Serum Zinc and Lead Levels in Different Clinical Types of Eczema

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**Abstract**

**Background:** Zinc is an essential micronutrient for normal functioning of the immune and antioxidant systems. Inflammation and oxidative stress are major pathogenic mechanisms in the development of eczema. The role of zinc in eczema has been investigated in a limited number of studies, although the results are contradictory. The incidence of eczema has been increasing in developed countries. Although air and food pollution with heavy metals (e.g. lead) have been considered as possible culprits, these factors have never been investigated in different clinical types of eczema.

**Objective:** To assess the possible role of zinc and lead levels in different types of eczema.

**Results:** We found that patients’ serum zinc levels were significantly lower than control group. While on the other hand, patients’ serum lead levels were significantly higher than control group.

**Conclusion:** Evaluation of zinc and lead serum levels in cases with eczema could prove useful. The role of micronutrients in the pathogenesis and course of eczema warrants further study.

**Keywords:** Eczema; Zinc; Lead; Zinc deficiency; Dermatitis; Atopic dermatitis

**Introduction**

Eczema is a common relapsing disease affecting both children and adults. Eczema can present with different clinical phenotypes and is classically distinguished into an intrinsic and extrinsic form [1]. The increasing prevalence of allergic diseases in childhood in the last decades could be linked to concomitant dietary changes, especially with the modified and lower consumption of fruit, vegetables and minerals [2].

Zinc is an essential micronutrient for the proper functioning of more than 100 enzymes. Zinc plays a central role in modulating the immune system. It is essential for cellular function in the immune response, and acts as an antioxidant [3]. In the fields of environmental health and medicine, lead exposure remains one of the most important problems in terms of the prevalence of exposure and public health. The permeation of lead via the human skin has not been systematically evaluated due to its intense risk [4].

**Patients and Methods**

This is a case-control study including one hundred patients diagnosed with different types of eczema and fifty age and sex matched healthy volunteers who served as controls. All participants were recruited from the outpatient clinic of the Department of Dermatology, Faculty of Medicine, Benha University between March 2014 to February 2015. All participants provided an informed consent and the study protocol was approved by the ethical committee of human research in Benha University. Exclusion criteria were the use of topical steroids or antibiotics in the previous 2 weeks and any systemic anti-inflammatory or any medication known to interfere with serum zinc level in the previous 4 weeks. Pregnant and lactating females and patients suffering from gastrointestinal diseases were also excluded.

A five ml blood sample was taken from all patients and control groups under complete aseptic precautions. Blood sampling was done from antecubital vein. Blood samples were centrifuged at 3000 rpm for 10 min. The separated sera were immediately stored at -80°C until analysis.

Serum zinc level was detected spectrophotometrically with direct colorimetric method using 2-(5-bromo-2-pyridylazo-5-(N-n-propyl-N-3-sulfopropyl-amino) phenol (5-BR-PAPS) [5]. Zinc present in serum was chelated first and then, it reacted with a specific color reagent forming a stable and colored chelate. Then the result complex was measured at a wavelength of 560 nm. The intensity of the color was directly proportional to the amount of zinc in the sample. Males=70-125 μg/dl and females=68-115 μg/dl were considered of normal values.

Serum lead level was measured by atomic absorption spectrophotometer. The ermo Electro-SOLAAR M6 Dual Zeeman comfort with zemman background correction and with appropriate hydrogen burner head or quartz tube furnace, and lead hollow cathode lamp [6]. External calibrators for lead were prepared by serial dilution of parent stock which contain 1000 μl /ml using the diluents (deionized water). For reading lead concentration and standard (calibrator), it was important to choose proper wave length (283.3 nm) with the optimum lamp current band supplied with the lamp.
Statistical analysis

Data were tabulated and analyzed using the computer program Statistical package for social science (SPSS) version 16 (SPSS Inc., Chicago, IL). Descriptive statistics were calculated for the data in the form of mean and standard deviation for quantitative data while, frequency and percentage for qualitative data. Student t-test was used to compare mean of two groups while F test was used to compare between more than two groups. Inter-group comparison of categorical data was performed by using Chi square test (X^2-value) and fisher exact test (FET). Correlation coefficient was also used to find relationships between variables. A p-value less than 0.05 was considered statistically significant.

Results

Figure 1: Distribution of sex among different types of eczema (FET=20.52, p=0.002).

This study included 100 patients with eczema (38% males and 62% females with mean age 28.18 ± 15.69 years) and 50 age and sex matched healthy volunteers who served as control (20% males and 30% females with mean age 27.08 ± 17.13 years). Eight different clinical types of eczema were diagnosed in this study but the most common types were hand eczema (28%) and allergic contact dermatitis (25%).

