Relation between serum zinc levels and recurrent urinary tract infections in female patients: A case-control study

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Abstract

Background: Zinc deficiency can increase the risk of infectious diseases. Given that recurrent urinary tract infection is a common complication, this study examines the association between serum zinc levels and recurrent urinary tract infections.

Methods: In this case-control study, serum zinc levels for 48 patients with recurrent urinary tract infections were compared with the serum zinc levels of the same number of people in the control group who were matched in terms of location and age. Using SPSS ver. 18, univariate analysis was performed through t-test, correlation coefficient; and multivariate analysis was carried out through multiple regression tests. Significant level was considered as less than 0.05.

Results: There was a weak correlation between age and serum zinc level (r=0.205, p=0.045). Mean serum zinc level of the test group and the control group were 96.83 (±11.25) and 76.72 (±17.06) microgram/deciliter (p=0.001), respectively. Level of zinc reduced with aging; in addition, the group with recurrent UTIs had lower zinc levels than the control group (p=0.010, R2=0.377).

Conclusion: According to the results of this study, serum zinc levels of people with recurrent urinary tract infections were lower than that in the control group. It seems that zinc levels are a risk factor for recurrent urinary tract infections.

Keywords: Urinary tract infection, Micronutrients, Zinc, Recurrent infections, Nutrition

Introduction

Urinary tract infections (UTIs) are more common in women and become more prevalent with age (1-3). Prevalence of UTIs is 10% among people aged 4–7 years old while it is about 52% in people aged 18–26 years old (4,5). Recurrence is one of the complications of the disease, and its prevalence is different. In a follow-up study, the recurrent disease was observed once in 27% of patients and twice in 2.7% of UTI patients. Recurrent UTIs are defined as incidences of UTIs at least twice in six months or three or more times in one year (6).

Zinc is a micronutrient, and its deficiency can increase the risk of infectious diseases (7). Zinc is involved in the regulation of the host immune system, and its moderate deficiency leads to the dysfunction of the immune system. Zinc is necessary for the development and activity of T lymphocytes, and its deficiency leads to decreased levels of cellular immunity (8). Host cells can change the cytoplasmic and lysosomal level of zinc to make a response to the bacteria; in addition, the accumulation of zinc in phagolysosome and macrophages helps to control patho-

*What is “already known” in this topic:
According to the results of this study, It seems that serum zinc level is a risk factor for recurrent urinary tract infections.

—What this article adds:
There is a relationship between low serum zinc level and urinary tract infection. Therefore, a clinical trial is required for people with UTIs.
Zinc and urinary tract infection
gens. The bacterial poisoning caused by zinc can be a de-
defense mechanism used by macrophages to clear the infe-
tion (9). Zinc deficiency is associated with bad outcomes in
response to bacterial infections and sepsis (10). So, it
seems that zinc levels can be a risk factor for recurrent
UTIs. This study compared serum zinc levels between
women with and without recurrent UTIs.

Methods
This case-control study was conducted after aproval
by the Ethics Committee of Kurdistan University of Medical
Sciences (MUK.REC.1392.158). Considering a 1% error
rate of 0.05, mean zinc level of 105.9 (±23.7) in healthy
subjects and 95.4 (±21.8) in patients, and second type er-
ror of 10%, sample size was calculated as 48 in each
group (10). To enroll the subjects into the two groups,
they were briefed about the objectives of the study and
informed consent was obtained. The study participants
included women with recurrent UTIs who referred to
Tohid Hospital or the Clinic of Infectious Diseases. Initial
screening was performed by an infectious diseases spe-
cialist who examined patients to detect signs and sym-
ptoms of UTIs.

UTIs are defined as: presence of dysuria, or/and fre-
quency, and suprapubic pain or/and tenderness, or/and
costovertebral tenderness, or/and fever, or/and chills with
WBC equal or more than 10 /hpf in centrifuged urine
smear and presence of organism compatible with UTI
more than 100000 in urine culture. After initial screening,
the inclusion criteria were defined as recurrent UTIs or
UTI at least twice in the last six months, or UTI at least
two times over the past year, and being older than 12
years. It is worth noting that only incidences were enrolled
into the study (i.e. those who had not been treated for re-
cent infection). Considering the exclusion criteria, we did
not enroll those who consumed zinc in the past year, im-
munocompromised patients, dialysis patients, patients
receiving corticosteroid therapy, patients with cancer, and
patients with malabsorption.

The control group consisted of those referred to clinics
to undergo routine tests or to accompany patients and con-
sented to participate in this study. They underwent pri-
mary screening, which was performed by an infectious dis-
 ease specialist; in the absence of UTI symptoms or a his-
 tory of past UTIs, they were selected as members of the
control group. The control group matched with the cases
in terms of age and place of residence (urban/rural) by
group matching. To ensure the absence of UTIs, partici-
pants in the control group underwent urinalysis and a
urine culture test. The exclusion criteria used for the
control group were similar to those used for test group.

