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ORIGINAL ARTICLE

Evaluation of Serum Level of Zinc, Copper and Magnesium in Asthmatic Children and Their Correlation to Disease Severity

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ABSTRACT

Background: Trace elements are essential micronutrients found in the body in extremely small amounts. The generation of free radicals may be linked to trace element deficiencies and is known to cause damage to cells and tissues. They are assumed to have a role in the etiology of numerous diseases, including bronchial asthma. Zinc (Zn), copper (Cu), and magnesium (Mg) are necessary for antioxidant enzymes and therefore for the optimal functioning of the immune system. Changes in trace elements level decrease the efficacy of these antioxidant enzymes and lead to hyperactivity and inflammation of the respiratory tract .

Aim: To find the relationship between serum level of zinc , copper and magnesium and severity of bronchial asthma in children (who are subdivided into intermittent , mild persistent , moderate persistent and severe persistent) .

Methods: This case–control study was conducted on 124 children at the Pediatric Pulmonology Outpatient Clinic of the Faculty of Medicine, Zagazig University. The children were divided into two groups. Group A comprised 62 children diagnosed with bronchial asthma. We subsequently subdivided this group into four subgroups according to asthma severity: intermittent, mild persistent, moderate persistent and severe persistent. Group B comprised 62 clinically healthy controls. The serum levels of Zn, Cu, and Mg were measured by Atomic Absorption Spectrophotometer and pulmonary function tests were done to studied groups.

Results: Compared to the control group, the asthmatic group had significantly lower serum levels of Zn and Mg and higher levels of Cu. There was significant relation between asthma severity and serum level of Zn and Mg .The severe persistent subgroup had significantly lower levels of Zn and Mg than the intermittent and mild persistent subgroups. Serum copper showed no significant correlation with asthma severity .

Conclusion: Children with bronchial asthma have lower serum levels of zinc and magnesium and higher levels of copper compared to healthy children. A disruption of these trace elements serum levels could be a factor in the development of bronchial asthma.

Keywords: Serum Level; Zinc; Copper; Magnesium; Asthmatic Children.

INTRODUCTION

Bronchial asthma is a long-term inflammatory illness of the airways that results in bronchial hyperactivity, excessive mucus production, wall remodelling, and airway narrowing. It is caused by a variety of immune system cells, both innate and adaptive [1]. It is the leading cause of pediatric hospital stays, ER visits, and absences from school. It also increases morbidity and death in children. The three most typical asthmatic symptoms are dyspnoea, wheezing, and cough [2]. Numerous genetic and environmental factors can impact the development of asthma [3]. Numerous researchers have hypothesized that dietary

modifications could contribute to an increased risk of developing asthma [4].

Minerals and trace elements are chemical elements that are found in trace concentrations in living tissues. Certain trace elements are nutritional minerals that are necessary for proper human growth and function [5]. The structures of antioxidant enzymes contain trace amounts of components. These enzymes function as components of the immune system and, through controlling the host immune system, have the ability to modify viral DNA [6]. A deficiency in trace elements can lead to the generation of free radicals, which can cause damage to tissue. Additionally, viral disorders are frequently observed concurrently, creating intricate interactions[7].

Zinc has antiapoptotic, stabilizing microtubule, antioxidant, and growth cofactor properties that protect the respiratory system [8]. Zinc reduces oxidative stress by blocking the synthesis of reactive oxygen species (ROS) through the activation of antioxidant enzymes, including catalase (CAT), superoxide dismutase (SOD), and glutathione-related enzymes, as well as through the inhibition of pro-oxidant enzymes, such as NADPH oxidase [9]. Increased inflammatory responses may arise from a shift in the Th1/Th2 balance toward a Th2 response caused by dysregulation of zinc (Zn) homeostasis[10]. A primary aberration in asthma is an enhanced Th2 response to normally harmless environmental antigens. Th2 cells release cytokines that promote inflammation and the production of IgE and other antibodies by B cells. These cytokines include IL-4, which stimulates the synthesis of IgE; IL-5, which activates locally recruited eosinophils; and IL-13, which stimulates the formation of mucus from bronchial submucosal glands and stimulates B cells to create IgE [11]. Reduced zinc levels hinder the cell membrane's defense against free radicals, which damages the membrane's stability and integrity by releasing enzymes from lysosomes and histamine from mast cells [12]. Asthma onset, severity, and exacerbation are all associated with low zinc levels. Ingesting less zinc increases the chance of atopy, bronchial reactivity, and allergy-like symptoms by up to five times [13].

