Zinc Deficiency and Gastrointestinal Parasitic Infections Among Children

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ABSTRACT
Zinc is an important component of the immune response and the immune-regulation against parasitic infections. This study aimed to find out the relation between Zinc deficiency and intestinal parasitic infections among children. A cross sectional, comparative study was conducted from December 2012 to July 2013 on children attending the outpatient clinic of the Pediatric department of Benha University Hospital. The study included 129 children. They were of both sexes and their age ranged from four to ten years. The serum of the children was examined for the level of Zinc. Stool examination was done. The results revealed that the low Zinc group constitute 69% while the normal Zinc group constitute 31%. Low Zinc group reported higher parasitic infections regarding Entamaeba histolytica (55.1%), Giardia lamblia (49.4%), Hymenolipes nana (13.5%) and Ascaris lumbricoides (1.1%) with statistically significant results only for giardiasis. Also variable gastro intestinal manifestations were higher among the low zinc group as abdominal pain (41.6%), diarrhea (29.2%), abdominal distention (27%) and anorexia (14.6%) with statistically significant differences between the two groups regarding abdominal pain and anorexia. Male children (60.7%), school children (59.6%), underweight (78.7%) and who had diarrhea had low zinc level. Regarding the relation between zinc level and age, there was negative correlation between zinc level and age yet it is insignificant. This study reveals an evidence about the relationship between zinc deficiency and parasitic infections among children. National-level programs to combat childhood Zinc deficiency should be initiated and promoted at the primary health care level.

KEYWORDS: Zinc, children, nutrition, gastrointestinal parasites

INTRODUCTION
The association between nutrition and infection have been linked for centuries especially between micronutrient deficiencies and immune impairment[1]. Micronutrient deficiencies and infectious diseases often coexist and exhibit complex interactions leading to the vicious cycle of malnutrition and infections among underprivileged populations of the developing countries particularly preschool children[2]. Malnutrition and infectious diseases has been well recognized, especially those of the gastrointestinal tract[3]. Parasitic infections of the gut are highly prevalent in developing countries and contribute to the severe malnutrition associated with persistent diarrhea in children[4].

Zinc(Zn) plays a central role in cellular growth and in the function of the immune system [5]. Zinc is an important component of the immune response and the immune-regulation against parasitic infections [6]. A central clinical feature of zinc deficiency is the increased susceptibility to infectious diseases [7], many studies have demonstrated the benefits of zinc supplementation in regard to infectious diseases in human populations ,zinc supplements are estimated to reduce diarrheal deaths by 13% and pneumonia deaths by 20 % [8]. The first evidence of zinc deficiency in humans appeared in Egyptian and Iranian populations subsisting mainly on bread made of whole wheat flour in which zinc is not in an available form due to high phytate content[9].

Mild to moderate Zn deficiency is now known to occur among children and adults of many countries and is thought to be an important public health problem; its global prevalence was estimated to be 31% in 2004, whereas rates ranged from 4% up to 73% in developing countries[1].
The body’s need for zinc is greatest during periods of growth, such as infancy, adolescence, and pregnancy, and during lactation. The United States Recommended dietary allowances (RDA) for zinc rises from 5mg/day for newborn infants to 19mg/day for females during their first 9 months of lactation. For adult males 15mg/day, whereas the figure for adult females who are neither pregnant nor lactating is 12mg/day.[10].

Although a considerable amount of research has recently been focused on specific nutritional deficiencies and zinc as an essential dietary trace element yet few studies have examined the relation between zinc level and parasitic infections among children.

The current work aimed to find out the relation between zinc deficiency and intestinal parasites infections among children and to assess the association between zinc level, underweight and some personal characteristics.

MATERIALS AND METHODS

This is a cross sectional comparative study conducted on randomly selected 129 child who were attending the pediatric outpatient clinic of Benha University Hospital in the period from December 2012 to July 2013.

Inclusion criteria: Underweight, normal weight, male and female children with ages range from 4 up to 10 years.

Exclusion criteria: Overweight, obesity and underweight due to chronic illnesses as congenital heart diseases, endocrine, neoplastic disorders and short stature.

All children were subjected to the following:

They were weighed to the nearest one kg, lightly dressed and barefooted.

