

# Serum Zinc Level and Its Correlation with Vesikari System Scoring in Acute Pediatric Diarrhea

Ayman E. Eskander<sup>1</sup>, Lobna S. Sherif<sup>2</sup>, Mohammad Nabih<sup>1</sup>, Nevine R. El Baroudy<sup>1</sup>, Ghobrial C. Marcos<sup>1</sup>, Ehsan A. Badawy<sup>3</sup>, Amira S. El Refay<sup>2\*</sup>

<sup>1</sup>Department of Pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt; <sup>2</sup>Department of Child Health, National Research Centre, Cairo, Egypt; <sup>3</sup>Department of Biochemistry, National Research Centre, Cairo, Egypt

## Abstract

**Citation:** Eskander AE, Sherif LS, Nabih M, El Baroudy NR, Marcos GC, Badawy EA, El Refay AS. Serum Zinc Level and Its Correlation with Vesikari System Scoring in Acute Pediatric Diarrhea. Open Access Maced J Med Sci. 2017 Aug 15; 5(5):677-680. <https://doi.org/10.3889/oamjms.2017.097>

**Keywords:** Acute diarrhoea; zinc deficiency; Vesikari score; infants.

\***Correspondence:** Amira S. El Refay, PhD, Department of Child Health, National Research Centre, El-Bohouth Street, Dokki, Cairo, Egypt P.O:12622, Affiliation ID: 60014618. Tel: +20 012 298 3076; Fax: +37601877. E-mail: amirasayed.ak@gmail.com

Received: 01-Apr-2017; Revised: 06-May-2017; Accepted: 25-May-2017; Online first: 12-Aug-2017

**Copyright:** © 2017 Ayman E. Eskander, Lobna S. Sherif, Mohammad Nabih, Nevine R. El Baroudy, Ghobrial C. Marcos, Ehsan A. Badawy, Amira S. El Refay. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0).

**Funding:** This research did not receive any financial support.

**Competing Interests:** The authors have declared that no competing interests exist.

**BACKGROUND:** Diarrhea remains the most common infectious disease worldwide. Zinc has been studied extensively recently for its potential effect on prevention, control and treatment of acute diarrhoea.

**AIM:** This study was designed to correlate the level of zinc with the severity of pediatric diarrhoea estimated by Vesikari Scoring System.

**PATIENTS AND METHODS:** The present study included 80 children aged two months to 30 months from those suffering from the acute diarrheal episode and admitted to Pediatric Hospital "Abo El Rish" Cairo University. Serum Zinc level was assessed by a colorimetric method with a spectrophotometer.

**RESULTS:** Zinc deficiency was detected in 45 (56.2%) patient of the studied group. Significant negative correlations were found between serum zinc level and severity of dehydration and duration of hospitalization ( $p < 0.05$ ).

**CONCLUSION:** Zinc level has an essential role in acute pediatric diarrhoea. Zinc therapy should be considered beside Oral rehydration salts (ORS) to achieve maximum impact on diarrheal diseases; clinical trials are recommended to support the zinc supplementation in developing countries.

## Introduction

Diarrheal disease remains the most common infectious disease worldwide and still presenting the third cause of mortality among children younger than five years of age [1, 2]. In developing countries, acute diarrhoea was reported to cause a significant mortality rate. On the other hand, it is rarely fatal in the developed countries. However, acute diarrhoea was considered a leading cause of emergency department visits and hospitalizations causing a significant economic burden [3].

The clinical spectrum of the diarrheal disease range from a self-limiting disease with the potential of short hospitalization for few days up to more prolonged disease that may be complicated by severe dehydration, malnutrition, and death [4].

These differences had generated different definitions.

Moreover; different treatment protocols and diversity in recommendations of diarrheal diseases [5].

According to the WHO recommendations; acute diarrheal main treatment is the prevention of dehydration with adequate liquids and oral rehydration salts (ORS) maintenance of oral feeding, and supplementation of zinc [6].