Blood samples (5 cc) were taken from the subjects who
met the inclusion criteria; to measure the serum level, the
collected blood samples were sent to the laboratory. The
subjects in the control group underwent the same pro-
dure and the tests were performed by one laboratory. To
measure the serum zinc levels, a zinc calorimetry test was
performed using the BT 3000 auto analyzer device (made
in Italy) and the Bio rex kit (made in the UK).

Results
The mean age of the participants in the test group and
the control groups was 53.37 (±19.2) and 52.70 (±19.33)
years, respectively (p=0.865). The mean serum zinc levels
of the participants from urban and rural areas were 86.78
(±17.32) and 86.75 (±20.6) microgram/deciliter, respecti-
vely (p=0.995). There was a weak correlation between age
and serum zinc level (r=-0.205, p=0.045). Mean se-
rum zinc level of the test group and the control group was
96.83 (±11.25) and 76.72 (±17.06) microgram/deciliter
(p=0.001), respectively.

The results of multiple linear regression (Table 1) shows
that the level of zinc reduced with age; in addition, the
group with recurrent UTIs had lower zinc levels than the
control group (p=0.010, R²=0.377).

Decreased serum zinc levels was related to increased
age and recurrent infections after adjusting for other vari-
ables.

Discussion
According to the results of this study, people with recurr-
ent UTIs had lower serum zinc levels than the control
group; this difference was also observed after adjusting
for age and location. Javadinia et al. (11) showed that se-
rum zinc levels were significantly lower in children with
UTIs than in the control group. In our study, we observed
the same result. This confirms that serum zinc levels in
patients with UTIs are lower than healthy individuals. It
should be noted that our study was conducted on patients
with recurrent UTIs, which was different from Javadinia
et al. (11). The results of our study showed that serum zinc
levels decreased with age and it was observed in both
groups, which indicates a reverse relationship between age
and serum zinc level. Given the fact that with aging there

Table 1: Relationship between serum zinc level and other variables after adjusting for other factors using a regression model

<table>
<thead>
<tr>
<th>Model</th>
<th>Non-standard coefficients</th>
<th>Standard coefficients</th>
<th>p</th>
<th>95% CI for B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta Coefficient</td>
<td>Std. Error</td>
<td>Beta Coefficient</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant coefficient</td>
<td>1.0782</td>
<td>6.75</td>
<td>-0.051</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.198</td>
<td>0.076</td>
<td>-0.215</td>
<td>0.010</td>
</tr>
<tr>
<td>Location (urban / rural)</td>
<td>-0.384</td>
<td>4.35</td>
<td>-0.007</td>
<td>0.930</td>
</tr>
<tr>
<td>Group (recurrent infection / control)</td>
<td>-20.23</td>
<td>2.87</td>
<td>-0.579</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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is an increase in the incidence of UTIs, it can be hypothe-
sized that, in addition to various causes for the increased
incidence of UTIs in old age, zinc deficiency can also be
regarded as one of the reasons.

Hancock et al. (12) indicated that the antimicrobial and
anti-biofilm effects of zinc on urinary tract pathogens, E.
coli, and Klebsiella was investigated; it was observed
that the divalent zinc was able to inhibit the mechanisms
of biofilm formation by the studied organisms in order
to apply its antimicrobial mechanism. Therefore, it might
be concluded that frequent recurrences may be due to the
formation of biofilm in the urinary tract or stones in the
urinary system.

Combination of some antibiotics with zinc results in a
synergistic effect against organisms and might be effective
in decreasing recurrent infections (13). Zinc is a cofactor
of more than 200 enzymes that are necessary for the met-
abolic activity of cells. Additionally, zinc has an important
role in immune system physiology and is important for the
development and activity of T lymphocyte. Decreased
serum zinc levels cause decreased immune system activity.
Zinc has an important role to play in the production of
gamma interferon, interleukin-2, and interferon alpha (14).
Zinc is necessary for radical detoxification and antioxidant
defenses (15). In patients with UTIs, oxidative stress is
increased and antioxidant levels is decreased. Markers of
oxidative stress such as malondialdehyde in UTIs is in-
creased; whereas, serum cations such as Cu, Ca, and Zn
are decreased (16).

The above-mentioned conclusions are consistent with the
results of our study. The administration of antibiotics
together with an appropriate level of serum zinc could
result in a synergistic ability to eradicate organisms in the
urinary system.

This study had some limitations. We could not follow
patients with low levels of serum zinc. Follow up of these
patients can clearly define the possible relation of zinc
deficiency and recurrent UTI.

Conclusion

It can be suggested that recurrent UTIs are associated
with low serum zinc levels. Therefore, it is recommended
to conduct a clinical trial to study the effects of zinc sup-
plementation on patients with recurrent UTIs and to de-
termine their effectiveness in the prevention or treatment
of recurrent UTIs.

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Conflict of Interests

The authors declare that they have no competing interests.

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