A statistically significant difference (p<0.001) was noticed among patients with different types of eczema regarding to gender distribution. Hand eczema (33.9%) and allergic contact dermatitis (32.3) were the most common in females while pityriasis alba (28.9%) and hand eczema (18.4%) were more common in males (Figure 1).

The mean serum zinc level was statistically lower (p<0.001) in case group (71.52 ± 22.44 µg/dL) compared to control group (106.5 ± 13.49 µg/dL). Both males and females in case group showed a statistically (p<0.001) lower mean serum zinc level (75.04 ± 22.57, 69.35 ± 22.27 µg/dL respectively) in comparison to those in control group (108.3 ± 9.68, 105.3 ± 15.56 µg/dL respectively) (Table 1).

Within the case group a statistically significant difference (p<0.05) was also found between the mean serum zinc levels of patients with atopic dermatitis (91.26 µg/dL) versus seborrhoeic dermatitis (63.79 µg/dL), allergic contact dermatitis (70.75 µg/dL) and eye lid eczema (49.23 µg/dL). The latter also had a significant difference when compared to hand eczema (73.2 µg/dL) (Table 2).

Table 3 shows no statistically significant differences (p>0.05) between different serum lead levels among different types of eczema included in this study. Table 4 showed a high statisticaly significant negative correlation (p=0.001) between zinc and lead serum level in cases of seborrhoic dermatitis (r=-0.888), hand eczema (r=-0.49), allergic contact dermatitis (r=-0.682) and atopic dermatitis (r=-0.873), and there was also a statistically negative correlation(P<0.05) to pityriasis alba (r=-0.636).

Table 1: Comparison between mean serum zinc and lead levels (µg/dL) in studied groups (case and control) regarding to sex.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>Case group</th>
<th>Control group</th>
<th>Student t test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>Male</td>
<td>75.04 ± 22.57</td>
<td>108.3 ± 9.68</td>
<td>6.27</td>
<td>0.001  HS</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>69.35 ± 22.27</td>
<td>105.3 ± 15.56</td>
<td>7.94</td>
<td>0.001  HS</td>
</tr>
<tr>
<td>Lead</td>
<td>Male</td>
<td>5.77 ± 2.87</td>
<td>2.7 ± 1.83</td>
<td>4.34</td>
<td>0.001  HS</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>5.85 ± 2.9</td>
<td>2.14 ± 1.34</td>
<td>6.66</td>
<td>0.001  HS</td>
</tr>
</tbody>
</table>

Table 2: Comparison between mean serum zinc and lead levels (µg/dL) in studied groups (case and control) regarding to type of eczema.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean zinc</th>
<th>± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous eczema</td>
<td>72.54</td>
<td>22.02</td>
<td>40.7-94.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Seborrhoeic dermatitis</td>
<td>63.79</td>
<td>21.15</td>
<td>41.4-103.2</td>
<td>0.489 NS</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3: Comparison between mean serum zinc and lead levels (µg/dL) in studied groups (case and control) regarding to type of eczema.
Pityriasis alba  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>70.42</td>
<td>22.73</td>
<td>42.7-113.7</td>
<td>0.859 NS</td>
<td>0.508 NS</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lichen simplex chronicous  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>68.45</td>
<td>17.79</td>
<td>42.7-102.8</td>
<td>0.719 NS</td>
<td>0.641 NS</td>
<td>0.835 NS</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hand eczema  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>73.2</td>
<td>21.89</td>
<td>42.5-114.5</td>
<td>0.951 NS</td>
<td>0.288 NS</td>
<td>0.704 NS</td>
<td>0.579 NS</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Eye lid eczema  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>49.23</td>
<td>12.32</td>
<td>40.9-67.5</td>
<td>0.102 NS</td>
<td>0.238 NS</td>
<td>0.096 NS</td>
<td>0.084 NS</td>
<td>0.042 S</td>
<td>-</td>
</tr>
</tbody>
</table>

Allergic contact dermatitis  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>70.75</td>
<td>22.3</td>
<td>40.2-114.9</td>
<td>0.871 NS</td>
<td>0.443 NS</td>
<td>0.965 NS</td>
<td>0.793 NS</td>
<td>0.689 NS</td>
<td>0.073 NS</td>
</tr>
</tbody>
</table>

Atopic dermatitis  
<table>
<thead>
<tr>
<th>Mean lead ± SD</th>
<th>Range</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
<th>p5</th>
<th>p6</th>
<th>p7</th>
</tr>
</thead>
<tbody>
<tr>
<td>91.26</td>
<td>26.07</td>
<td>60.1-121.4</td>
<td>0.21 NS</td>
<td>0.036 S</td>
<td>0.064 NS</td>
<td>0.06 NS</td>
<td>0.056 NS</td>
<td>0.013 S</td>
</tr>
</tbody>
</table>