Zinc considered as an essential trace element required for normal intestinal mucosal integrity, sodium and water transport and immune function [7]. Unfortunately, 30% of the world's population is zinc deficient [8].

The role of zinc level and its association with the outcome of acute pediatric diarrhoea has been studied evidently over the last years in both developing and developed countries showing a potential effect of zinc in reducing complications and mortality rates [9-11].

In developed countries, some guidelines recommend the use of zinc in addition to the ORS and oral feeding maintenance [12-14].

The present study was designed to estimate serum zinc level in children with acute diarrhoea and its correlation with the severity of diarrhoea estimated by Vesikari Scoring System.

## Subjects and Methods

The present study was conducted on 80 children aged from 2 months to 30 months from those diagnosed as having acute diarrheal episodes according to the WHO criteria and admitted to Abo El Rish Pediatric Hospital, Cairo University from February 2016 to October 2016.

Children came to the clinic suffered from acute diarrhoea was screened for inclusion and exclusion criteria. Those fulfilled the criteria were considered for sampling. According to their number, a systematic technique random sampling was used to select the desired number. Children with acute diarrhoea were included. Any child with history suspecting surgical or extra intestinal causes of diarrhoea or receiving immunosuppressive therapy were excluded from the study.

The study followed the regulations of the medical ethical committee of the Cairo University. Signed informed consents were collected from mothers of the children enrolled in the study before participation. Demographic data and medical history were collected from the mothers via questionnaires.

Acute diarrhoea was defined as caregiver's report of  $\geq$  three loose or watery stools in a 24-hour period [7]. The clinical picture and severity degree of each case was assessed based on a direct examination and categorized into mild, moderate and severe using a clinical scoring system (Vesikari Scoring System) [15].

**Table 1: Vesikari Scoring System**

Parameter	1	2	3
Diarrhea			
Maximum number stools per day	1-3	4-5	$\geq 6$
Diarrhea duration (day)	1-4	5	$\geq 6$
Vomiting			
Maximum number per day	1	2-4	$\geq 5$
Vomiting duration (day)	1	2	$\geq 3$
Maximum body temperature ( $^{\circ}$ C)	37.1-38.4	38.5-38.9	$\geq 39.0$
Severity of dehydration (%)	N/A	1-5	$\geq 6$
Treatment	Rehydration	Hospitalization	N/A
Severity rating scales	<7 (mild)	7-10 (moderate)	$\geq 11$ (severe)

Vesikari Scoring System (VSS) can be considered a useful and reliable infectious marker for pediatric gastroenteritis are enabling development of an early treatment plan and recently verified by many studies [16, 17] (Table 1).

## Laboratory investigations

Blood Sample was collected using plain tubes and let to stand until clotting. Clotted blood was centrifuged, separated, and serum transferred into aliquots stored frozen at  $-20^{\circ}$ C. Zinc level was estimated by using the colorimetric method with a spectrophotometer wavelength 560 nm (Atomic Absorption Spectrometer equipped with a graphite furnace atomizer and an auto-sampler; Quimica Clinica Aplicada S.A. Company, Amposta, Spain). The normal serum zinc level was considered for values of 60-110  $\mu$ g/dl.

## Statistical analysis

Statistical analysis was performed using the SPSS statistical package software for windows version 21 (SPSS Inc, Pennsylvania, USA). Parametric variables are described as the mean  $\pm$  SD. Pearson's correlation coefficients were used to evaluate correlations between the data exhibiting parametric distribution. P value < 0.05 was considered significant difference and p < 0.005 was considered highly significant difference.

## Results

The descriptive and clinical data are demonstrated in table 2. The mean age of the included children was  $5.9 \pm 11.2$  months.

According to the collected clinical data, 57 (71.3%) cases were reported to have a fever and 52 (65%) cases were associated with vomiting.

