Serum Zinc Levels in Asthmatic and Non-Asthmatic Children Aged 5-15 Years - A Case Control Study

Reyaz A Malik[1], Muzaffar Rather[2]

ABSTRACT

Introduction: Asthma is the most common chronic disease in childhood, and the prevalence has increased considerably in recent decades. Zinc is a trace mineral involved in many functions in the body. Studies have examined abnormal distributions of trace minerals, including zinc; some of them have reported the effect of the lower zinc status in asthma/ wheezing.

Material and methods: This study was a case and control study in 50 asthmatic (cases) and 50 non-asthmatic (controls) children.We measured the serum Zn level in controls and then compared the levels with those of cases. Zinc concentration was measured by means of semi automatic analyser.

Results: The median age in the asthma group was ±9.4 while as in the non-asthma group it was ±9.6 years**.** There were 29 males and 21 females in both the case as well as the control groups. 28 patients were deficient (mean serum zinc level of 52.75ng/dL), while as 72 of them had sufficient serum zinc level (mean value of 81.65ng/dL) (p=0.002). Investigating the serum zinc levels in case and control patients, which was further evaluated within case groups, we found that mean serum zinc levels in cases was 58.14ng/dL while in controls it was 88.98ng/dL (p.value of 0.0001). Among the four case groups of asthma severity; mean serum zinc levels in intermittent group was 56.18ng/dL, in mild group it was 55.88ng/dL, in moderate group it was 64.3ng/dL and in severe group it was 57.1ng/dL. The same does not reflect any association between serum zinc deficiency & disease severity in asthmatic children (p>0.05).

Conclusion: Serum zinc levels were considerably lower in children with asthma than in healthy children. Serum zinc levels in asthmatics were found to have no relation with severity of asthma.

Keywords: Bronchial Asthma, Serum Zinc Levels, Asthma Severity

INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways, characterized by recurrent, reversible, airway obstruction. Airway inflammation leads to airway hyper reactivity, which causes the airways to narrow in response to various stimuli, including allergens, exercise, and cold air[1]. Asthma has also been described in children as, a common chronic disease with a high rate of mortality and morbidity among children that leads to emergent visits, hospitalization, and absence from school. It seems that the prevalence of this disease has increased during recent decades, which could be due to genetic susceptibilities and/or environmental, economic, and nutritional factors[2]. Asthma is the most common chronic disease in childhood, and the prevalence has increased considerably in recent decades[3]. According to international guidelines, the ultimate goal of asthma management is to control the disease in terms of symptoms, pulmonary function, preventing asthma exacerbations and avoiding adverse effects from asthma medications. The main controller medications are inhaled corticosteroids that switch off the inflammation of asthmatic airways.[4,5]

Zinc (Zn) is a trace mineral involved in many functions in the body[6]. Zn, an essential dietary metal & contributes partly to the structure and function of many biological enzymes. It also regulates ion transporters relevant to pulmonary diseases. Zn is known to exhibit powerful antioxidant activity in the lungs and several body organs[6,7,8,9]. Reactive oxygen species (ROS) have a role in initiating inflammation in asthmatic airways. Excessive ROS production in asthma leads to an oxidant-antioxidant imbalance in airways[10]. It is possible that Zn deficiency can disturb the equilibrium between type 1 and type 2 T helpers[11], which leads to increased inflammation and eosinophilia. This is the same mechanism detected in allergic airway hypersen-sitivity[12]. Chronic asthmatics take prophylactic inhaled steroids daily, which may have an important contributing effect on serum Zn status. Such a study has not been reported in the literature, but there are some studies that demonstrated a relationship between oral steroids and Zn levels in normal humans, asthmatic patients, burn patients, and patients with rheumatoid arthritis[13,14,15].

Zinc serves as an enzyme cofactor and protects cell membranes from lysis caused by complement activation and toxin release[16,17]. It was proposed that adequate dietary intake and Zn supplementation may decrease the severity of asthmatic attacks[18].

According to Mayo Clinic Laboratories, the normal reference range for Zn is 0.60-1.20 mcg/mL for children under age 10 and it is 0.66-1.10 mcg/mL for children over age 10 and for adults.

[1]Associate Professor, Department of Pediatrics, SKIMS Medical College & Hospital, Srinagar J&K., [2]Resident Pediatrics, Department of Pediatrics, SKIMS Medical College & Hospital, Srinagar J&K.

Corresponding author: Dr. Reyaz A Malik. Department of Pediatrics, SKIMS Medical College & Hospital, Srinagar J&K.

How to cite this article: Malik RA, Rather M. Serum zinc levels in asthmatic and non-asthmatic children aged 5-15 years - a case control study. International Journal of Contemporary Medical Research 2021;8(10):J1-J4.

