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Original Research Article

Assessment of Trace Elements Status in Bronchial Asthma

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ABSTRACT

Bronchial asthma is a chronic inflammatory disease of the respiratory tract. Trace elements are essential micronutrients that exist in very low concentrations in the body. Deficiency of trace elements may be associated with production of free radicals with subsequent tissue damage and infectious diseases. Major trace elements such as zinc and copper are part of the structure of antioxidant enzymes like super oxide dismutase. These enzymes act as antioxidant defense and are able to regulate the host immune system, and alter viral genome. Changes in the Zinc and copper level decrease the efficiency of this antioxidant system and this leads to hyper-reactivity and inflammation in the respiratory tract.

Aim: To determine serum levels of the trace elements Zn, and Cu in asthmatic patients and healthy controls.

Materials And Methods: 50 patients of bronchial asthma in age group of 20-70 years and 50 age and sex matched healthy controls were included in the study. 3 ml of venous blood was aseptically collected, serum was separated and serum Zinc and Copper level was estimated by colorimetric kit method.

Result: Out of 100 subjects enrolled in the study, mean serum zinc levels of 50 healthy subjects and 50 patients were 87.71±15.05 µg/dl and 65.92±21.29 µg/dl respectively and mean serum copper levels of 50 healthy subjects and 50 patients were 129.93±7.44 µg/dl and 178.38±21.26 µg/dl respectively. Serum zinc level was significantly low in patients as compared to control group. The data was statistically significant (p = 0.00). Serum copper level was significantly high in patients as compared to control group. The data was statistically significant (p = 0.00).

Conclusion: The present study confirmed, the presence of an oxidant-antioxidant imbalance in patients of bronchial asthma, supporting the concept of systemic oxidative stress in these conditions. Also, quantitative determination of zinc and copper in the serum of asthmatic patients may help in the early detection of the disease and evaluation of therapeutic agents.

Key Words: Bronchial asthma, Zinc, Copper, oxidative stress

INTRODUCTION

Bronchial asthma is a chronic inflammatory disease of the respiratory tract. Different genetic and environmental factors are involved in the pathogenesis of asthma. [1] Epidemiological study of asthma revealed that asthma is still common among lower socioeconomic classes including African Americans and Hispanics two to four times relative to Caucasians. There is increasing evidence that reactive oxygen species can be of particular importance in the pathophysiology of several lung diseases. Reactive oxygen species can even

induce an autonomic imbalance between muscarinic receptor-mediated contraction and the beta-adrenergic-mediated relaxation of the pulmonary smooth muscles. Increased tissue vulnerability to oxidant stress is likely to increase the risk of development of asthma. [2]

In recent years, nutrition has also been considered as an important conditioning factor of many cardiovascular, gastrointestinal and pulmonary chronic diseases. [3] Trace elements are essential micronutrients that exist in very low concentrations in the body, forming 0.01% of the total body weight. [4] They play an important role in various physiological processes, and are crucial for proper functioning of the immune system. These elements and the minerals should present in the body in appropriate amounts and must be available for reacting with other elements to form critical molecules as well as to participate in various important chemical reactions. [5] Deficiency of trace elements may be associated with production of free radicals with subsequent tissue damage and infectious diseases are often concomitantly observed and result in complex interactions. [6]

The major trace elements such as zinc and copper have imunomodulatory effects and thus influence susceptibility and the course of a variety of infections. This is mainly due to the fact that these elements are part of the structure of antioxidant enzymes like super oxide dismutase. These enzymes act as antioxidant defense and are able to regulate the host immune system, and alter viral genome. [4] Changes in the Zinc and copper level decrease the efficiency of this antioxidant system and this leads to hyper-reactivity and inflammation in the respiratory tract. [7]

Objective: This study was conducted to determine serum levels of the trace elements Zn, and Cu in asthmatic patients and healthy controls and to determine the correlation between Zinc and Copper in patients of bronchial asthma.

MATERIALS AND METHODS

This was the cross-sectional study conducted among out patients attending the Respiratory Medicine OPD/ IPD for the management of bronchial asthma for a period of one year. Subjects included for the study were categorized into 2 groups: Group 1- 50 patients of bronchial asthma in age group of 20-70 years and Group 2- 50 age and sex matched healthy controls.

INCLUSION CRITERIA:

- Patients from 20-70 years of age.
- Patients being diagnosed by spirometry with reversibility.
- Stable asthmatic patients with no co-morbidities.

