect neurons and respiratory

mucosa from oxidant damage; it can significantly reduce the incidence of asthma and relieve respiratory mucosa inflammation (Yuqing, et al., 2016). Vitamin A is an antioxidant that plays a role in lung development and regeneration of epithelial lung tissue (Checkley et al., 2010). Asthmatic symptoms are associated with airway inflammation, infection, exertion, or stress have appeared within asthmatic children. These factors have been shown to decrease serum retinol levels by increasing cellular demand for retinol and increasing its urinary elimination (Filteau et al., 1993). Airway inflammation in asthmatic patients is associated with increased production of reactive oxygen species (ROS) by peripheral blood eosinophils, neutrophils, and alveolar macrophages (Maier 1993). B-Carotene, by quenching singlet oxygen, may reduce airway inflammation in asthma (Burton et al., 1994). The utilization of vitamin A as an antioxidant may be reducing serum vitamin A levels. Hypovitaminosis A induces respiratory epithelial changes, such as metaplasia (Zachman 1994), and may predispose to respiratory infections (Bloem et al., 1990), which may exacerbate acute asthmatic attacks in children.

CONCLUSION:

Despite the low level of intake antioxidants or there in serum within asthmatic children with no significant differences, they showed signs of asthma.

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Table (1): Basic Characteristics of the Study Population

Variables		Normal N=61	Asthmatic Individuals N=43
		N (%) or Mean \pm SD	N (%) or Mean \pm SD
Age	Years	7-10	7-10
Sex	Boys	29 (47.5)	25 (58.1)
	Girls	32 (52.5)	18 (41.9)
BMI	Kg/m ²	17.3 \pm 5.9	20.8 \pm 7
History of Food allergy	Yes	17 (27.9)	9 (20.9)
	No	44 (72.1)	34 (79.1)
No. of siblings	1	25(41)	18(41.9)
	>2	36(59)	25(58.1)
Maternal Smoking	Yes	4(6.6)	4(9.5)
	No	57(93.4)	39(90.5)
Paternal Smoking	Yes	20(32.8)	21(48.8)
	No	41(67.2)	22(51.2)
Maternal History of Asthma	Yes	8(13.1)	7(16.3)
	No	53(86.9)	36(83.7)
Paternal History of Asthma	Yes	3(4.90)	3(7.1)
	No	58(95.1)	40(92.9)
Vigorous exercise > 3 / week	Yes	6(9.8%)	14(32.6%)
	No	55(90.2)	29(67.4)
Maternal Education	Illiterate	14(23.3)	6(14)
	Primary, Prep	11(18.3)	6(14)
	Secondary, Intermediate	25(41.7)	24(55.8)
	University	10(16.7)	7(16.3)
Paternal Education	Illiterate	12(20)	4(9.3)
	Primary, Prep	10(16.7)	6(14)
	Secondary, Intermediate	28(46.7)	26(60.5)
	University	11(16.7)	7(16.3)

Table (2): Daily Nutrient Intake of some Antioxidant Vitamins in the Study Group (mean ± SD)

Group Vitamins	Normal cases (n=61)	Asthmatic Individuals (n=43)	P value
Vitamin A (µg / day)	504.9 ±112.6	470.9 ±103.9	0.319
RDAs	500 µg/ day		
% from RDA	101%	94%	
Vitamin E (mg / day)	7.75 ±2.39	7.09 ±2.24	0.904
RDAs	9 mg/day		
% from RDA	86%	79%	
Vitamin C (mg / day)	30.09 ±2.84	25.51 ±4.10	0.022*
RDAs	35 mg/day		
% from RDA	86%	73%	

*Significant differences $p < 0.05$ RDI of vitamins A, C from WHO and FAO 2002
 Vitamin. E *Adequate Intake (AI) from National Institutes of health

Table (3): Serum Level of Antioxidant Vitamins in the Study Group (Mean \pm SD)

Group Vitamins	Normal range	Normal cases (n=61)	Asthmatic Individuals (n=43)	P value
Vitamin A ($\mu\text{g} / \text{dl}$)	12.8-81.2 mcg/dl	84.7 \pm 40.6	80.4 \pm 51.7	0.902
% change vs normal case		-	-5%	
Vitamin E (mg/l)	3.8-18.4 mg/l	13.6 \pm 5.2	13.2 \pm 6.1	0.793
% change vs normal case		-	-2.9 %	
Vitamin C (mg/dl)	0.6 -2 mg/dl	0.76 \pm 0.38	0.63 \pm 0.58	0.417
% change vs normal case		-	-11%	

Significant $P \leq 0.05$

التأثير المحتمل لتناول فيتامينات أ، ج، هـ ومستوياتها في مصل الدم لدى الأطفال المصابين بالربو

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الملخص العربي

مرض حساسية الجهاز التنفسي هو حالة التهاب مصحوبة بالاجهاد التأكسدي . قد يكون لمضادات الاكسدة تأثير علاجي مضاد للالتهاب. تناولت هذه الدراسة تأثير الفيتامينات (أ، ج، هـ) في غذاء ومصل بعض الاطفال المصريين المصابين بالربو التحسسي المترددين على عيادات المعهد القومي للتغذية . اشتملت الدراسة على ١٠٤ طفل من عيادة الاطفال الخارجية في خلال شهري اغسطس وسبتمبر ٢٠١٤ . تم اختيار المشاركين في الدراسة ، من البنات والاولاد بشكل عشوائي وكانوا من الفئة العمرية من ٧-١٠ سنوات . ثم تم تقييم أعراض الربو من خلال النسخة الصينية من استبيان الدراسة الدولية للربو والحساسية في الاطفال . تم جمع البيانات المتعلقة بالحالة التغذوية باستخدام استبيانات تناول الطعام (استرجاع على مدار ٢٤ ساعة) والنمط الغذائي لتكرار الطعام للعناصر المختارة . تم حساب مؤشر كتلة الجسم بناء على وزن الجسم بالكيلو جرام مقسوما على مربع الطول بالمتر . بعد صيام طوال الليل لمدة ١٢ ساعة، تم جمع عينة دم من الوريد ٥مل من الاطفال لتحديد مستويات الفيتامينات (أ، ج، هـ) في المصل . النتائج أظهرت انخفاض المدخول اليومي ومحتوي المصل من تلك الفيتامينات في الاطفال المصابين بالربو مقارنة بالاطفال الطبيعيين ولكن مع عدم وجود فروق معنوية . الخلاصة على الرغم من انخفاض مستوى تناول مضادات الاكسدة أو وجودها في مصل الدم لدى الاطفال المصابون بالربو مع عدم وجود فروق ذات دلالة احصائية مقابل الحالات الطبيعية ، فكانت لديهم علامات الربو، مما يؤكد ان الانخفاض في تلك الفيتامينات ولو قليل يؤدي الى حساسية الربو .

الكلمات المفتاحية: مضادات الاكسدة - الربو - الاطفال