Enzymes involved in energy metabolism, such as cytochrome c oxidase, and oxidant-antioxidant equilibrium, such as Cu-Zn-superoxide dismutase, contain copper as a component or cofactor. Copper excess and zinc deficiency are observed simultaneously. This can be explained by the fact that elevated copper levels counteract zinc influx across intestinal membranes. Elevated copper levels could result from inflammation-induced tissue damage that releases copper [9]. Both an excess and a shortage of copper can cause oxidative stress and persistent inflammation [14]. Phosphatidyl-inositol-3-kinase (PI3K) is an enzyme that is activated by copper and, in turn, promotes inflammatory mediators, recruitment of inflammatory cells, and remodelling of airways [15]. Therefore, copper ions may act as a second messenger in the development of inflammation and the body's reaction to an inflammatory burden [16].

Magnesium dilates airways and relaxes the smooth muscles in the bronchi, most likely by changing the flow of calcium ions. On the other hand, bronchoconstriction may result from hypomagnesemia. In certain people, bronchial spasms may cause disruption of the neuromuscular process [17]. Moreover, magnesium decreases the release of acetylcholine from motor nerve terminals, which in turn inhibits the excitability of muscle fibres. Additionally, it prevents the release of inflammatory mediators by impeding mast cell degranulation and aiding in T-cell stability. Additionally, it decreases the intensity of inflammation in individuals with asthma by promoting the synthesis of prostacyclin and nitric oxide. However, studies performed to prove this connection have produced contradictory findings[6, 18]. Thus, research is required to determine whether the levels of zinc, copper, and magnesium are related to bronchial asthma severity.

We aimed to assess bronchial asthma severity in children in relation to serum levels of zinc, copper and magnesium.

PATIENTS AND METHODS

This case–control study was conducted on 124 children at the Pediatric Pulmonology Outpatient Clinic in the Faculty of Medicine, Zagazig University, from July 2023 to February 2024 after protocol approval by our local ethics committee (institutional review board number 10911-21-6-2023). Informed consent was also obtained from the parents of the children who participated in the study. The study protocol conformed to the ethical guidelines of the World Medical Association (Declaration of Helsinki 1975) for studies involving humans.

The children were divided into two groups. Group A comprised 62 children of both sexes who were diagnosed with asthma. We subsequently subdivided this group into four subgroups according to asthma severity: intermittent (14 patients), mildly persistent (14 patients), moderately persistent (20 patients) and severely persistent (14 patients). Asthmatic children were

classified by severity according to GINA guidelines [19]. Group B comprised 62 clinically healthy children of both sexes who didn't have family or personal history of asthma or other allergies and composed the control group. They were matched to the children in group A regarding age,weight and height.

Children aged 5-14 years, diagnosed with asthma based on the child's history of frequent severe episodes of cough, dyspnoea, and wheezing and diagnosed with bronchial asthma according to history, clinical findings and pulmonary function test results with a family history of asthma or other allergies were included in the study.

The exclusion criteria were children aged <5 years and >14 years with potential causes of wheezing other than asthma, such as congenital lung lesions, reflux disease, heart problems, chest conditions other than asthma, severe systemic sickness, protein energy deficiencies or a history of vitamin or mineral supplementation in the last 6 months.

All children were subjected to family history of asthma and other atopic diseases, socioeconomic status, age at onset of symptoms, frequency of daytime symptoms, frequency of night awakening from exacerbations, effect on normal activities including school attendance, types and route of drugs used, previous hospital admissions, careful clinical examination including general examination of anthropometric measurements, local pulmonary examination and other systems examination to exclude other chronic diseases. BMI was calculated by dividing the child's weight in kilograms by their height in meters squared (kg/m2) and then plotted on the BMI-for-age table. Laboratory investigations included routine complete blood counts, eosinophil counts, serum IgE levels, and serum zinc, copper and magnesium levels.

Pulmonary function testing:

It was carried out in our pulmonology unit using the Jaeger Master Screen™ IOS, version 5.2, produced in Hoechberg, Germany, by VIASYS Healthcare GmbH under standard conditions according to the manufacturer's instructions.

Based on the established standards, the following parameters were measured by Miller et al. : forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio by Miller et al. [20]. These parameters are expressed as a percentage of the predicted value for each subject as calculated by the machine according to the data entered, which include age, sex, weight and height.

For pulmonary function tests, medication for the chest was prohibited for 12 hours before the examination. The child was at ease and dressed in loose-fitting clothing without any girdles or belts that might restrict his or her breathing.