Standing height was measured to the nearest one cm, with shoes off, feet together and head in the horizontal plane[11].

The body mass index (BMI) was calculated from a child’s weight in kilograms and height in meters (kg/m²). BMI and ages of the children were plotted on the Egyptian percentile for boys and girls. Children below the third percentile were considered underweight and from 3rd to 97th percentile were considered normal weight[12].

The data were collected from the parents of the children who agreed to participate in the study through a well-designed structured questionnaire including some personal characteristics; age and sex and thorough history taking with special concern to gastrointestinal symptoms as diarrhea, anorexia, abdominal pain and abdominal discomfort.

Sample collection:

A) Stool samples were examined for detection of parasites.

B) Blood samples for assessing the level of zinc in serum.

A) Parasitological examination of stool was done by:

* Direct smear [13]

* Formol ether sedimentation technique [14]

* Modified Ziehl-Neelsen stain technique[15]

* Trichrome stain technique [16]

* Standard method for counting the number of cysts in the stool: According to Danciger and Lopez (1971) [17] with some modifications.

All stool samples were examined fresh within three hours after collection. If there is a delay of more than 3 hours after collection the stool was refrigerated at 4°C for 24 hours.

* Harada-Mori Culture (Test-Tube Cultures)[18]

B) Assessment of serum zinc level:

According to Homsher and Zack (1985) [19] zinc level (68-108 µg/dl) was considered normal. Thus the studied children were divided into two groups based on zinc level; low zinc level group (below 68 µg/dl) and normal zinc level group.

The study was conducted according to the rules of Benha faculty of medicine Ethical Committee including a written consent from each child parent with explanation of the purpose of the study and ensuring privacy.

Statistical analysis of the data including data coding, entry, sorting and statistical manipulations were performed. The collected data were tabulated and analyzed statistically using SPSS program version 16. The qualitative data were expressed as number and percentages while the quantitative data were expressed as mean ±standard deviation .chi square test used to test the differences between the qualitative variables and the t test was used to test the differences between the quantitative variables .The accepted level of significance will be p<0.05.

RESULTS

This study was conducted on 129 children .They were divided into two groups according to the zinc level; low zinc level group (below 68 µg/dl) and normal zinc level group (68-108 µg/dl). The results revealed that the low zinc group constitute 69 % with mean zinc level (57.16±6.8 µg/dl ) while the normal zinc group constitute 31% with mean zinc level of (87.92±11.4 µg/dl ). The majority of the studied group were males (58.1% ) ,school children (50.4% ) and underweight (67.4% ). The studied children shows 53.5 % with Entameba hisolytica infection, 43.4 % with Giardia lamblia, 11.6 % with Hymenolepis nana and 0.8 % with Ascaris lumbricoides. Also a number of intestinal manifestation were presented ; 36.4 % show abdominal pain, 27.1 % with abdominal distention , 25.6% with diarrhea and only 11.6 % show anorexia. Comparison of the two groups were conducted which reveals the following:

Table 1 shows that the low zinc group reported higher parasitic infections regarding entameba histolytica (55.1%), giardia lamblia (49.4%), hymenolipes nana (13.5%) and ascaris lumbricoides (1.1%) with statistically significant results only for giardiasis.
Table 1: Comparison between the studied groups regarding the parasitic infections.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Low zinc level Group</th>
<th>Normal zinc level</th>
<th>Total</th>
<th>p. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (89)</td>
<td>% (69%)</td>
<td>No (40)</td>
<td>% (31%)</td>
</tr>
<tr>
<td>Entamaeba histolytica</td>
<td>Yes</td>
<td>49 (55.1)</td>
<td>20 (50.0)</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>40 (44.9)</td>
<td>20 (50.0)</td>
<td>60</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>Yes</td>
<td>44 (49.4)</td>
<td>12 (30.0)</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>45 (50.6)</td>
<td>28 (70.0)</td>
<td>73</td>
</tr>
<tr>
<td>Hymenolipes nana</td>
<td>Yes</td>
<td>12 (13.5)</td>
<td>3 (7.5)</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>77 (86.5)</td>
<td>37 (92.5)</td>
<td>114</td>
</tr>
<tr>
<td>Ascaris lumbericoides</td>
<td>Yes</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>88 (98.9)</td>
<td>40 (100)</td>
<td>128</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>89 (100.0)</td>
<td>40 (100.0)</td>
<td>129</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\* \(x^2\) test

Table 2 illustrates that the low zinc group reported higher parasitic infection’s manifestations in the form of abdominal pain (41.6%), diarrhea (29.2%), abdominal distention (27%) and anorexia (14.6%) with statistically significant differences between the two groups regarding abdominal pain and anorexia (Table 2).