DOI: http://dx.doi.org/10.21276/ijcmr.2021.8.10.3

The literature on zinc as a potent antioxidant is vast, but the role played by zinc in airway inflammation remains unclear. Studies have examined abnormal distributions of trace minerals, including zinc; some of them have reported the effect of the lower zinc status in asthma/wheezing[19].

We conducted this study to study the difference in serum zinc levels in asthmatic and non-asthmatic children in order to assess possible association between zinc deficiency and asthma risk.

MATERIAL AND METHODS

This study was a case and control study, which was conducted on 50 asthmatic children denoted as cases and 50 non-asthmatic children denoted as controls who attended the Department of Pediatrics in a tertiary care institution. The study was conducted in afore mentioned department for a period of two years. The following inclusion criteria for selecting asthmatic children was used: (i) age between 5 and 15 years and (ii) the diagnosis of asthma was based on a physician's diagnosis according to the American Thoracic Society guidelines in accordance with guidelines of the Global Initiative for asthma and the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. The following patients were excluded from the study;

- Malnourished asthmatic patients.
- Patients with chronic illness like chronic kidney disease, chronic liver disease, metabolic diseases, etc.
- Patients on zinc supplements in preceeding 3 months.

Patients were classified as intermittent asthma, mild persistent asthma, moderate persistent asthma & severe persistent asthma as per the GINA guidelines.

Asthma control was assessed using the Asthma Control Test (ACT) that includes five items (activity limitations, shortness of breath, nocturnal symptoms, rescue medication, and overall control in the past 4 weeks). Each item was scored from 1(worst) to 5 (best). The ACT ranged from 5 to 25 (better indicated by higher values). A score of >20 indicates well-controlled asthma, 16–19 partially controlled, and <16 uncontrolled asthma.

We measured the serum Zn level in controls and then compared the levels with those of cases. None of the subjects in either the cases or control group had acute respiratory infection for more than 4 weeks prior to enrollment. For the measurement of serum zinc level, blood samples were collected by vein puncture from ante cubital vein and collected in blood vacutainer system CAT-plain tubes. After 25-30 minutes, the serum was separated and collected in Eppendorf tubes and stored at -20ºC for estimation of serum zinc level. Zinc concentration was measured by means of semi automatic analyser.

All the clinical & demographic data about the cases & controls, viz age, gender, severity of asthma, dose of control class medication being used, asthma control & serum zinc levels were entered in Microsoft excel sheet & analyzed statistically.

RESULTS

This study was a prospective case-control study which was conducted over a period of two years with the primary objective of ascertaining serum zinc levels in asthmatic and non-asthmatic patients. We enrolled a total of 100 pediatric patients (50 cases and 50 controls). We further categorized the patients into two age groups; one of them being 5-10 years and another one being 11-15 years (Table 1). The median age in the asthma group was ±9.4 while as in the non-asthma group it was ±9.6 years. There was no significant difference regarding the mean ages of the groups ($p > 0.05$). There were 29 males and 21 females in both the case as well as the control groups. Severity of asthma was based on ISAAC questionnaire. Amongst the cases, 11 had intermittent asthma, 8 of them had mild asthma, 10 of them had moderate asthma and 21 of them had severe asthma (Table2). Hypozincemia was defined as serum Zn level below 60.0 ng/dL. As an assessment of zinc deficiency in studied subjects, we analysed the case and control groups in terms of overall state of being deficient or having sufficient serum zinc levels which was further evaluated within case groups. In a total of 100 patients 28 of them were deficient in serum zinc levels with mean serum zinc level of 52.75ng/dL, while as 72 of them had sufficient serum zinc level

Age in years	Frequency	Percent
5-10	34	68%
11-15	16	32%
Total (n=50)	50	100%
Mean±SD (Range)=9.42±2.92 (5-15)		

Table 1- Age wise frequency in asthma subjects.

Grade of asthama	Frequency	Percent
Intermittent	11	22
Mild	8	16
Moderate	10	20
Severe	21	42
Total	50	100

Table-2: Distribution of Asthma patients as per severity.