After receiving the child's information, which included name, age, sex, height, and weight in kilograms, the system automatically used regression equations to determine the expected normal values of the ventilatory function parameters. The child was instructed to make three consecutive attempts. The child was instructed to inhale deeply, exhale as strongly and quickly as they could, and then reinspire as forcefully and quickly as they could to trace the flow-volume loop.

Biochemical estimation of serum micronutrient levels:

To estimate the serum micronutrient levels of zinc, copper and magnesium, blood specimens were collected in sterile tubes. Three-millilitre blood samples were centrifuged for 15 min in the centrifugation device of the Central Laboratory of Zagazig University Hospitals. One milliliter of each resulting serum sample was separated and stored in Eppendorf tubes at −80°C until the time of the assay. The quantitative determination of zinc, copper and magnesium was carried out by a "Buck Scientific 210VGP Atomic Absorption Spectrophotometer AAS" at the Central Laboratory, Zagazig University. The device was calibrated by the following measuring units: µg/dL for zinc, µg/dL for copper and mg/dL for magnesium.

Statistical analysis:

The statistical package for the social sciences, SPSS, version 26, was used to examine the collected data. The chi-square test was used to compare and characterize categorical variables based on their absolute frequencies. Depending on the type of data, quantitative variables were described using their means, standard deviations, medians, and interquartile ranges. Pairwise comparisons and the Bonferroni correction were utilized when the difference was significant. The correlation coefficients for Pearson and Spearman ranks were also employed. In this work, we employed one-way ANOVA, the ROC curve test, the Mann–Whitney test, the Kruskal–Wallis test, the independent sample T test, and the Kolmogorov–Smirnov test. To determine the ideal cut-off of a certain quantitative parameter for diagnosis, a receiver operating characteristic (ROC) curve was generated. The level of statistical significance was set at $P<0.05$. A highly significant difference was indicated by $p\leq0.001$.

RESULTS

There was no significant difference observed among studied groups regarding age, sex , height , weight or BMI . There was a statistically

significant difference between the studied groups regarding family history, haemoglobin and the eosinophil count. There was a statistically significant difference in the IgE concentration between the studied groups. FEV1, FVC, FEV1/FVC and PEF were all significantly lower in the asthmatic group. Regarding serum zinc, copper and magnesium, the asthmatic group had significantly greater serum copper and lower zinc and magnesium. (Table 1).

The FEV1, FVC, FEV1/FVC, and PEF were significantly positively correlated with the serum zinc and magnesium concentrations. The relationships between the serum copper concentration and the FEV1, FVC, FEV1/FVC, or PEF were not statistically significant. (Table 2).

There was a significant positive relationship between asthma severity and IgE.. All of FEV1, FVC, FEV1/FVC and PEF were negatively correlated with asthma severity . There was a significant negative coerrelation between asthma severity and serum zinc and magnesium . Severe persistent group had significantly lower serum zinc and magnesium compared to intermittent and mild persistent groups . There was no significant correlation between copper concentration and the severity of asthma (Table 3).

Serum IgE was significantly higher in uncontrolled group when compared to the controlled and partly controlled groups . There was a statistically significant relationship between asthma control and all of FEV1, FEV1/FVC , FVC and PEF . There was a significant relationship between asthma control and serum zinc and magnesium . Serum zinc and magnesium were significantly lower in uncontrolled group while there was no significant correlation between copper and asthma control (Table 4).

The best cut-off of serum zinc and magnesium for the diagnosis of controlled asthma was ≥71.5 µg/dL and ≥1.815 mg/dl respectively . The best cut-off of serum zinc and magnesium for the diagnosis of uncontrolled asthma was ≤69.7 µg/dL and ≤1.745 mg/dl respectively . The best cut-off for serum zinc and magnesium for the diagnosis of severe persistent asthma was ≤69.7 µg/dL and ≤1.645 mg/dl respectively. (Figure 1).