EXCLUSION CRITERIA:

- Patients with active infection finding.
- Iron deficiency anemia.
- Acute severe attack of asthma.
- Malnourished patients.
- Patients with multivitamin supplementation.

Serum Zinc and Copper levels were evaluated in all the selected patients and control.

The study was conducted after obtaining informed and written consent form from the individual following whom the study participant was assessed using questionnaire tool.

3 ml of venous blood was aseptically collected from the antecubital vein. Sample was centrifuged and serum was separated and serum Zinc and Copper level was estimated by colorimetric kit method described by Abe A, Yiamashita S, Noma A. [8]

Normal Reference Values for zinc and copper: Serum zinc: 60-120 µg/dl and **Serum copper:** 80-140 µg/dl (Males); 80-155 µg/dl (Females)

Statistical Analysis: Mean and standard deviation of all parameters in serum were calculated. Students t-test was used for comparison of means and $p < 0.05$ was considered significant.

RESULTS

The study included 50 patients of bronchial asthma and 50 controls in which there were 34 males (68%) and 16 females (32%) in each group. Mean age of patients was 52.86±14.52 years and of controls was 42.36±15.12 years and the difference was not statistically significant. 20-70 years of age group was taken in the study out of which 50 patients and 50 healthy controls were enrolled. There were 5 patients and 15 controls in age group of 20-30 years, 7 patients and 13 controls in age group of 31-40 years, 7 patients and 7 controls in age group of 41-50 years, 12 patients and 8 controls in age group of 51-60 years and 19 patients and 7 controls in age group of 61-70 years. (Figure 1)

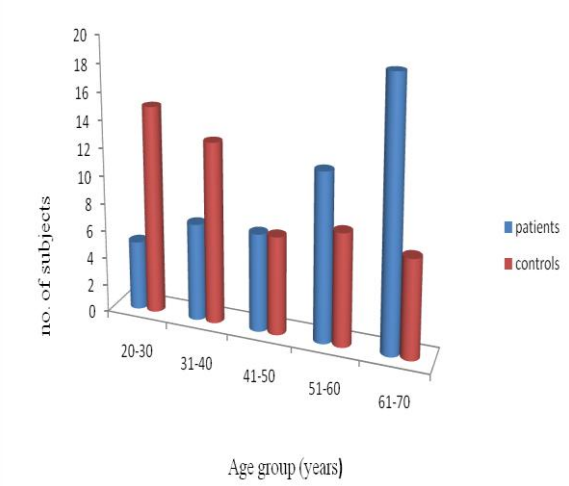

Fig 1. Showing age distribution of patients and controls in Bronchial Asthma.

Out of 100 subjects enrolled in the study, mean serum zinc levels of 50 healthy subjects and 50 patients were 87.71±15.05 µg/dl and 65.92±21.29 µg/dl respectively and mean serum copper levels of 50 healthy subjects and 50 patients were 129.93±7.44 µg/dl and 178.38±21.26 µg/dl respectively. Serum zinc level was significantly low in patients as compared to control group. The data was statistically significant (p = 0.00). Serum copper level was significantly high in patients as compared to control group. The data was statistically significant (p = 0.00). (Table1, Fig 4)

Table:1 Showing mean serum Zinc and Copper levels in controls and patients

(Mean±SD)	Controls (n=50)	Patients (n=50)	p-value
Serum Zinc (µg/dl)	87.71±15.05	65.92±21.29	0.00*
Serum copper (µg/dl)	129.93±7.44	178.38±21.26	0.00*
*p-value < 0.05 have been considered to be significant.			