Serum zinc status	Mean	Std. Deviation	N
Deficient	52.75	4.07	28
Sufficient	81.65	14.361	72
Total	73.56	17.959	100
p=0.002			

Table-3: Overall Serum zinc levels in subjects

Grade of Asthma	Defficient (n=25)	Sufficient (n=22)	Total
Intermittent	7	4	11
Mild	6	2	8
Moderate	3	7	10
Severe	12	9	21
P=0.001			

Table-4: Severity of Asthma and serum zinc levels

Serum Zinc level	Group	N	Mean	Std. Deviation	Std. Error Mean
	Asthmatic	50	58.14	7.318	1.035
	Non asthmatic	50	88.98	10.622	1.502
p=0.0001					

Table-5: Serum zinc levels in subjects

Asthma Severity	Mean	Std. Deviation	N
Intermittent	56.18	6.983	11
Mild	55.88	10.035	8
Moderate	64.3	5.539	10
Severe	57.1	5.787	21
Total	73.56	17.959	39
p>0.05			

Table-6: Serum zinc level with asthma severity

with mean value of 81.65ng/dL (Table 3) The difference was statistically significant (p=0.002). Within the case sub-groups, in the intermittent group 7 patients were deficient whereas 4 patients had sufficient serum zinc levels, in mild group 6 patients were deficient whereas 2 patients had sufficient serum zinc levels, in moderate group 3 patients were deficient whereas 7 patients had sufficient serum zinc levels, intermittent group 7 patients were deficient whereas 4 had sufficient serum zinc levels and in severe group 12 patients were deficient whereas 9 patients had sufficient serum zinc levels (Table 4). Investigating the serum zinc levels in case and control patients, which was further evaluated within case groups, we found that mean serum zinc levels in cases was 58.14ng/dL while in controls it was 88.98ng/dL (taking 60ng/dL as the lowest normal range), which reflected a significant decrease in serum zinc levels in cases as compared to controls (p.value of 0.0001) (Table 5). Among the four case groups of asthma severity; mean serum zinc levels in intermittent group was 56.18ng/dL, in mild group it was 55.88ng/dL, in moderate group it was 64.3ng/dL and in severe group it was 57.1ng/dL (Table 6), the same does not reflect any increased deficient state of serum zinc levels with disease severity (p>0.05).

DISCUSSION

Zinc deficiency is common in children from developing countries and often it is aggravated by inter current acute and chronic infections. A regular intake of dietary zinc is essential for maintenance of physiological zinc need. Zinc deficiency occurs as a result of either high dietary phytate intake with inadequate intake of zinc-rich animal protein or from increased loss of zinc in infections such as diarrhea. It is claimed that nutritional deficiency of zinc may affect nearly 2 billion people in the developing world. In Bangladesh, prevalence of zinc deficiency is 44.6% in the preschool aged children and 57.7% in slum children[20].

Further, chronic inflammation events cause a characteristic decline in plasma or serum zinc levels in experimental studies. The explanation of this hypozincemia is the redistribution of plasma zinc in the body. Activation of the phagocytic cells occurs in IgE-mediated allergic reactions, leading to the release of Leukocyte Endogenous Mediator which increases the movement of zinc from plasma to the hepatocytes, decreasing its serum level. It appears that hypozincemia plays a role in producing, or at least exacerbating, the allergic diseases. Zinc deficiency seems to have a role in the pathogenesis of asthma. The results of this study confirm previous observations that there is low serum zinc level in asthmatic children. In this study, a significant frequency of hypozincemia was detected in the studied subjects [28/100]. And a decreased level of mean serum zinc [58.14ng/dL] was found in cases, which was in agreement with some previous studies. Mao et al[21] suggested a different zinc status between asthmatic and healthy subjects. In the study by Di Toro et al[21], mean hair zinc level was lower in asthmatic and healthy children ($p < 0.05$). Our study didn't showed that severity of asthma can be associated with increased deficiency in serum zinc level which is in concordance with the works of Urushidate et al[22], who noted a similar onservation in their study in Japanese subjects Measurement of zinc level could be recommended in asthmatic children, especially in countries with a higher prevalence of zinc deficiency. Zinc supplementation might be suggested in asthmatic patients with hypozincemia.

CONCLUSION

To conclude, in our study, we found that:

- Serum zinc levels were considerably lower in children with asthma than in healthy children.
- Serum zinc levels in asthmatics were found to have no relation with severity of asthma.

REFERENCES

1. D. Behera, Inderpaul Singh Sehgal. Bronchial asthma - Issues for the developing world. Indian J Med Res. 2015 Apr; 141(4): 380–382.
2. G Khanbabaee, A Omidian, F Imanzadeh, F Adibeshgh, M Ashayeripanah, N Rezaei. Serum level of zinc in asthmatic patients: A case---control study. Allergol Immunopathol (Madr) ;42.1:19-21.
3. Gelfand, E.W. Pediatric asthma: A different disease, Proc. Am. Thorac. Soc 2009;6:278 –282.
4. Reddel, H.K., Bateman, E.D., Becker,A., Boulet, L.P.,