**Table 2: Demographic and clinical data of studied children**

	"Minimum and maximum."	Mean $\pm$ SD
Age (months)	3 - 30	11.2 $\pm$ 5.9
Weight (Kg)	4 - 13.5	8.1 $\pm$ 2.3
Duration of hospitalization (days)	1 - 6	2.3 $\pm$ 1.3
	No	%
Vomiting	52	65.0
Fever	57	71.3
Dehydration	66	82.5
Mild	27	40.9
Moderate	27	40.9
Severe	12	18.2
ICU admission	9	11.3
VVS Score:		
Mild <7	0	0
Moderate 7-10	10	12.5
Severe $\geq 11$	70	87.5

Dehydration degree ranged from mild to severe. Out of 80 studied cases, 66 children (82.5%) suffered from dehydration. Out of them, 27 (40.9%) child as a mild dehydration, 27 (40.9%) child as a moderate degree of dehydration while 12 children (18.2%) suffered from a severe degree of dehydration with 9 cases with ICU admission. The duration of hospitalization ranged from 1 to 6 days.

The VSS was applied to all cases; 10 (12.5%) cases were scored as moderate, and 70 (87.5%) cases were scored as severe.

Zinc level ranged from 50 – 101 µg/dl with the mean  $65.0 \pm 13.5$  µg/dl. The studied cases were then subdivided into two groups according to the cutoff value of serum zinc level which is 60 µg/dl. Zinc deficiency was present in 45 (56.2%) cases (Table 3).

**Table 3: Zinc level in studied children**

	Range	Mean $\pm$ SD
Serum Zinc level (µg/dl)	50 – 101	65.0 $\pm$ 13.5
Zinc level:	No	%
< 60 µg/dl	45	56.2
> 60 µg/dl	35	43.8

A significant negative correlation was noticed between zinc level and the diarrhoea severity parameters as the severity of dehydration ( $p < 0.001$ ), duration of hospitalization ( $p < 0.01$ ) and VSS scoring ( $p < 0.001$ ) as shown in (Table 4).

**Table 4: Correlations between serum zinc and diarrheal severity parameters**

Zinc level	Pearson Correlation	Age in months	Dehydration severity	Duration of hospitalization	VSS score
		0.593**	-0.429**	-0.269*	-0.496**
	Sig. (2-tailed)	0.000	0.000	0.016	0.000

\* Correlation is significant at the 0.01 level (2-tailed). \*\* Correlation is highly significant at the 0.001 level (2-tailed).

## Discussion

Acute diarrhoea considered as a leading cause of childhood mortality despite the remarkable achievement of oral rehydration therapy (ORT) in acute diarrheal diseases treatment over the years [1].

Oral rehydration salts (ORS) solution and ORT were adopted by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) since 1978 as the first line tool in dehydration management, causing reduction in the mortality rate of children aged five and less diagnosed as acute diarrhea from 4.5 million to 1.8 million every year. However, in spite of this undeniable achievement, acute diarrhoea remains a leading cause of death in children in developing countries [14, 18].

Frequent episodes of acute diarrhoea can compromise zinc level due to increased faecal zinc losses during the episode that could be associated with negative zinc balance. Additionally, zinc stores are limited and rapidly depleted by acute intestinal illness [19]. In the developing countries, the high prevalence of diarrheal episodes was reported to increase the risk of zinc deficiency [20].

In the present study, zinc deficiency was detected in 45 (56.2%) cases of the studied children. A significant negative correlation was noticed between zinc level and the severity of the disease measured by VSS.

This finding is in favour to many studies that reviewed the degree of diarrhoea control and treatment achieved by zinc supplementation. Some studies focused on the mechanisms by which zinc might contribute to the pathogenesis of acute diarrhoea [21-26].

Zinc deficiency has been linked to the severity of diarrheal episodes [21]. Moreover, Zinc supplement significantly reduced the duration of illness [22].

The current WHO/UNICEF Joint Statement on Clinical Management of Acute Diarrhea recommends 10–20 mg zinc/d (dependent on age) for 10–14 d for a reduction in diarrhoea duration and severity (the therapeutic benefit) and prevention of subsequent episodes (the “secondary prevention” benefit) [18].

