Research Article

Serum Levels of Selenium, Zinc, and Magnesium in Children with Bronchial Asthma

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Abstract
Bronchial asthma is a chronic inflammatory disease of the respiratory tract, characterized by air way hyper responsiveness**.** Zinc (Zn) is an important antioxidant element, possesses antiapoptotic and anti-inflammatory feature indicating a possible role in asthma pathogenesis and treatment**.** Selenium (Se) has been hypothesized to ameliorate oxidative stress which significantly contribute to the pathogenesis of asthma and thus reducing asthma. Magnesium (Mg) is an important mineral in the body and is essential to good health. **Aim of the work:** The aim of this work was to measure serum selenium, zinc, and magnesium in children with bronchial asthma and compare them with that of normal children. **Patients and Methods:** This study was carried upon ٢ groups: (group ١) consisted of ٥٠ patients with bronchial asthma ٢٦ males (٥٢٪) and ٢٤ females (٤٨٪) with age ranged from ٣ to١٢ years with a mean ٦.٩±٢.٧. The ٢nd group (control group) consisted of ٣٠ apparently healthy volunteers with age and sex matched to the diseased patients. Serum levels of zinc, Se, Mg were measured. **Results:** hemoglobin, Zinc, and Selenium levels were highly significantly decreased in patients than in controls and to a lesser extinct, there was a decrease in Mg level in patients than in controls. **Conclusion:** serum levels of zinc, selenium, and magnesium in asthmatic children are lower than that of controls; also, serum levels of zinc, selenium, and magnesium in asthmatic children are lowered with increasing asthma severity.
Key words: Asthma, Selenium, Zinc, and Magnesium.

Introduction
Bronchial asthma is one of the most common diseases in childhood. It is a chronic inflammatory disease of the respiratory tract; asthma is a multifactorial inflammatory syndrome characterized by air way hyper responsiveness[١].

Zinc (Zn) is an important antioxidant element, it is found in the respiratory tract epithelium, plays a role in the regulation of cellular and humeral response and possesses anti apoptotic and anti-inflammatory feature indicating a possible role in asthma pathogenesis and treatment[٢].

Selenium (Se) has been hypothesized to play an important role as a potent nutritional antioxidant which can serve to ameliorate oxidative stress which signify-cantly contribute to the pathogenesis of asthma and thus reducing asthma[٣].

Magnesium (Mg) is an important mineral in the body and is essential to good health. Approximately ٥٠٪ of total body magnesium is found in bone. The other half is found predominantly inside cells of body tissues and organs. Only ١٪ of magnesium is found in blood[٤].

Aim of the work:
The aim of this work was to measure serum selenium, zinc, and magnesium in children with bronchial asthma and compare them with that of normal children and also correlate their levels with the severity of asthma.

Patients and method

This study included ٨٠ children, ٥٠ patients, with bronchial asthma and ٣٠ controls, during the period from Jan ٢٠١٣ to June ٢٠١٣. Informed consent was obtained in every case from his/her legal guardians. The patients were ٢٦ males (٥٢٪) and ٢٤ females (٤٨٪) and the control children were ١٥ males (٥٠٪) and ١٥ females (٥٠٪) who were apparently healthy and of the same age and sex, the studied groups were subjected to the followings: full history taking, clinical examination, laboratory investigations. Full history taking including age and gender, family history of similar condition, history of consanguinity, age of onset of the disease, number of attacks, frequency of exacerbation of the attacks and duration of free symptoms, history of medications including the type, dose, method of administration, and compliance to treatment, and if use inhalational treatment or not. Clinical examination: general examination including: anthropo-metric measurements (weight, length), pallor, cyanosis, signs of distress as working ala nasi, restlessness, irritability, fighting for breathing, vital signs (heart rate, respiratory rate, temperature, and blood pressure), systemic examination, cardiac examination (inspection, palpation, percussion, and auscultation), chest exami-nation (inspection, palpation, percussion, and auscultation), abdominal examination (inspection, palpation, percussion, and auscultation). Laboratory investigations including: complete Blood Count by using automated cell counter (Sysmex NE. ١٥٠٠. Japan), assessment of serum magnesium, zinc, and selenium by using semi-auto-mated spectrophotometer (Humalyer ٣٠٠٠, Germany). The patients were diagnosed by: data obtained from history as age, age of onset of the disease, family history of similar condition, history of recurrent attack of wheezing, time of exacerbation of the attack, time of free symptoms, type of medications, and doses, symptoms as cough, tight chest, wheezing, tachypnea.