Table 2: Comparison of the studied groups regarding parasites manifestations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Low zinc level group</th>
<th>Normal zinc level group</th>
<th>Total</th>
<th>p. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (89)</td>
<td>% (69%)</td>
<td>No. (40)</td>
<td>% (31%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>YES</td>
<td>37 (41.6)</td>
<td>10 (25.0)</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>52 (58.4)</td>
<td>30 (75.0)</td>
<td>82</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>YES</td>
<td>26 (29.2)</td>
<td>7 (17.5)</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>63 (70.8)</td>
<td>33 (82.5)</td>
<td>96</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>YES</td>
<td>24 (27.0)</td>
<td>11 (27.5)</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>65 (73.0)</td>
<td>29 (72.5)</td>
<td>94</td>
</tr>
<tr>
<td>Anorexia</td>
<td>YES</td>
<td>13 (14.6)</td>
<td>2 (5.0)</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>76 (85.4)</td>
<td>38 (95.0)</td>
<td>114</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>89 (100.0)</td>
<td>40 (100.0)</td>
<td>129</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\* \(x^2\) test

Table 3 shows that the low zinc level group were presented more among male students (60.7%), school children (59.6%) and those with underweight (78.7%). The differences between the two groups were significant regarding age and weight status (Table 3). Table 4 illustrates that regarding the relation between zinc level and age, there was negative correlation between zinc level and age yet it is insignificant. In the present study, male children, schoolchildren, underweight and who had diarrhea had low mean zinc level (less than 68µg/dl). There were differences in the zinc level among the studied groups with higher levels among females, preschool children, normal weight and those who do not had diarrhea with statistically significant differences regarding their age, weight status and diarrhea (Table 5).
### Table 3: Comparison of the studied groups according to some personal characteristics and the weight status

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Low zinc level group</th>
<th>Normal zinc level group</th>
<th>Total</th>
<th>p. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (89)</td>
<td>% (69%)</td>
<td>No. (40)</td>
<td>% (31%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>54</td>
<td>21</td>
<td>75</td>
<td>58.1</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>35</td>
<td>19</td>
<td>54</td>
<td>41.9</td>
</tr>
<tr>
<td>Age</td>
<td>Preschool children</td>
<td>36</td>
<td>28</td>
<td>64</td>
<td>49.6</td>
</tr>
<tr>
<td></td>
<td>School children</td>
<td>53</td>
<td>12</td>
<td>65</td>
<td>50.4</td>
</tr>
<tr>
<td>Weight status</td>
<td>Normal weight</td>
<td>19</td>
<td>23</td>
<td>42</td>
<td>32.6</td>
</tr>
<tr>
<td></td>
<td>Underweight</td>
<td>70</td>
<td>17</td>
<td>87</td>
<td>67.4</td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td>100.0</td>
<td>40</td>
<td>100.0</td>
<td>129</td>
</tr>
</tbody>
</table>

* χ² test

### Table 4: Correlation between zinc level and age among the studied group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc level</td>
<td>66.6±16.6</td>
<td>-0.105</td>
<td>P&gt;0.05</td>
</tr>
<tr>
<td>Age</td>
<td>6.7±1.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 5: Comparison of the zinc level among the studied children regarding some personal characteristics, weight status and diarrhea

<table>
<thead>
<tr>
<th>Variables</th>
<th>Zinc level</th>
<th>T test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low zinc level</td>
<td>57.16±6.8</td>
<td>-19.11</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Normal zinc level</td>
<td>87.92±11.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>64.72±16.3</td>
<td>-1.606</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>69.44±16.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool children</td>
<td>69.92±16.5</td>
<td>2.2</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>School children</td>
<td>63.52±16.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>79.38±19.2</td>
<td>7.107</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Underweight</td>
<td>60.57±10.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>61.79±17.9</td>
<td>-1.994</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>no</td>
<td>68.39±15.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### DISCUSSION

Zinc is an essential trace element in the diets of humans for optimal health and growth. It is required for the genetic makeup of every cell and considered as an absolute requirement for all biologic reproduction hence, widespread sub optimal zinc nutrient constitutes a notable health risk for children in terms of growth and development[20],[21]. Also parasitic diseases represent a major cause of morbidity and mortality in childhood in most parts of the world, as parasites are endemic in many parts of the world with no specific area is spared[22].