**P1=** serum zinc level (ug/dl) in venous eczema versus other types of eczema  
**P2=** serum zinc level (ug/dl) in seborrhoeic dermatitis versus other types of eczema  
**P3=** serum zinc level (ug/dl) in pityriasis alba versus other types of eczema  
**P4=** serum zinc level (ug/dl) in lichen simplex chronicous versus other types of eczema  
**P5=** serum zinc level (ug/dl) in hand eczema versus other types of eczema  
**P6=** serum zinc level (ug/dl) in eye lid eczema versus other types of eczema  
**P7=** serum zinc level (ug/dl) in allergic contact dermatitis versus other types of eczema

**Tables 2:** Comparison between mean serum zinc (µg/dL) levels in different types of eczema.

**Diagnosis**  
**Mean lead ± SD**  
**Range**  
**p1**  
**p2**  
**p3**  
**p4**  
**p5**  
**p6**  
**p7**

**Venous eczema**  
5.35  
3.85  
2.04-9.8  
-  

**Seborrhoeic dermatitis**  
6.45  
3.14  
2.3-10.8  
0.583 NS  
-  

**Pityriasis alba**  
5.34  
2.52  
1.9-9.4  
0.996 NS  
0.374 NS  
-  

**Lichen simplex chronicous**  
5.39  
3.4  
1.2-9.1  
0.985 NS  
0.527 NS  
0.971 NS  
-  

**Hand eczema**  
5.67  
2.74  
1.6-10.5  
0.82 NS  
0.497 NS  
0.707 NS  
0.808 NS  
-  

**Eye lid eczema**  
7.62  
1.94  
4.9-9.5  
0.322 NS  
0.515 NS  
0.117 NS  
0.258 NS  
0.183 NS  
-  

**Allergic contact dermatitis**  
6.23  
2.99  
1.06-10.8  
0.568 NS  
0.862 NS  
0.351 NS  
0.505 NS  
0.478 NS  
0.382 NS  
-  

**Atopic dermatitis**  
5.08  
3.07  
1.9-9.8  
0.89 NS  
0.391 NS  
0.828 NS  
0.85 NS  
0.60 NS  
0.166 NS  
0.35 NS  

**P1=** serum lead level (ug/dl) in venous eczema versus other types of eczema  
**P2=** serum zinc level (ug/dl) in seborrhoeic dermatitis versus other types of eczema  
**P3=** serum zinc level (ug/dl) in pityriasis alba versus other types of eczema  
**P4=** serum zinc level (ug/dl) in lichen simplex chronicous versus other types of eczema  
**P5=** serum zinc level (ug/dl) in hand eczema versus other types of eczema  
**P6=** serum zinc level (ug/dl) in eye lid eczema versus other types of eczema  
**P7=** serum zinc level (ug/dl) in allergic contact dermatitis versus other types of eczema

**Table 3:** Serum lead level (µg/dl) in different types of eczema.

**Lead-Zinc correlation**  
**r test**  
**P value**  
**Eye lid eczema**  
0.091  
0.909 NS  

**Allergic contact dermatitis**  
-0.682  
0.001 HS  

**Atopic dermatitis**  
-0.873  
0.005 HS  

**Table 4:** Correlation between zinc and lead serum level in different groups of eczema.
Discussion

The term “dermatitis” (synonym: eczema) refers to a non-infectious, inflammatory disorder of the skin. There are different forms of dermatitis including seborrheic dermatitis, primary irritant dermatitis, allergic contact dermatitis, dermatitis associated with venous hypertension, dyshidrotic dermatitis, photoallergic dermatitis, HIV-associated dermatitis, nummular dermatitis and atopic dermatitis (AD) [7]. Atopic dermatitis is one of the most common chronic inflammatory skin disease [8].

The essential trace element zinc (Zn) has a large number of physiologic roles, in particular being required for growth and functioning of the immune system. Adaptive mechanisms enable the body to maintain normal total body Zn status over a wide range of intakes, but deficiency can occur because of reduced absorption or increased gastrointestinal losses. Deficiency impairs physiologic processes, leading to clinical consequences that include failure to thrive, skin rash, and impaired wound healing. Mild deficiency that is not clinically overt may still cause nonspecific consequences, such as susceptibility to infection and poor growth [9].

Human exposure to lead occurs through inhalation, ingestion and through the skin. Lead is a heavy metal with no apparent biological function. Despite the extensive evidence concerning the toxic effects of lead on human health, the molecular mechanisms underlying this metal’s poisonous effects on the central nervous system (CNS) and other vital systems have yet to be clarified [9].

Based on these facts, this study was set to determine the serum levels of zinc and lead in patients with different clinical types of eczema in an attempt to investigate the possible relation of these elements with eczema [10].