Inclusion Criteria: age ranged from ٣-١٢y, family history of similar condition, symptoms of airway obstruction.

Exclusion criteria: age less than ٣ y and more than ١٢ y and other causes of respiratory distress as allergic rhinitis, chronic rhinitis, sinusitis, adenoidal or tonsillar hypertrophy, bronchopulmonary dysplasia, viral bronchiolitis, Bronchie-ctasis, cystic fibrosis, chronic aspiration, interstitial lung diseases, tuberculosis, pneumonia, pulmonary edema, congestive heart failure. Medications associated with chronic cough as acetyl cholinesterase inhibitors, B ١ adrenergic antagonists.

Sampling: five ml of venous blood were withdrawn, one ml in EDTA containing tube for CBC and the other four ml in plain tube, left to be clotted and centrifuged then sera were separated and stored at -٢٠c for assessment of zinc, selenium and magne-sium. Atomic Absorption Spectrophoto-meter was used for determination of serum level of zinc, selenium, and magnesium.

Normal levels of serum zinc is (٦٠-١١٠ ug/dl), serum selenium is (٧٠-١٥٠ ng/ml), serum magnesium is (١.٩-٢.٥mg/dl).

Statistical analysis:

Statistical analyses were performed using the SPSS statistics version ١٦. Differences in the mean of continuous variables was analyzed using parametric test (independent sample T. test, One-way ANOVA test). And differences between categorical variables were analyzed using Chi Square test. For all tests, the values P<٠.٠٥ were regarded statistically significant.

Results

This study was carried on ٨٠ patients divided into ٢ groups. Group ١ consisted of ٥٠ patients with bronchial asthma ٢٦ males (٥٢٪) and ٢٤ females (٤٨٪) with age ranged from ٣ to١٢ years with a mean ٦.٩±٢.٧, this group was subdivided into mild intermittent (٣٤ patients) and moderate persistent (١٦ patients). Group ٢ (control group) consisted of ٣٠ apparently healthy volunteers with age and sex

matched to the diseased patients during the period from January to June ٢٠١٣ in Minia University Hospital. An approval was obtained from the ethical committee of the Faculty of Medicine of Al-Minia university. There were no statistical differences regarding age, weight, height, and sex between the patients and controls (table ١).

There were no significant statistical differences between the severity of asthma and age, sex, weight, height, age of onset, family history, seasonal variation, socioeconomic state, smoking, and animal exposure in asthmatic patients (table ٢). There were highly significant higher levels of hemoglobin, zinc, selenium, in controls compared to patients (P value <٠.٠٠١) and significant higher level of magnesium in controls compared to patients, (P value ٠.٠١) and significant lower level of eosinophils in controls compared to patients (P value ٠.٠٢) while no statistical difference between patient and controls regarding white blood cells (P value ٠.٦). Normal level of Hb (١٢-١٤g/dl), WBCs (١٠+-٥x (١٠)٣/ul, Eosinophils (٢٪) (table ٣).

There were highly significant higher levels of hemoglobin, zinc, selenium, and magnesium in patients with mild intermittent asthma, compared to those with moderate persistent asthma (P value <٠.٠٠), while no statistical difference regarding white blood cells and Eosinophils (table ٤).

Table (١): Base line demographic data of the studied groups.