Table 1: Comparison between the studied groups regarding baseline data, Spirometric data and trace elements

		Case group (N= 62)	Control group (N=62)	χ^2	p
Gender	**Female** **Male**	28 (45.2%) 34 (54.8%)	25 (40.3%) 37 (59.7%)	0.297	0.586
Family history		39 (62.9%)	0 (0%)	56.894	<0.001**
Age (year)		7.98 ± 1.88	8.24 ± 2.31	-0.683	0.496
Weight (kg)		25.34 ± 5.91	25.4 ± 6.1	-0.06	0.952
Height (cm)		123.69 ± 10.46	125.16 ± 11.83	-0.736	0.463
BMI (kg/m^2)		16.46 ± 1.4	16.04 ± 1.19	1.081	0.074
Hemoglobin (g/dl)		10.97 ± 1.14	11.6 ± 1.17	-3.036	0.003*
Eosinophil (cells/ml)		440.97 ± 110.21	128.23 ± 38.77	21.077	<0.001**
IgE (IU/ml)		395(185 – 550)	65(60 – 73)	-9.613	**<0.001****
FEV1 %		68.24 ± 13.59	84.92 ± 3.42	-9.368	<0.001**
FVC%		84.76 ± 8.84	94.47 ± 3.1	-8.16	<0.001**
FEV1/FVC		79.31 ± 9.21	89.42 ± 2.74	-8.285	<0.001**
PEF %		72.63 ± 15.78	90.06 ± 4.04	-8.426	<0.001**
Serum Zinc (µg/dL)		70.44 ± 9.51	89.3 ± 15.01	-8.36	<0.001**
Serum copper (µg/dL)		124.98 ± 12.24	100.6 ± 13.77	10.415	<0.001**
Serum Magnesium (mg/dl)		1.77 ± 0.13	1.96 ± 0.17	-7.077	<0.001**

Date presented as mean ± SD, median (IQR) or frequency (%), χ^2Chi square test t independent sample t test
*p<0.05 is statistically significant **p≤0.001 is statistically highly significant t independent sample t test

Table 2: Correlation between trace elements and pulmonary functions :

	Zinc		Copper		Magnesium	
	r	p	r	p	r	P
FEV1%	0.335	0.008*	-0.174	0.176	0.725	<0.001**
FVC%	0.417	0.001**	-0.067	0.605	0.64	<0.001**
FEV1/FVC	0.349	0.005*	0.058	0.656	0.678	<0.001**
PEF%	0.398	0.001**	-0.055	0.672	0.697	<0.001**

r Spearman rank correlation coefficient *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

Table 3: Relation between asthma severity and demographic , laboratory , spirometric data and serum trace elements of the studied patients :

		Intermittent N=14	Mild persistent N=14	Moderate persistent N=20	Severe persistent N=14	χ^2 /F/KW	p
Gender	**Female**	6 (42.9%)	8 (57.1%)	6 (30%)	8 (57.1%)	0.023	0.879
	Male	8 (57.1%)	6 (42.9%)	14 (70%)	6 (42.9%)		
Family history		8 (57.1%)	9 (64.3%)	12 (60%)	10 (71.4%)	0.403	0.525
Age (year)		7.79 ± 1.98	7.64 ± 2	7.95 ± 1.74	8.57 ± 1.91	0.654	0.584
Weight (kg)		25.43 ± 5.35	24.29 ± 5.45	25.2 ± 5.97	26.5 ± 7.14	0.322	0.81
Height (cm)		123.71 ± 12.77	119.18 ± 9.16	125.2 ± 19,23	126 ± 9.1	1.249	0.3
BMI (kg/m^2)		16.47 ± 1.23	16.88 ± 1.11	16.23 ±1.18	16.37 ±2.02	0.612	0.61
Hemoglobin (g/dl)		11.04 ± 1.21	11.25 ± 1.34	11.19 ± 1.21	10.48 ± 1.11	1.211	0.314
Eosinophil cells/ml		401.43± 84.57	411.43±55.31	450±103.92	497.14±157.65	2.337	0.083
IgE(IU/ml)		142 (111.3–276.3)	350 (200 – 460)	400 (395 – 456)	550 (272 – 722.3)	10.72	0.013*
		P1= 0.146	P2= 0.285	P3= 0.649	P4= 0.006*	P5=0.003*	P6= 0.16
FEV1%		82.71 ± 1.07	80.93 ± 1.07	62.7 ± 2.94	49 ± 2.72	732.26	<0.001**
		P1 >0.999	P2 <0.001**	P3 <0.001**	P4 <0.001**	P50.001**	P6 0.001**
FVC%		93.43 ± 2.82	90.36 ± 2.93	83.7 ± 3.92	72.0 ± 6.0	75.214	<0.001**
		P1 >0.999	P2 <0.001**	P3 <0.001**	P4 <0.001**	P50.001**	P6 0.001**
FEV1/FVC		88.29 ± 2.2	88.64 ± 3.15	74.5 ± 3.25	67.86 ± 3.26	169.24	<0.001**
		P1 >0.999	P2 <0.001**	P3 <0.001**	P4 <0.001**	P50.001**	P6 0.001**
PEF%		86.71 ± 3.95	88.21 ± 2.08	67.9 ± 5.68	49.71 ± 5.17	221.51	<0.001**
		P1 >0.999	P2 <0.001**	P3 <0.001**	P4 <0.001**	P50.001**	P6 0.001**
Zinc (µg/dL)		75.96 ± 6.55	72.49 ± 9.48	70.86 ± 9.2	63.33 ± 9.6	5.092	0.003*
		P1 >0.999	P2 >0.999	P3 0.106	P4 0.618	$P_5$0.002*	P_6 0.048*
Copper (µg/dL)		123.57 ± 9.24	125.42 ± 12.2	126.07 ± 12.74	124.39 ± 15.08	0.126	0.944
Magnesium (mg/dl)		1.89 ± 0.1	1.84 ± 0.1	1.71 ± 0.06	1.64 ± 0.12	23.218	<0.001**
		P1 >0.999	P2 <0.001**	P3 0.254	P4 <0.001**	$P_5$0.001**	P6 0.001**