The present study revealed that zinc levels were below the lower references in 56 patients with different clinical types of eczema (56%) while, another study revealed it in 66 patients (60%). This difference may be attributed in part to difference in target population (child vs adulthood). Moreover, Mrinal et al. [11] stated that endemic zinc deficiency is found in rural Iran, Egypt and Turkey due to eating whole grain bread with high fibre and phytate content that renders zinc nearly unabsorbable.

Serum zinc levels were statistically lower in case group than control pointing out the possible role of zinc in the pathogenesis of eczema. Until now, most of the studies [12] measured serum zinc levels in atopic patients with contradictory results, some authors reported lower levels [12,13], whereas others found no differences [14,15]. Dogramaci et al. [16] measured the serum levels of selenium, copper, zinc, iron and lead in 35 patients with hand eczema and 35 matched, healthy controls. Their results showed that the serum levels of trace but essential minerals (selenium, copper, iron and zinc) were lower in the eczema patients than in controls. The researchers concluded that low levels of zinc, selenium and iron contributed to the development of hand eczema. Another study [17] also measured the serum levels of lead, mercury, cadmium, selenium, copper and zinc in 110 children with eczema and 41 children with other skin conditions and showed that low zinc level was more pronounced in eczema than in the other skin conditions considered.

Parasad, [18] in a human study found that a mild deficiency of zinc led to reduction in Th1 functions, as measured by the production of IFN-γ, IL-2, and tumor necrosis factor-α (TNF-α). Thus, zinc deficiency in humans resulted in an imbalance between Th1 and Th2 cells. Furthermore, Parasad [19] stated that in a cell culture model, zinc deficiency decreased NF-kB activation, leading to reduced generation of inflammatory cytokines including TNF-α, IL-1β and IL-8. These data suggest that zinc deficiency may reduce anti-inflammatory effects and cause a relative increase of Th2 cytokines, which are the cytokines mainly implicated in eczema.

Female patients had a lower serum zinc levels than males in this study. Differences in serum zinc concentration by sex were noted previously [20]. Possible reasons for sex-based differences include differences in serum albumin concentrations and in lean body mass [21]. Estrogen and progesterone are also associated with lower serum zinc concentrations in women [22]. All of which may partly explain the lower serum zinc concentrations found in women.

A statistically significant difference was found between the mean serum zinc levels of patients with atopic dermatitis versus seborrheic dermatitis, allergic contact dermatitis and eye lid eczema. The latter also had a significant difference when compared to hand eczema. To the best of our knowledge serum zinc level was never compared in different types of eczema as designed in this study.

Lead poisoning is a serious problem world-wide. Although none of the participants in this study had lead levels beyond local upper limits, yet patients in eczema group showed significantly higher lead levels compared to control group. These results were in accordance with two studies [23,17], the first study revealed that lead levels were positively correlated with disease severity and long transformed IgE level (as a marker of atopy) and the second study found that in eczema patients, lead levels were generally within normal limits, but their levels were positively correlated with poor quality of life (QOL), disease severity and atopy. This positive correlation between atopy and lead was explained by Shaheen et al. [24] as they declared that evidence in animals suggests that high exposure to the heavy metals lead and mercury promotes Th2 cytokine responses in vivo, and that high lead exposure in utero causes persistent elevation of IgE in the offspring. Moreover, Hataguchi [25] stated that drinking deep sea water may be useful in treatment of AEDS (atopic eczema/dermatitis syndrome) as it significantly decreases the levels of the essential mineral, potassium (K) and significantly decreased the levels of the toxic minerals, mercury and lead.

On the other hand, the results of this study were opposed by Yamada et al. [26]. They found that hair lead level was not significant to the onset of eczema. The discrepancy between our findings and the medical literature may be the result of differences in age and study methodology and as our study was not limited to AD but included other clinical types of eczema.

In the current study there was a significant difference between serum zinc levels of cases of AD and those of allergic contact dermatitis, seborrhoeic dermatitis and eye lid eczema. There was no scientific explanation to this result but it might predict that those patients having AD might present later either with allergic contact dermatitis, seborrhoeic dermatitis or eye lid eczema.

A statistically negative correlation were detected in this study between the serum zinc and lead levels especially in patients with hand eczema, atopic dermatitis, seborrhoeic dermatitis and allergic contact dermatitis.

To the best of our knowledge, the present study is the first to evaluate the correlation between zinc and lead levels in different types
of eczema as other studies showed this correlation in patients with atopic dermatitis only.

Conclusion and recommendations: Evaluation of zinc and lead serum levels in cases with eczema could prove useful. The role of micronutrients in the pathogenesis and course of eczema warrants further study.

References