

## Original Article

# Serum zinc levels in patients with multiple warts

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**Abstract** *Background* Although zinc sulphate has been used successfully for the treatment of warts, its mechanism of action is not fully understood. It may work by deficient body stores. The aim of this study was to compare the serum concentration of zinc in patients with multiple warts with normal subjects.

*Patients and methods* In this case-controlled study, 30 patients less than 15 years of age with multiple warts and 30 individuals from the normal population who were matched for age and sex were included. The level of zinc in the serum was measured using flame atomic absorption spectrometry in the two groups.

*Results* The mean serum zinc concentration in the patient and control groups was  $55.2 \pm 9.6$  and  $55.8 \pm 8.2 \mu\text{g } 100 \text{ mL}^{-1}$ , respectively. No significant difference in serum zinc concentration was found between the two groups ( $p=0.795$ ). However, there was a significant inverse correlation between serum zinc concentrations and the number of warts ( $\beta=-1.793$ ,  $\text{SE}=0.646$ ,  $P=0.002$ ). There was no significant relationship between serum zinc concentration and duration of disease in the patient group ( $\beta=-0.129$ ,  $\text{SE}=0.083$ ,  $p=0.124$ ).

*Conclusion* Serum zinc concentration in patients with multiple warts was not statistically different from control subjects. However, there was an inverse relationship between serum zinc concentration and the number of warts.

### Key words

Zinc, wart, human papillomavirus, immunity, Iran

## Introduction

Zinc belongs to the group of essential trace elements. It is present in high concentrations in shellfish, legumes, nuts, whole grain and green leafy vegetables, while its levels are usually insignificant in fruits.<sup>1</sup> Adequate intake of zinc is required for the immune system to function efficiently, and its deficiency comprises the functions of immune cells, especially T cell

function.<sup>2,3</sup> Zinc deficiency leads to a decreased number of T cells and disruption of their function, including a shift of the T helper (Th1) cell response to a Th2 predominance.<sup>2,4</sup> It also results in reduced killing activity in natural killer (NK) cells.<sup>2,3</sup> Neutrophil count is reduced and their recruitment is diminished during zinc deficiency.<sup>5</sup> Although monocytes and macrophages are more resistant to zinc deficiency, this condition can impair intercellular signaling pathways in them.<sup>6</sup>

Warts are benign tumors of the skin and other epithelial surfaces, caused by the human papillomavirus (HPV) infection.<sup>7</sup> They are one of the most common diseases seen in the dermatology clinics. The role of immune system in wart regression is well-documented.<sup>8-10</sup>

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Although a humoral immune response is mounted against papillomavirus infection,<sup>11</sup> the importance of this in disease modulation is not known. However, cell-mediated immunity appears to be the principle mechanism involved in wart regression.<sup>12</sup> In fact, in persistent disorders of cell-mediated immunity, the prevalence and incidence of warts are increased.<sup>13</sup>

Zinc sulphate has been used orally and topically for the treatment of warts in some clinical trials with favorable results.<sup>14-16</sup> Considering the role of zinc in immune function and the efficacy of zinc sulphate in wart resolution, we measured serum concentration of zinc in patients with multiple warts and compared it with control subjects.

### **Patients and methods**

In this case-controlled study, 30 patients less than 15 years of age with multiple warts (the number of warts  $\geq 3$ ) who had been referred to Shahid Faghihi Hospital in Shiraz were included. Also, 30 individuals from the normal population who were matched for age and sex were selected as the control group. A special questionnaire was completed through an interview and the following data were included for analysis: 1. demographic characteristics: age and gender; 2. socioeconomic status: education level of their fathers (categorized to three levels of low [illiterate or primary school], medium [junior high school or senior high school] and high [college or university degree]), income of their family (categorized as low income [less than 200 dollars per month], medium (200 to 400 dollars per month), and high [ $>400$  dollars per month]); and 3. information related to disease: the number and location of warts, duration of the disease, types and duration of previous treatments. Patients with acute

infections or systemic diseases were excluded. Individuals who agreed to participate the study met with the researcher or research assistant who explained the purpose of the study and informed consent was obtained from all participants. This study was approved by Shiraz University of Medical Sciences ethical committee.

Sera were collected from the patients between 9.00 a.m. and 12.00 a.m. After centrifugation, the serum was kept at  $-80^{\circ}\text{C}$  until further testing. The blood samples then were transferred to zinc-free test tubes. The level of zinc in the serum was measured using a flame atomic absorption spectrometer.

Results were reported as mean $\pm$ standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the student's *t*-test for the continuous variables and the chi-square test (or Fisher's exact test if required) and Mantel-Haenszel chi-square test for trend for the categorical variables. This study was done with a power of 90%. *p* values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

### **Results**

Demographic characteristics and the socioeconomic status of the studied population are shown in **Table 1**. In both studied groups, 47% of the patients were male and 20% of all patients were between 4 to 7 years old. There was no significant difference in education level of the family between the patients and control groups ( $p=0.098$ ), whereas the level of income in the family of patients group was significantly lower than the family of the controls ( $p<0.001$ ).