Cruz, A.A., Drazen, J.M et al. A summary of the new GINA strategy: A roadmap to asthma control, Eur. Respir. J; 46:622–639
5. Castro-Rodriguez, J.A., Rodrigo, G.J., Rodriguez-Martinez, C.E. Prin-cipal findings of systematic reviews for chronic treatment in childhood asthma. J. Asthma 2015;52: 407–416.
6. Prasad A.S. Zinc deficiency in women, infants, and children, J. Am. Coll. Nutr;15: 113–120.
7. Zalewski, P.D. Zinc metabolism in the airway: Basic mechanisms and drug targets. Curr. Opin. Pharmacol; 6: 237–243.
8. Childers, M., Eckel, G., Himmel, A., Caldwell, J.A new model of cystic fibrosis pathology: Lack of transport of glutathione and its thiocyanate conjugates, Med. Hypotheses, 68: 101–112.
9. Zsembery A, Fortenberry J.A, Liang L, Bebok Z, Tucker T.A, Boyce A.T. et al. Extracellular zinc and ATP restore chloride secretion across cystic fibrosis airway epithelia by triggering calcium entry, J. Biol. Chem 2004; 279:10720–10729.
10. Taylor C.G, Bray T.M. Effect of hyperoxia on oxygen free radical defense enzymes in the lung of zinc-deficient rats. J. Nutr; 121:460–466.
11. Nadeem, A, Masood A, Siddiqui N. Oxidant-antioxidant imbalance in asthma: Scientific evidence, epidemiological data and possible therapeutic options, Ther. Adv. Respir. Dis;2:215–235.
12. Honscheid A, Rink L, Haase H. T-lymphocytes: A target for stimulatory and inhibitory effects of zinc ions. Endocr. Metab. Immune Disord. Drug Targets; 9:132–144.
13. Ai.Q Truong-Tran, Ruffin, R.E., Foster, P.S., Koskinen, A.M., Coyle, P., Philcox, J.C. et al. Altered zinc homeostasis and caspase-3 activity in murine allergic airway inflammation, Am. J.Respir. Cell Mol. Biol ;27:286-296.
14. El-Kholy, M..S. Gas Allah, M.A. el-Shimi S, El-Baz, F. el-Tayeb, H. Abdel M.S. Zinc and copper status in children with bronchial asthma and atopic dermatitis., J.Egypt Public Health Assoc;65:657–668. https://pubmed.ncbi.nlm.nih.gov /2134 100
15. Kadrabova, J., Madaric, A., Podivínsky, F., Gazdík, F., Ginter, F. Plasma zinc, copper and copper/zinc ratio in intrinsic asthma, J. Trace. Elem. Med. Biol 1996;10:50–53.
16. Peretz A, Neve J, Famaey J.P. Effects of chronic and acute corticosteroid therapy on zinc and copper status in rheumatoid arthritis patients, J. Trace Elem. Electrolytes Health Dis; 3:103–108. https://pubmed.ncbi.nlm.nih.gov/2535323
17. Vasto S, Candore G, Listì F, Balistreri C.R, Colonna Romano G, Malavolta M, Lio D et al. Inflammation, genes and zinc in Alzheimer's disease, Brain Res Rev; 58:96-105.
18. Pasternak, CA. A novel form of host defence: a membrane protection by Ca2+ and Zn 2+. BiosciRep;7:81-91.
19. Rita de Cássia Ribeiro-Silva, Rosemeire Leovigildo Fiaccone , Maurício Lima Barreto , Luce Alves da Silva, Luis Fernandes Pereira Santos , Neuza Maria Alcantara-Neves. The preval-ence of wheezing and its association with serum zinc concentration in children and adolescents in Brazil. J Trace Elem Med Biol;28,3:293-297.
20. Islam, S.N., Kamal, M.M., Rahmatullah, R., Sadi, S.K.S., Ahsan, M. Serum zinc levels in children with acute respiratory infections: Association with sociodemography and nutritional status. Clinical Nutrition Experimental; 2018;22:11-18.
21. Mao,S., Wu,L., Shi,W. Association between trace elements levels and asthma susceptibility. Respiratory Medicine 2018;;145:110–119.
22. Di Toro R, Galdo Capotorti G, Gialanella G, Miraglia del Giudice M, Moro R, Perrone L. Zinc and copper status of allergic children. Acta Paediatr Scand. 1987;76:612-7.
23. Urushidate S, Matsuzaka M, Okubo N, Iwasaki H, Hasebe T, Tsuya R, et al. Association between concentration of trace elements in serum and bronchial asthma among Japanese general population. J Trace Elem Med Biol. 2010;24:236-42.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 26-08-2021; **Accepted:** 27-09-2021; **Published:** 30-10-2021