Date presented as mean ± SD, median (IQR) or frequency (%), χ2Chi square for trend test F One way ANOVA test KW Kruskal Wallis test p1 difference between intermittent and mild persistent asthma, p2 difference between mild and moderate persistent p3 difference between moderate and severe persistent p4 difference between intermittent and moderate persistent p5 difference between intermittent and severe persistent p6 difference between mild and severe persistent *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

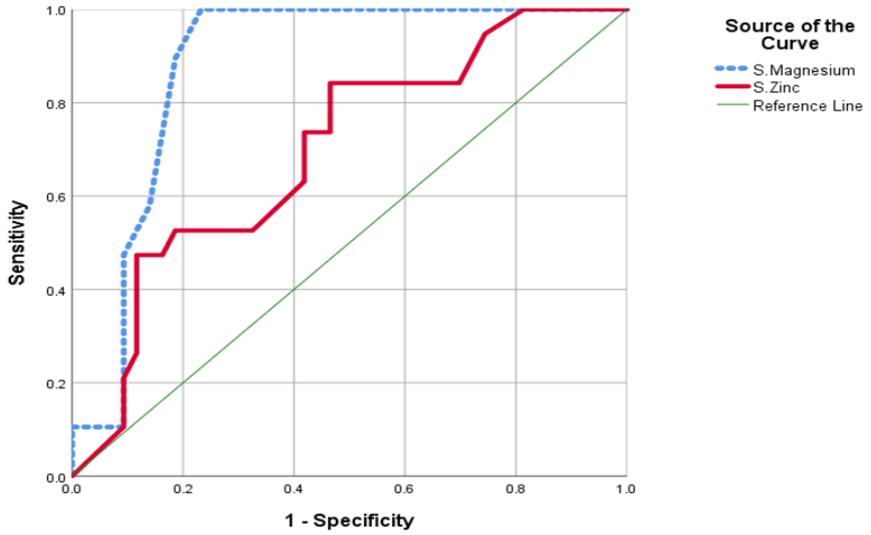
Table 4: Relation between asthma control and demographic, laboratory, spirometric data and serum trace elements among studied patients**:**

		Uncontrolled N=28	Partly controlled N=15	Controlled N=19	χ^2 /F/KW	p
Gender	**Female**	12 (42.9%)	7 (46.7%)	9 (47.4%)		
	Male	16 (57.1%)	8 (53.3%)	10 (52.6%)	0.099	0.754
Family history:		16 (57.1%)	13 (86.7%)	10 (52.6%)	0.011	0.918
Age (year)		8.43 ± 1.86	7.53 ± 2.01	7.68 ± 1.73	1.483	0.235
Weight (Kg)		26.36 ± 6.76	24.27 ± 5.43	24.68 ± 4.89	0.773	0.466
Height (cm)		26.93 ± 9.42	120.0 ± 9.77	121.82 ± 11.51	2.724	0.074