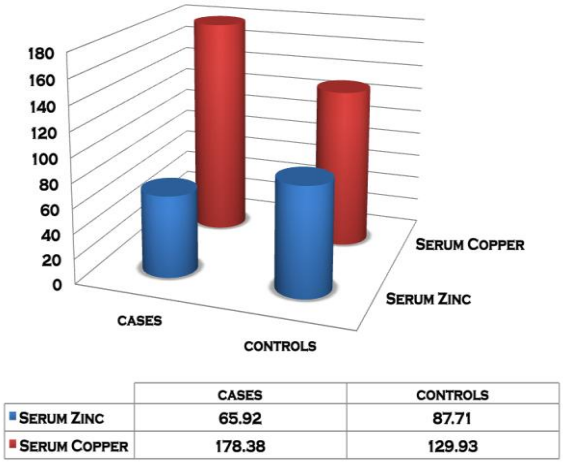

Fig 4: Mean Serum zinc and Mean Serum copper levels in patients and controls

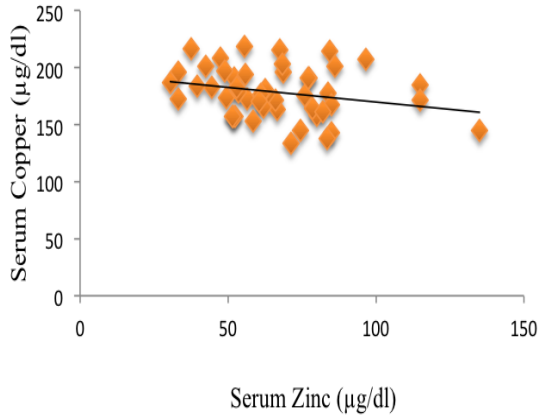

Fig 2: Correlation between serum zinc and copper in patients

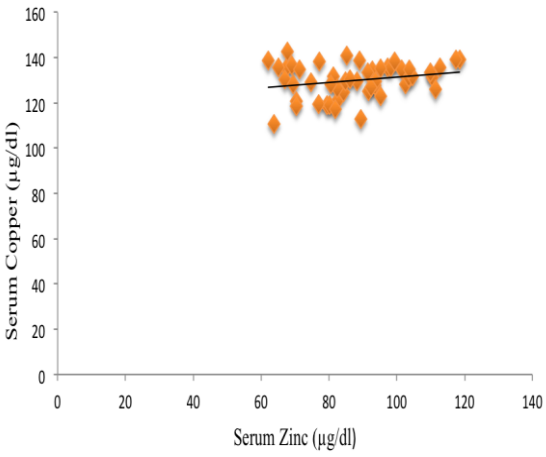

Fig 3: Correlation between serum zinc and copper in controls

There was negative correlation between serum zinc and copper in patients (r=−0.25, p= 0.08) and positive correlation serum zinc and copper in healthy controls (r= 0.24, p= 0.09) though it was not statistically significant. (Figure 2 & 3)

Table 2 shows that out of 50 patients enrolled in the study, there were 34 males with mean serum zinc levels and mean serum copper levels of 61.37±18.75 µg/dl and 184.92±20.88 µg/dl respectively while there were 16 females whose mean serum zinc levels mean serum copper levels came out to be 72.13±24.66 µg/dl and 169.97±19.81 µg/dl respectively. The statistical analysis shows that the difference between serum zinc levels between male and female in patient was not statistically significant but difference between serum copper levels between male and female in patient was statistically significant.

Table:2 Comparison of serum Zinc levels and serum Copper levels between males and females in healthy controls.

Group	Serum zinc (µg/dl) (Mean±SD)	Serum copper (µg/dl) (Mean±SD)
Males (n=34)	90.7±15.34	129.17±7.35
Females (n=16)	81.36±12.61	131.55±7.60
p-value	0.029*	0.30*
*p-value < 0.05 have been considered to be significant.		

Table 3 shows that out of 50 healthy controls enrolled in the study, there were 34 males with mean serum zinc and mean serum copper levels were 90.7±15.34 µg/dl and 129.17±7.35 µg/dl respectively while there were 16 females whose mean serum zinc and mean serum copper levels came out to be 81.36±12.61 µg/dl and 131.55± 7.60 µg/dl respectively. The statistical analysis shows a significant difference between serum zinc levels of healthy male and female and non significant difference between serum copper levels of male and female in controls.

Table: 3 Comparison of serum Zinc levels and serum Copper levels between males and females in patients

Group	Serum zinc (µg/dl) (Mean±SD)	Serum copper (µg/dl) (Mean±SD)
Males (n=34)	61.37±18.75	184.92±20.88
Females (n=16)	72.13±24.66	169.97±19.81
p-value	0.11*	0.018*
*p-value < 0.05 have been considered to be significant.		

DISCUSSION

Oxidants-antioxidants balance is essential for the normal lung function. Both, an increased oxidant and/or decreased antioxidant may reverse the physiologic oxidant-antioxidant balance in favor of oxidants, leading to lung injury. A number of diseases involving the lung, such as COPD, emphysema, bronchiectasis and bronchial asthma have been associated with a disturbance of these balances. [9]

Bronchial asthma is a chronic inflammatory disease of the respiratory tract with an unknown etiology where inflammation is often associated with an increased generation of ROS. Asthma itself may cause physiological changes in serum antioxidant status, perhaps because of increased oxidant burden associated with the disease. Numerous disturbances of antioxidant defense mechanisms have been described in asthma, as that of the epithelial lining fluid of the lung which contains high a concentration of antioxidants providing a first line of defense against inhaled and endogenously oxidant agents. [10] The most important antioxidant systems are the SODs and the GSH-Px which contain zinc/copper and selenium in their structures respectively. [4]