	Patients (No. = ٥٠)	**Controls (No. = ٣٠)**	**P value**
Age(year)			
Mean±SD	٦.٩±٢.٧	٧.٣±٣.١	٠.٥
Range	٣-١٢	٣-١٢	
Sex No.(%)			
Male	٢٦(٥٢٪)	١٥(٥٠٪)	٠.٨
Female	٢٤(٤٨٪)	١٥(٥٠٪)	
Weight(kg)			
Mean±SD	٢٠.٧±٦.٢	٢١.٩±٦.٩	٠.٤
Range	١٢-٤٠	١٢-٣٥	
Height(cm)			
Mean±SD	١١٥.١±١٥.٣	١١٧.٨±١٧.٢	٠.٤
Range	٩٠-١٥٠	٨٩-١٤٣	

Table ٢: The relation between the severity of bronchial asthma and the demographic data.

	Severity of BA		P value
	Mild intermittent No. (٣٤) ٦٨٪ of total	Moderate persistent No. (١٦) ٣٢٪ of total	
Age(year)			
Mean±SD	٧.١±٢.٨	٦.٧٥±٢.٥	٠.٧
Range	٣-١٢	٣-١١	
Sex			
Male (٢٦)	١٧(٦٥.٤٪)	٩(٥٦.٣٪)	٠.٧
Female (٢٤)	١٧(٧٠.٨٪)	٧(٤٣.٧٪)	
Weight(kg)			
Mean±SD	٢٠.٧±٦.٣	٢٠.٤±٦.٣	٠.٩
Range	١٣-٤٠	١٢-٣٥	
Height(cm)			
Mean±SD	١١٥.٤±١٥.٧	١١٤.٥±١٥.٣	٠.٨
Range	٩٢-١٥٠	٨.٦-٩.٦	
Age of onset			
Mean±SD	٣.٦±١	٣.٥±٠.٩	٠.٧
Range	٢.٥-٦	٢.٥-٥	
Family history			
Siblings(١٢)	٩(٧٥٪)	٣(١٨.٧٥٪)	٠.٨
Paternal(٨)	٥(٦٢.٥٪)	٣(١٨.٧٥٪)	
Maternal(٣٠)	٢٠(٦٦.٧٪)	١٠(٦٢.٥٪)	
Seasonal variation			
Winter(٢٤)	١٨(٧٥٪)	٦(٣٧.٥٪)	٠.٦
Spring(٢٠)	١٢(٦٠٪)	٨(٥٠٪)	
Autumn (٦)	٤(٦٦.٧٪)	٢(١٢.٥٪)	
Socioeconomic status			
Low(٣٢)	٢١(٦٥.٦٪)	١١(٦٨.٧٥٪)	٠.٦
Intermediate(١٨)	١٣(٧٢.٢٪)	٥(٣١.٢٥٪)	
Smoking			
-ve(١٤)	١٠(٧١.٤٪)	٤(٢٥٪)	٠.٧
+ve(٣٦)	٢٤(٦٦.٧٪)	١٢(٧٥٪)	
Animal exposure			
No(٢٣)	١٥(٦٥.٢٪)	٨(٥٠٪)	٠.٧
Yes(٢٧)	١٩(٧٠.٤٪)	٨(٥٠٪)	

Data is presented by No. (%)

Table (٣): Comparison between cases and control groups as regarding studied laboratory data

	Patients (No. = ٥٠)	Controls (No. = ٣٠)	P value
Haemoglobin(g/d)			
Mean±SD	٩.٩±٠.٨	١٢.٩±٠.٨	<٠.٠٠١**
Range	٦.٤-١٠.٧	١٢-١٥	
White blood cells(x١٠)٣/ul			
Mean±SD	٧.٩±٢.٦	٧.٦±١.٨	٠.٦
Range	٤.٢-١٣.٦	٤.٣-١١	
Eosinophils(%)			
Mean±SD	١.٥٤±١.٣	١±٠.٠	٠.٠٢*
Range	١-٨	١-١	
Zn(ug/dl)			
Mean±SD	٤٩.١±٨.٥	٩٥±١٠.٨	<٠.٠٠١**
Range	١٧-٥٩	٧٠-١١٠	
Mg(mg/dl)			
Mean±SD	١.٥±٠.٣	٢.٩±٣.٨	٠.٠١*
Range	٠.٧-١.٨	١.٩-٢٣.٣	
Se(ng/ml)			
Mean±SD	٥٤.٥±١٠.٩	١٢٨.٤±١٢.٧	<٠.٠٠١**
Range	٢٩-٦٩	١٠٦-١٥٠	