Unfortunately, the WHO/UNICEF strategy for zinc supplementation as adjunctive therapy for diarrhoea is poorly implemented [27].

A significant negative correlation was noticed between zinc level and the diarrhoea severity parameters as the severity of dehydration ( $p < 0.001$ ), duration of hospitalization ( $p < 0.01$ ) and VSS scoring ( $p < 0.001$ ).

These findings are in favour to the finding of a systematic review by Lamberti et al., [28] that confirm and highlight the benefits of therapeutic zinc supplementation for diarrhoea among children aged five and less in low- and middle-income countries. The effects of zinc treatment, which include reductions in episode duration, stool output, stool frequency and length of hospitalization.

In conclusion, zinc level has an essential role in acute pediatric diarrhoea. For maximum impact on diarrheal diseases, improvement zinc therapy should be considered beside ORS. Clinical trials are recommended to support the zinc supplementation in developing countries.

## References

1. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet*. 2003;361(9376):2226–34.

[https://doi.org/10.1016/S0140-6736\(03\)13779-8](https://doi.org/10.1016/S0140-6736(03)13779-8)

2. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2095–12. [https://doi.org/10.1016/S0140-6736\(12\)61728-0](https://doi.org/10.1016/S0140-6736(12)61728-0)
3. Schnadower D, Finkelstein Y, Freedman SB. Ondansetron and probiotics in the management of pediatric acute gastroenteritis in developed countries. *Curr Opin Gastroenterol*. 2015;31(1):1–6. <https://doi.org/10.1097/MOG.0000000000000132> PMID:25333367
4. Farthing M and Kelly P. Infectious diarrhoea. *Medicine*. 2007; (35) 5:251–256. <https://doi.org/10.1016/j.mpmed.2007.02.009>
5. WHO. The treatment of diarrhoea: a manual for physicians and other senior health workers. In: Organization WH, editor, 2005.
6. WHO/UNICEF. WHO/UNICEF joint statement: clinical management of acute diarrhoea. Geneva, Switzerland, and New York, NY: WHO, UNICEF, 2004.
7. Olmez A, Yaçın SS, Yurdakök K, Coskun T: Serum zinc levels in children with acute gastroenteritis. *Pediatr Int*. 2007;49:314–317. <https://doi.org/10.1111/j.1442-200X.2007.02371.x> PMID:17532827
8. Caulfield L, Black RE. Zinc deficiency. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Edited by: Ezzati M, Lopez AD, Rodgers A, Murray CJL. Geneva: World Health Organization, 2004.
9. Patel A. Zinc for Acute Diarrhea and Amoxicillin for Pneumonia, Do They Work? *Indian J Pediatr*. 2015; 82(8):703–6. <https://doi.org/10.1007/s12098-015-1712-8> PMID:25731896
10. Sazawal S, Black RE, Jalla S, Mazumdar S, Sinha A, Bhan MK: Zinc supplementation reduces the incidence of acute lower respiratory infections in infants and preschool children: a double-blind, controlled trial. *Pediatrics*. 1998; 102 (1 Pt 1): 1–5. <https://doi.org/10.1542/peds.102.1.1> PMID:9651405
11. Hambidge M, Krebs N. Zinc, diarrhea, and pneumonia. *J Pediatr*. 1999; 135 (6): 661–664. [https://doi.org/10.1016/S0022-3476\(99\)70080-6](https://doi.org/10.1016/S0022-3476(99)70080-6)
12. Guarino A, Albano F, Ashkenazi S, Gendrel D, Hoekstra JH, Shamir R, et al. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: executive summary. *J Pediatr Gastroenterol Nutr*. 2008;46(5):619–2117–18.
13. Women's NCCf, Health Cs. Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years. London: RCOG Press, 2009.