Zinc is absorbed most efficiently from meat, liver, eggs, and seafood, and less efficiently from vegetables and cereal food containing large amounts of phytates and fibers[23]. Giardia lamblia is the most commonly isolated intestinal parasite throughout the world. Rates of 20.0-40.0% are reported in developing countries, especially in children[24].
Many studies proved the association between giardiasis and zinc levels in human hosts. A consistent change in level of zinc in the blood of children infected with G. lamblia has been noted by some investigators who have also reported decreased serum levels during giardiasis [25-30]. On the other hand, eradication of G. lamblia led to a significant improvement in the mean serum Zn levels six months after treatment in schoolchildren from northwestern Mexico [31].

The current work results coincide with this. They show that giardia lamblia infection were reported in (49.4%) of the low zinc group and (30.0%) of the normal zinc group with statistically significant results (P<0.05). This is in agreement with Jendryczko et al. [25] who studied the disturbances in zinc metabolism in children with Giardia intestinalis infection. The mean serum zinc concentration and the zinc concentration in the erythrocytes of children in the infected group was lower than that of control group. Also the effects of giardiasis on serological levels of zinc, copper and iron elements were assessed in a study by Ertan et al., [27] in Turkey. The study revealed that zinc and iron levels decreased during giardiasis due to malabsorption.

These findings were also proved by Karakas et al., [26] study which was designed to evaluate the serum zinc and copper levels in Turkish children infected with giardiasis and amebiasis. They added that after metronidazole therapy a significant increase in zinc level was observed, also Cu/Zn ratio level decreases and return to normal level. The authors concluded that zinc deficiency and increased Cu/Zn ratio level could be acute-phase responses to parasitic infections in children with giardiasis or amebiasis, and that a successful treatment of the primary disorder will lead to complete recovery.

The current work reveals that there are insignificant results between the two studied groups regarding Entamaea histolytica (p>0.05). On the contrary Vega-Robledo et al., [32] conducted a study to analyze the effects of zinc on Entamoeba histolytica activity and on its pathogenicity. The results indicated that zinc altered the functionality of the Entamoeba in vitro as reflected by a decrease in replication and adhesion and in vivo as manifested by inhibition of amoebic pathogenicity.

The current work shows that, there is statistically significant difference (P<0.05) in zinc level between children who have diarrhea and the others with lower zinc levels among children with diarrhea (61.79±17.9 ) and higher percentage of diarrhea among the low zinc level group (29.2%).

This is in agreement with Penny [33] who concluded that zinc deficiency contributes to an increased incidence and severity of diarrhea. Also Ghishan [34], reported that there are many studies which emphasize the possible explanations for the link between zinc deficiency and diarrhea such as, the functional impairment of the intestinal mucosal cell transport mechanisms during diarrhea which can cause losses of zinc or failure of absorption. Infections with intestinal parasites that cause diarrhea, malabsorption or bleeding into the bowel are considered to be a potential cause of zinc deficiency[35]. Many trials concluded that oral zinc supplementation is a simple and effective therapeutic intervention in the management of acute diarrhea.

Sazawal et al. [36] reported that daily supplementation with elemental zinc reduced the risk of continued diarrhea by 21% and also reduced the severity of the diarrhea particularly in stunted children. Zulfiqar et al.[37], reported that,锌-supplemented children had a 15% lower probability of continuing diarrhea on a given day in the acute-diarrhea trials and a 24% lower probability of continuing diarrhea and 42% lower rate of treatment failure or death in the persistent-diarrhea trials. Chaitali and Vijay [5] concluded that oral zinc administration provides substantial benefit in the reduction of stool output, frequency, and duration, combined with safety, efficacy, and affordability in acute diarrhea.