Table ٤: The relation between the severity of bronchial asthma and laboratory data in patients group

	Severity of BA		P value
	Mild intermittent No. (٣٤)	Moderate persistent No. (١٦)	
Haemoglobin(g/dl)			
Mean±SD	١٠.٣±٠.٣	٨.٩±٠.٣	<٠.٠٠١**
Range	٩.٧-١٠.٧	٦.٤-٩.٦	
White blood cells(x(١٠)٣/ul			٠.٢
Mean±SD	٨.٢±٢.٥	٧.١±٢.٩	
Range	٤.٢-١٣.٤	٤.٤-١٣.٦	
Eosinophils(%)			
Mean±SD	١.٦٥±١.٥	١.٣±٠.٥	٠.٤
Range	١-٨	١-٢	
Zn(ug/dl)			
Mean±SD	٥٣.٤±٤	٤٠±٦.١	<٠.٠٠١**
Range	٤٥-٥٩	٣١-٥٥	
Mg(mg/dl)			
Mean±SD	١.٧±٠.١	١.١±٠.١	<٠.٠٠١**
Range	١.٥-١.٨	١-١.٢	
Se(ng/ml)			
Mean±SD	٦٠.٨±٥.٩	٤١.٢±٤.٩	<٠.٠٠١**
Range	٤٨-٦٩	٣٠-٤٩	

Discussion

Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible obstruction, and bronchospasm[٦].

Zinc is protective for respiratory epithelium by virtue of being an anti-oxidant, organelle stabilizer and possessing anti-apoptotic activity (as an inhibitor of caspase-٣ activation), also stimulates DNA synthesis and cell proliferation, tissue regeneration and acting as an anti-inflammatory agent [٧].

There is a high relationship between Se deficiency and asthma through the antioxidant effects of glutathione peroxidase, the asthmatic patients had significantly lower concentrations of selenium measured in plasma and whole blood [٨].

Magnesium plays an important role in the bronchial asthma including inhibition of vascular and bronchial smooth muscle contraction, inhibition of acetylcholine release from cholinergic nerves, promotion of nitric oxide and prostacycline generation, and stabilization of smooth muscle [٩].

Numerous studies investigated the zinc, magnesium, and selenium status of bronchial asthmatics. It was proposed that adequate dietary intake and Zn, Mg, and Se supplementation may decrease the severity of asthmatic attacks [١٠].

The present study was done to estimate serum zinc, magnesium, and selenium in children with bronchial asthma.

Regarding anthropometric measures it was found that patients with bronchialasthma had no significant differences compared with control group.

As regards laboratory data, this study showed that there is a highly significant difference in Zn, Hb and Se being lower in patients compared to controls.

Zinc has anti-oxidant and anti-apoptotic effect, so it has a protective role in asthma, excessive and inappropriate apoptosis in airway epithelium play a role o in asthma pathogenesis [١١].

In our study, the serum level of Zn ishighly significantly lower inpatients than in controls.

This is matched with Emmanouil et al., ٢٠١٠, Ermis et al., ٢٠٠٤ who found marked lowering in serum zinc in asthmatics than controls.
Zinc deficiency leads to airway epithelial damage which plays an important role in asthma pathogenesis, the damage to this barrier is related to caspase ٣ activation and the proteolysis of proteins that provide intercellular connection. Zinc protects airway epithelial integrity by preventing caspase ٣ activation and lysis of proteins, so zinc acts ascytoprotectant for airway epithelium [١٣].

This is in variance with Arik Yilmaz et al, ٢٠١١ whose study showed that there was no significant difference in Zn between asthmatics and controls .

In Arik study all cases of hypozincemia were from central Anatolian region Zn is deficient in ٥٠٪ of agricultural soil and most of these area is located in Central Anatolian Region, it is known that Zn deficiency is seen commonly in communities with a grain based diet and the high phytate, Zn in food is one of the main factors, the Zn availability decreases markedly when this ratio is over ٢٥-٣٠, this ratio can increase up to ١٢٠ in wheat raised in Central Anatolian Region [١٤].