**Table 1** Demographic characteristics and socioeconomic status of patients and control groups

Characteristic	Patient group (n=30) n (%)	Control group (n=30) n (%)	p value
Male	14 (47.0)	14 (47.0)	0.999
Age			
4-7 years	6 (20.0)	6 (20.0)	
8-11 years	11 (36.7)	11 (36.7)	0.999
12-15 years	13 (43.3)		
Education level			
Primary	15 (50.0)	7 (23.3)	
Secondary	11 (36.7)	16 (53.4)	0.098
Higher	4 (13.3)	7 (23.3)	
Income			
Less than 200 DPM*	20 (66.6)	7 (23.4)	
200 to 400 DPM	4 (13.4)	18 (60.0)	<0.001
More than 400 DPM	6 (20.0)	5 (16.6)	

\* Dollars per month

**Table 2** Clinical description of the study groups by certain variables (n=30)

Characteristics	n (%)
Location of warts	
Upper limbs	15 (50.0)
Lower limbs	3 (10.0)
Head and neck	4 (13.4)
Trunk	5 (6.7)
Head, neck and limbs	6 (20.0)
Duration of the disease	
< 1 year	21 (70.0)
1-2 years	4 (13.3)
> 2 years	5 (16.7)
Number of warts	
Four	5 (16.7)
Five	8 (26.7)
Six	3 (10.0)
Ten	8 (27.6)
Twenty	4 (13.3)
Fifty	2 (5.7)

Information related to warts in the patient group has been summarized in **Table 2**. The number of warts in 19% of patients was  $\geq 20$  warts on the body surface and half of them were located on the upper extremities. Among these patients, 43.3% had no history of treatment for warts and 13.4% of them were administered traditional medicines. The duration of disease was less than one year in 70% of patients and more than 2 years in 16.7% of them.

The mean serum zinc concentration in the patient and control groups was  $55.2 \pm 9.6 \mu\text{g}$

$100\text{mL}^{-1}$  and  $55.8 \pm 8.2 \mu\text{g } 100\text{mL}^{-1}$ , respectively which was not statistically significant ( $p=0.795$ ). In the patient group, regression analysis showed a significant inverse correlation between serum zinc concentration and the number of warts ( $\beta=-1.793$ ,  $\text{SE}=0.646$ ,  $p=0.002$ ), however there was no significant relationship between serum zinc concentration and duration of disease in these patients ( $\beta=-0.129$ ,  $\text{SE}=0.083$ ,  $p=0.124$ ).

## Discussion

Although zinc sulphate has been used successfully for the treatment of viral warts, its mechanism of action is not fully understood.<sup>16</sup> It has been stated that local irritation which is produced by topical zinc application may trigger immune response.<sup>17</sup> However, it may be due to replacement of zinc deficiency or by immunomodulatory functions of the zinc. The possibility that serum zinc level may lead to an increased risk of acquiring warts may be evident as one study showed that all the lesions regressed completely in conjunction with the increment of serum zinc.<sup>16</sup>

In the present study, 20% of patients with multiple warts were less than 7 years of age and 56% of them were less than 11 years old.

Furthermore, in our study, multiple warts were observed more commonly on the upper extremities. Similarly, in a study by Kilkenny *et al.*<sup>18</sup> it was shown that the prevalence of warts was 22% overall, ranging from 12% in 4 to 6 year olds to 25% in 10 to 12 year olds and no difference in prevalence was noted between boys and girls. The majority of warts in their study occurred on the upper extremities. Also, in a large epidemiological study among British school children between 11 and 16 years, the prevalence of warts was between 3.9% and 4.9% and there was no difference in prevalence between both sexes.<sup>19</sup>

In our study, no significant difference in zinc concentration was found between the two groups. In a similar study by Al-Gurairi *et al.*<sup>16</sup> serum zinc of all patients with viral warts ( $62.5 \pm 10.7 \mu\text{g } 100\text{mL}^{-1}$ ) was statistically lower than at baseline in comparison with the level of serum zinc in the healthy control group ( $87.8 \pm 10.0 \mu\text{g } 100\text{mL}^{-1}$ ). Also, in another study by Gaby *et al.* the mean serum zinc concentration was approximately 27% lower in patients than in healthy controls.<sup>20</sup> The similarity of serum zinc concentration between patients and control group in our study can be related to the small sample size of our study. It has also been stated that in cases of mild zinc deficiency, the assay of cellular zinc provides a more sensitive criterion.<sup>4</sup> Therefore, it would be better to measure cellular zinc levels for the detection of these mild deficient cases.

We found an inverse association between the number of warts and serum zinc concentration, but this association was not observed between the duration of warts and zinc concentration. Some studies have shown that several factors such as immunosuppression and the number of warts at presentation are associated with increased duration of warts.<sup>21,22</sup> However, the

present study is one of the firsts to demonstrate the relationship between the number and duration of warts and serum zinc concentration.

In conclusion, zinc deficiency can be associated with increased number of warts, but it is not associated with increased tendency towards wart development or increased duration of them. However, more investigations about the role of zinc in wart using a larger sample size are warranted.

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