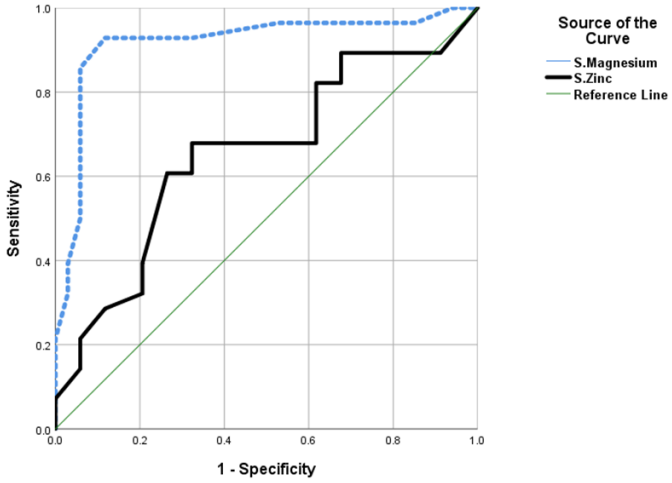
	Uncontrolled N=28	Partly controlled N=15	Controlled N=19	χ^2 /F/KW	p
BMI (Kg/m^2)	16.31 ± 1.7	16.69 ± 1.14	16.51 ± 1.1	0.361	0.699
Hemoglobin (g/dl)	10.76 ± 1.14	11.21 ± 1.48	11.21 ± 1.13	1.044	0.358
Eosinophil cells/ml	468.57 ± 131.37	436 ± 92.03	404.21 ± 77.84	2.015	0.142
IgE(IU/ml)	456(361.3 – 565)	350(200 – 400)	185(115 – 550)	9.004	0.011*
	P_1 0.036*	P_2 0.66	P_3 0.006*		
FEV1%	56.0 ± 7.7	73.4 ± 9.78	82.21 ± 1.36	82.446	<0.001**
	P_1 <0.001**	P_2 0.002*	P_3 <0.001**		
FVC%	77.5 ± 7.64	88.53 ± 2.92	92.47 ± 3.75	42.715	<0.001**
	P_1 <0.001**	P_2 0.155	P_3 <0.001**		
FEV1/FVC	71.71 ± 5.05	81.6 ± 8.4	88.68 ± 2.75	54.72	<0.001**
	P_1 <0.001**	P_2 0.001**	P_3 <0.001**		
PEF%	58.64 ± 10.41	80.73 ± 11.17	86.84 ± 3.52	62.066	<0.001**
	P_1 <0.001**	P_2 0.171	P_3 <0.001**		
Zinc (µg/dL)	67.94 ± 10.08	70.36 ± 9.4	74.97 ± 8.1	3.21	0.047*
	P_1 >0.999	P_2 0.147	P_3 0.042*		
Copper(µg/dL)	126.19±13.68	121.28 ± 11.19	126.11 ± 10.71	0.9	0.412
Magnesium (mg/dl)	1.67 ± 0.09	1.81 ± 0.11	1.88 ± 0.08	31.779	<0.001**
	P_1 <0.001**	P_2 0.079	P_3 <0.001**		

Data presented as mean ± SD, median (IQR) or frequency (%), Date presented as mean ± SD, median (IQR) or frequency (%), χ2Chi square for trend test F One way ANOVA test KW Kruskal Wallis test p1 difference between uncontrolled and partly controlled, p2 difference between controlled and partly controlled p3 difference between uncontrolled and controlled *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

To assess symptoms control of the asthmatic children according to GINA guidelines, they were asked about the following over the past four weeks: frequency of daytime and nighttime asthma symptoms, reliever use for relief of symptoms and activity limitation. Levels of asthma related symptoms were classified as well controlled if none of these are present, partly controlled if 1 or 2 of these are present and uncontrolled if 3 or 4 of these are present.



(A)



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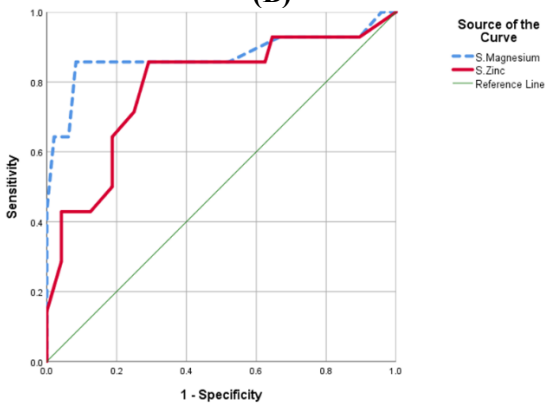

(C)

Figure 1: ROC curve showing (A) performance of serum zinc and magnesium in diagnosis of controlled asthma, (B) performance of serum zinc and magnesium in diagnosis of uncontrolled asthma, (C) performance of serum magnesium and zinc in diagnosis of severe persistent asthma

DISCUUSION

Chronic airway inflammation and hyperresponsiveness, which repeatedly restrict airflow, are the hallmarks of bronchial asthma [21]. Due to their significant roles in inflammation, trace elements may influence the pathophysiology of asthma directly or indirectly. High concentrations of free radicals, particularly reactive oxygen species such as superoxide and hydrogen peroxide, have been shown to be closely associated with asthma. [22].