Red meat and sea food have the highest Zn content among food products and in other study there is little evidence that asthmatics receive low Zn level in diet[١١].

The present study also showed a highly significant statistical difference in the serum zinc between cases of mild intermittent and moderate persistent asthma as zinc level decrease with increased severity and increase with decreased severity and this is in agreement with Arik Yilmaz et al, ٢٠١١ who found that level of Zn in patients with history of hospital admission was significantly lower than those who had not been admitted.

Taylor et al., ١٩٩٧has reported that zinc deficiency increase oxidative stress in mice and that the oxidant damage in the

respiratory tract can be prevented when zinc is added to their diet[١٥]

Our study found that there is a highly significant differences between Hb in asthmatics and controls in form of decreased level in patients and normal levels in controls.

Hambidge, ٢٠٠٠ reported that Zn deficiency leads to increase level of copper which interfere with iron metabolism, also Zn is essential for RBCs division and growth. Zn is essential for immunity and it is anti-infection also essential for DNA and RNA synthesis in the body so Zn deficiency leading to anemia [١٦].

In this study there is a highly significant difference in serum Se between asthmatics and controls in the form of decreased level in asthmatics and normal level in controls, this is in agreement with the study done by Hoffman et al., ٢٠٠٧ who found similar association between selenium intake and allergic airway inflammation in mice,also our study is in accordance with the study of Kocabas et al., ٢٠٠٦ who found significant association between serum Se and asthma[١٧, ١٨].

A study done by GUO et al., ٢٠١١ found that asthma group had low serum Se and higher indicators of oxidative stress as thiobarbituric acid reactive substances[١٩], also Kocyigit et al., ٢٠٠٤ reported that serum Se and glutathione peroxidase activity were reduced in children with asthma than in controls[٢٠].

The observational studies of Emmanouil et al., ٢٠١٠ found an association between lower Se level and asthmatic children.

Our study was in variance with the study done by Van Oeffelen et al., ٢٠١١ who found that the association between serum Se and asthma is inconsistent and not statistically significant, and couldnot confirm the hypothesized inverse associa-tions between serum Se and childhood asthma using cross sectional and prospective analyses but in his study there was a small sized samples which may decrease the power of the study[٢١].

Our study found that there is highly significant difference between serum Se

and asthma severity as it decrease with increased severity and vice versa, this matched with another study was done by Garcia-Larsen et al, ٢٠٠٧ suggested that Se level or glutathione peroxidase activity were positively associated with severity of asthma[٢٣]. But against Van Oeffelen et al., ٢٠١١ who found no association[٢١].

Results from intervention studies aimed at determining the effectiveness of Se supplementation for reducing the incidence or severity of asthma have not been entirely clear or consistent. For example, a study by Gazdik et al., ٢٠٠٢ reported significantly decreased consumption of corticosteroid after Se supplementation with ٢٠٠ug/day for ٩٦ weeks in corticosteroid dependent asthma[٢٥].

Se has a strong effect on the activation, proliferation and differentiation of T helper cell during initiation of immune response, and high Se intake significantly increase T cells proliferation capacity, and increase of Ca mobilization, oxidative burst, and translocation of nuclear factor of activated T cells (NFAT)[٢٧]

This study found that serum Mg is lower in patients than in controls and this matches with the study done by Emmanouil et al., ٢٠١٠ Gontijo-Amaral et al., ٢٠٠٧ who found that there was a significant lower Mg level in patients than controls[١٠,٢٨].

This association is interpreted as Mg has a bronchodilator effect and influence the immune system beneficially which could prevent or reduce asthma symptoms in children[٢٨].

In contrast to this study former studies of, Wang et al, ٢٠٠٧ who did not show any association between serum Mg and asthma[٢٩].

Mg also showed highly significant association with asthma severity in this current study as its level decrease with increased asthma severity and vice versa, but no study has been found talking about this association either by agreement or disagreement.

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