The present study showed relatively low serum levels of zinc (65.92 ± 21.29µg/dl) in patients with bronchial asthma comparing to healthy controls (87.71±15.05µg/dl). Our results are in corcordance with the studies conducted by Ermis B et al, [11] and Yousef et al. [12] Chronic inflammation causes a characteristic decline in serum zinc levels. It is well known that zinc deficiency affects the regulation of T-cell lymphocytes, which may play some part in the development of allergies. T-cell derived inflammatory mediator IL-2 is also involved in the cellular control of copper levels. Ceruloplasmin significantly increases IL-8 secretion and activation of NF- kappa B. This suggests that copper ion may cause some of the biologic effects of inhaled particulate air pollution. Proinflammatory Interleukins IL-

1induce synthesis of ceruloplasmin and are considered to be responsible for copper release in to plasma. [11]

Decreased Zinc levels enhancing respiratory diseases in adults can also be explained by decreased ability of the cell membrane to resist free radicals which lead to impairment of the stability and integrity of the cell membrane due to release of enzymes from lysosome and histamine from mastocytes. During excessive stress, release of leucocyte endogenous mediator from activated phagocytes occurs. This leads to redistribution in plasma Zn to the liver. Our data also showed that the serum copper levels were higher (178.28 ± 21.26µg/dl) in patients than in healthy controls (129.93 ±7.44 µg/dl). Previous studies have also reported that the serum Cu concentrations in bronchial asthma patients tended to be higher than in healthy individuals. [13,14] Cu/Zn-SOD is an antioxidant enzyme that contains Cu as an essential component. Some previous studies indicated that high Zn serum concentrations can lead to declines in both Cu/Zn-SoD and Cu concentrations, as Cu deficiency can reflect a high Zn concentration. [15] So, the high serum Cu concentrations in patients in this investigation are further evidence of Cu Zn antagonism in the pathophysiology of asthma. As both metals Zn and Cu form the prosthetic group of SOD, any alteration in their levels affect the activity of the enzyme. Decrease in this element impairs the enzyme activity. Such a condition may cause oxidative stress or may further increase an existing stress. [16] The present study shows negative correlation between zinc and copper in patients and positive correlation among controls. The negative correlation of copper and zinc may be explained by their competition either for the same absorptive binding sites on the intestinal mucosal cells or for similar functional protein systems. [17]

There are controversial reports regarding changes in serum level of zinc and copper in asthma. Magboula MH et al [4] conducted study on serum levels of selenium, zinc, copper and magnesium in asthmatic patients. Concentrations were measured in 150 asthmatic adult patients and 170 healthy control subjects matched for age and sex. Copper levels were found to be significantly decreased. Mean serum Cu for patients was 0.711± 0.37g/L (mean ±SD) while that for controls 0.939± 0.322g/L respectively (p value was <0.001). On the other hand the mean serum Zn level was significantly higher in patients compared to controls (1.2±0.51g/l and 0.94± 0.254g/l respectively) (p value was <0.001). They conducted that changes in the levels of trace elements which were a decrease in serum copper and selenium and increase in zinc may affect the antioxidant enzymes functions and decrease the antioxidant capacity in asthma.

Abnormal distributions of these trace minerals may aggravate oxidative damage and inflammation and decreased lung function in bronchial asthma. The changes in trace element status may be the effect of chronic disease state and do not associate with the cause of disease. Further studies on the relations between bronchial asthma and trace elements are needed to understand the details of these conditions.

CONCLUSION

The above results revealed the existence of an increased oxidative stress in asthmatic patients, with altered antioxidant capacities. The observed changes in the levels of the trace elements which were a decrease in serum zinc and an increase in serum copper levels may affect the antioxidant enzymes' functions, and decrease the antioxidant capacity in bronchial asthma.

The present study confirmed, the presence of an oxidant-antioxidant imbalance in patients of bronchial asthma, supporting the concept of systemic oxidative stress in these conditions. Also, quantitative determination of zinc and copper in the serum of asthmatic patients may help in the early detection of the disease and evaluation of therapeutic agents. Diet and nutrition are the important

modifiable risk factors for the development, progression and management of obstructive lung diseases such as asthma. Proper supplementations of zinc can be useful in the management of asthmatic patients due to increase the effect of antioxidant defense system and thereby, decrease the airway inflammation. However, further multi-centre studies with greater number of patients are needed to warrant the results of this study.

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