We divided 124 patients in our case–control study into two groups. According to the GINA guidelines, group A included 62 asthmatic children who were further classified into four subgroups: intermittent, mild persistent, moderate persistent, and severe persistent. Group (B) included (62) healthy children as the control group.

In the present study, we found no significant difference in weight, height or BMI between asthmatic children and normal children.

In contrast, a prospective study among school-aged children performed by Chen et al. [23] showed that children with early-life asthma are at increased risk of developing obesity during later childhood.

A family history of asthma was present in 62.9% of asthmatic patients. Zedan et al. [24] reported that a family history of bronchial asthma is one of the predominant risk factors for asthma development. In a prior cross-sectional survey, Mohammed et al. reported that children with a positive family history of asthma were 4.2 times more likely to develop asthma [25].

Compared to those in the control group in this study, the haemoglobin levels of the asthmatic children were considerably lower.

This was in line with the findings of Ramakrishnan and Borade [26], who discovered that children who are anaemic are 5.75 times more likely than those who are not to develop childhood asthma. Numerous studies have suggested that anaemia could be a potential risk factor for asthma [27,28]. However, a cross-sectional study by Ibrahim et al. revealed that the Hb level did not significantly differ between children with asthma and healthy controls [29].

Our results revealed a significant change in total IgE when comparing asthmatic children with healthy controls. Our results were in accordance with those of Sandeep et al. [30], who reported that IgE levels increased as the severity of asthma increased. Srivastava et al. [31] also reported that serum IgE levels were greater in asthmatic children than in healthy controls and that there was a significant difference in IgE levels among well-controlled, partly controlled and uncontrolled groups. In contrast, Davila et al. [32] found no evidence of a significant correlation between total serum IgE levels and airflow restriction or the severity of asthma.

In our study, compared with those in the control group, the mean eosinophil count in asthmatic patients in the asthma group was 440.97±110.21 cells/mm³, while in the control group, the mean eosinophil count was 128.23±38.77 cells/mm³; however, there was no significant correlation between the eosinophil count and asthma severity or asthma control.

This finding is in agreement with the findings of El-Sherbeny et al. [33], who reported that compared to children without asthma, children with asthma had significantly more eosinophils. Conversely, Casciano et al. [34] reported a strong correlation between peripheral blood eosinophil counts and the severity of asthma. Peripheral eosinophil counts are much greater in people with moderate-to-severe asthma than in people with mild asthma.

Our study revealed a significant decrease in the serum zinc concentration in asthmatic children compared with healthy controls, as the mean serum zinc concentration in the asthmatic group was 70.44±9.51 µg/dL, while it was 89.3±15.01 µg/dL in the control group.

Patients with asthma have low zinc levels for a variety of reasons, including increased excretion, redistribution, and excessive zinc requirements. Because zinc has antioxidant properties, asthmatic individuals who experience high levels of oxidative stress may have lower body zinc levels [21].

Özkan et al. showed that children with asthma have decreased serum zinc levels [6]. Xue et al. [35] carried out a meta-analysis that supported the hypothesis that circulating zinc is a promising measure of asthma susceptibility by showing that lower circulating zinc levels were linked to a greater risk for childhood asthma and its associated symptom wheezing.

Conversely, AbdulWahab et al. reported no marked difference in zinc levels between school-aged asthmatic children and healthy controls [36]. According to a meta-analysis by Ghaffari and colleagues, the zinc levels of individuals with asthma do not differ significantly from one another [2]. Increased serum zinc in asthmatic children is unexpected; however, some studies support this finding. Hussein et al. [37], El-Sayed and Essa [38] .As a result, there are conflicting findings about zinc levels in the serum of asthmatic patients.

Our results showed a significant relationship between serum zinc and asthma severity and asthma control level.