14. Victora CG, Bryce J, Fontaine O, Monasch R. Reducing deaths from diarrhea through oral rehydration therapy. *Bull World Health Organ*. 2000;78:1246–55. PMID:11100619 PMID:PMC2560623
15. Adapted from Ruuska T and Vesikari T. *Scand J Infect Dis*. 1990;22:259–67.
16. Shim DH, Kim DY, Cho KY. Diagnostic value of the Vesikari Scoring System for predicting the viral or bacterial pathogens in pediatric gastroenteritis. *Korean J Pediatr*. 2016;59(3):126–31. <https://doi.org/10.3345/kjp.2016.59.3.126> PMID:27186219 PMID:PMC4865623
17. Schnadower D, Tarr PI, Gorelick MH, O'Connell K, Roskind CG, Powell EC, Rao J, Bhatt S, Freedman SB. Validation of the modified Vesikari score in children with gastroenteritis in 5 US emergency departments. *J Pediatr Gastroenterol Nutr*. 2013;57(4):514–9. <https://doi.org/10.1097/MPG.0b013e31829ae5a3> PMID:23676445 PMID:PMC3788842
18. UNICEF/WHO. Diarrhoea: why children are still dying and what can be done. Geneva, Switzerland, and New York, NY: WHO, UNICEF, 2009.
19. Castillo-Duran C, Vial P, Uauy R. Trace mineral balance during acute diarrhea in children. *J Pediatr*. 1988;113:452–7. [https://doi.org/10.1016/S0022-3476\(88\)80627-9](https://doi.org/10.1016/S0022-3476(88)80627-9)
20. Manary MJ, Abrams S, Griffin M, Quimper R. Perturbed zinc homeostasis in rural 3–5-y-old Malawian children is associated with abnormalities in intestinal permeability attributed to tropical enteropathy. *Pediatr Res*. 2010;67:671–5. <https://doi.org/10.1203/PDR.0b013e3181da44dc> PMID:20496476
21. Fischer-Walker C, Lamberti L, Roth D, Black R. Zinc and Infectious Diseases. In: Rink L., editor. *Zinc in Human Health*. IOS Press; Amsterdam, The Netherlands, 2011: pp. 234–253.
22. Lazzarini M, Ronfani L. Oral zinc for treating diarrhoea in children. *Cochrane Database Syst. Rev*. 2013;1. <https://doi.org/10.1002/14651858.CD005436.pub4>
23. Fischer Walker CL, Black RE. Zinc for the treatment of diarrhoea: Effect on diarrhoea morbidity, mortality and incidence of future episodes. *Int J Epidemiol*. 2010;39:i63–i69. <https://doi.org/10.1093/ije/dyq023> PMID:20348128 PMID:PMC2845862
24. Sachdev HP, Mittal NK, Mittal SK, Yadav HS. A controlled trial on utility of oral zinc supplementation in acute dehydrating diarrhea in children. *J Pediatr Gastroenterol Nutr*. 1988;7:877–881. <https://doi.org/10.1097/00005176-198811000-00015> PMID:3058919
25. Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, Jalla S. Zinc supplementation in young children with acute diarrhea in India. *N Engl J Med*. 1995;333(13):839–44. <https://doi.org/10.1056/NEJM199509283331304> PMID:7651474
26. Bahl R, Bhandari N, Saksena M, Strand T, Kumar GT, Bhan MK, Sommerfelt H. Efficacy of zinc-fortified oral rehydration solution in 6- to 35-month-old children with acute diarrhea. *J Pediatr*. 2002;141:677–682. <https://doi.org/10.1067/mpd.2002.128543> PMID:12410197
27. United Nations. Every woman, every child. Essential Commodities Implementation Plan Sept 2012. New York, NY: UN Commission on Life-Saving Commodities for Women and Children, 2012.
28. Lamberti LM, Walker CL, Chan KY, Jian WY, Black RE. Oral zinc supplementation for the treatment of acute diarrhea in children: a systematic review and meta-analysis. *Nutrients*. 2013;5(11):4715–40. <https://doi.org/10.3390/nu5114715> PMID:24284615 PMID:PMC3847757