Regarding the differences of the zinc level among the studied group this study reported higher levels among preschool children (69.92±16.5) than the mean zinc level in schoolchildren (63.52±16.2). This is in agreement with Krebs et al., [38] and Krebs,[23] who explained that, healthy infants are usually able to get an adequate amount of zinc from breast feeding during the first six months of life, as long as the mother's milk supply is adequate and breast milk is not displaced by complementary foods. Krebs & Westcott [39]reported that, during the second six months of life when complementary foods are introduced, the risk for zinc deficiency increases because most traditional complementary foods are low in bio available zinc.

On the other hand Solomons,[40] reported that, the prevalence of zinc deficiency throughout childhood is estimated to be high, primarily related to the low consumption of foods high in bio available zinc.

In countries with known widespread zinc deficiencies and high levels of stunted children, preventive zinc supplementation has a small but significant positive effect on linear growth. The limited impact of zinc supplementation suggests that such an intervention should be part of more comprehensive efforts to improve the general nutritional status of children, particularly in the first two years of life [41]. Interventions that promote exclusive breastfeeding and appropriate complementary feeding along with micronutrient supplementation and fortification of foods may reduce the risk of stunting and are expected to provide substantial nutritional benefit to young children [42,43].

In this study there are statistically significant differences of the zinc level among the studied group regarding their weight status with higher levels among normal weight children (79.38 ± 19.2) than those who are underweight (60.57 ± 10.8) which reveals an association between zinc deficiency and underweight.

The link between zinc deficiency and weight status has been proved in different studies ;Sanstead et al., [44] who reported that, zinc deficiency can interfere with multiple organ systems development particularly when it occurs during a time of rapid growth and development, such as infancy, when nutritional demands are high, also in a study by Castillo-Duran et al. [45], which reported that infants with marasmus showed weight gain and increased host defense responses after 60 days of supplementation with 2 mg zinc/kg/day, another study by Rivera et al. [46] revealed that micronutrient deficiencies limited the growth of the Mexican infants, and they concluded that improving micronutrient intakes should be a component of interventions to promote growth in infants living in settings where micronutrient intakes are inadequate, a study from...
India identified 68% reduction in mortality in small-for-gestational-age term infants that were supplemented with zinc from 1 to 9 months of age [47].

Fraker et al. [48] reported that low serum zinc has been noted in children with protein calorie malnutrition (PCM), the parallels continue between zinc deficiency and PCM because both cause thymic atrophy, lymphopenia and impaired T cells and antibody-mediated responses in human, mice and primate. A syndrome of zinc deficiency has been described in Iran and Egypt with clinical manifestations of dwarfism, hypogonadism, hepatosplennomegaly, anaemia, poor hair growth, hyperpigmentation, and roughness of the skin [49]. Also indirect evidence for such effects in humans is also available. Intrauterine growth retardation, which has been linked to maternal zinc deficiency results in depressed cell-mediated immunity, which can persist for years[50].

CONCLUSION

This study reveals an evidence about the relationship between zinc deficiency and parasitic infections among children. Zinc was deficient in 69.0% of the studied groups while in 31.0% of the group the level were within the normal range. Higher percentages were reported for all intestinal parasites infections among the deficient zinc group with statistically significant results regarding Giardia infection. There are differences of the zinc level among the studied group with lower levels among males, school children, underweight and those who have diarrhea with statistically significant differences regarding their age, weight status and diarrhea.

RECOMMENDATIONS

National-level programs to combat childhood Zinc deficiency should be initiated and promoted at the primary health care level and school health services incorporating the private sector ; medical and non-medical Zinc supplementation for preschool and school aged children is an urgent strategy with more attention to the former age groups. School health team with good equipments should be focused on periodic regular screening and treatment for parasitic infections, promotion of personal hygiene awareness and practices and environmental sanitation among primary school children. Also more studies on big number of students in rural and urban areas of Egyptians are highly recommended.

CONFLICT OF INTEREST

There is no conflict of interest .There is no financial relationship with the organization that sponsored the research.

REFERENCES


41. Black, R.E.: Maternal and child under nutrition and overweight in low-income and middle-income countries. Lancet. 2013; S0140-6736(13)60937-X.


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