Our findings are in line with the findings of Ebraimi et al. [39], who discovered that the mean zinc level dramatically decreased as asthma severity increased, with the lowest zinc levels being found in children with severe asthma ($p = 0.009$). Rajkumar et al. [11] carried out a cross-sectional study on children with asthma and discovered that there was a statistically significant difference between the mean serum zinc levels and the degree of asthma symptom control, with patients in the control group having higher zinc values than those in the control group. This finding suggested that keeping zinc levels in check could aid in improving asthma control in pediatric patients.

However, some studies reported that zinc status does not affect asthma severity or control level Siripornpanich et al. [21], Bishopp et al. [40].

In our study, a positive correlation between serum Zn levels and FEV1 values as well as between FVC and the FEV1/FVC ratio was found.

Ghaffari et al. [2] demonstrated that giving asthmatic children a 50 mg/day Zn supplement for eight weeks greatly increased their FEV1 and FEV1/FVC ratio compared to those at baseline. Our results contradicted those of AbdulWahab et al. [36], who reported no significant association ($p = 0.405$) between Zn level and FEV1%.

Our serum copper concentration was significantly greater in the asthmatic group than in the control group (124.98±12.24 µg/dl and 100.6±13.77 µg/dl, respectively), but there was no significant correlation with asthma severity.

Similarly, Ali et al. [41] found that asthmatic patients had higher serum copper level and lower serum zinc and magnesium compared to healthy controls. Similar to our findings, they reported no difference in serum copper levels between patients with different asthma severity grades .

Our findings supported the findings of El Sherbeny et al. [33], Bhaskar et al. [42], Bilan et al. [43] and Elsayed et al. [27] which reported that asthmatic children had greater serum copper levels than controls. In contrast, Sagdic et al. [44]. Urushidate et al. [45] didn't observe a significant

difference in serum copper level between asthmatic patients and controls .

In the current study, there was no significant correlation between serum copper levels and asthma severity or asthma control. There was no correlation with pulmonary function tests.

In agreement with our results, in the study of Ariaee et al. [46], there was no discernible link between the severity of the disease and the copper concentration. Ali et al. also reported no difference in serum copper levels according to asthma severity or control grade [41]. El Sherbeny et al. reported that there was no correlation between the lung function indices FEV1, FVC, or FEV1/FVC and the serum copper concentration [33].

Our results showed a significant decrease in the serum magnesium concentration in the asthmatic group (1.77±0.13 mg/dl) compared to that in the healthy control group (1.96±0.17 mg/dl).

Our results were consistent with those of Alsharnoubi et al. [47], Al-Fartusie et al. [5] and Al-Salhen et al. [7] who reported that asthmatic patients had considerably lower serum magnesium levels, supporting the favourable effects of magnesium on lung function. On the other hand, Firoozi et al. [48] found no discernible difference in the serum magnesium levels of children with asthma and the control group, which might be explained by the measurement of serum levels alone; however, evaluating intracellular magnesium levels in addition to serum levels produced more accurate results.

According to our research, there is a significant correlation between serum magnesium levels and asthma control severity.

This finding is consistent with a study by Shaikh et al. [17], which revealed that as severity increases, serum magnesium levels decrease. They concluded that lower levels of magnesium are linked to increased asthma severity, poor asthma control, and frequent exacerbations in asthmatic patients. Magnesium levels in asthmatic patients should be checked and adjusted if they are found to be low, as magnesium levels may be useful indicators of the severity of asthma. However, Chitamanni et al. [49] found no significant difference in serum magnesium levels between children with asthma who were well, partially, or poorly controlled, nor was there a significant correlation between serum magnesium and pulmonary function tests.

Our study revealed a positive correlation between serum magnesium levels and FEV1, FVC, and FEV1/FVC. This finding implies that improved lung function is associated with elevated serum magnesium levels.

Somashekar et al. [18] suggested that low serum magnesium levels may play a part in the etiology of asthma. Even in the normal range, patients with asthma had significantly lower serum magnesium levels. The relationship between magnesium levels and lung function parameters was highlighted by Pearson's correlation coefficient, which showed a positive correlation between FEV1% and serum magnesium levels ($r=0.819$, $P<0.001$). This finding is consistent with our findings.

CONCLUSION

The present study indicated that the mean values of serum zinc and magnesium were lower in asthmatic patients than in healthy controls. A decrease in these elements may contribute to the manifestation of bronchial asthma due to their roles in the activity of some antioxidants or due to their impact on the immune system. Therefore, supplements and diets rich in magnesium and zinc may be helpful in preventing or treating asthma. Copper is significantly elevated in the serum samples of asthmatic patients compared with those of controls. The increased level may reflect its potential role in the pathogenesis of asthma.

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