

## Original Article

# ASSOCIATION OF LOW SERUM ZINC LEVEL WITH MULTIPLE VIRAL WARTS

Ayesha Anwar and Azam Bokhari

**Objective:** To determine the association of low serum zinc levels with multiple viral warts.

**Methods:** Comparative case control study was conducted from 28th February 2011 to 28th August 2011 in Department of Dermatology, Services Hospital, Lahore. 110 cases; 55 in each group calculated with 80% power of test, 5% level of significance and taking expected percentage of low serum zinc level i.e. 56% in patients presenting with warts, 32% in control group. Serum zinc analysis was carried out by atomic absorption spectrometry.

**Results:** Age of patients as well as of controls ranged from 12- 65 years with a mean of 30.02 + 10.04 years. Serum zinc level was low in 33(60%) patients and 19 (34.5%) controls. Among the patients, serum zinc level ranged from 680 - 1020 microgram/ litre with a mean of 812.33 + 105.57, whereas level ranged from 687-1020 microgram/ litre with a mean of 848.96 + 113.68 among controls. Odds ratio was 2.84.

**Conclusion:** As the Odds ratio is 2.84 (>2) it concludes that there is an association between the low serum zinc level and multiple viral warts. So, low serum zinc level is a risk factor of the multiple viral warts.

**Key words:** Zinc, multiple warts, human papillomavirus.

## Introduction

Warts are benign tumors of skin and other epithelial surfaces caused by Human Papilloma virus (HPV).<sup>1</sup> They are estimated to occur in 2-20% of school-age children. The incidence increases during school years to reach a peak in adolescence and early adulthood then declines rapidly through 20s and more gradually thereafter.<sup>2</sup> Any area of skin can be affected although hands and feet are by far the commonest sites.<sup>3</sup>

Role of immune system in wart regression is well documented. Human immune system uses both innate and adaptive immunity to recognize and combat foreign agents.<sup>4</sup> Humoral immunity to the viral capsid has been shown to be sufficient for protection against infection, while innate and adaptive cell-mediated immunity appears important for eventual elimination of HPV infection.<sup>5</sup>

Almost all nutrients in diet play a crucial role in maintaining an optimal immune response. Zinc is known to play a central role in immune system. Zinc is a trace element that affects many aspects of immune function, including thymic development and the activity of T, B cells, and NK cells.<sup>6</sup>

Zinc deficiency in humans decreases the activity of serum thymulin (a thymic hormone), which is required for maturation of T-helper cells. Thus zinc deficiency leads to cell-mediated immune dysfunction due to shifting of Th(1) to Th(2)

function. IL-2 production (Th(1) cytokine) is decreased, which leads to decreased activities of natural-killer and T cytolytic cells, which are involved in killing viruses, bacteria, and tumor cells.<sup>7</sup> Therapeutic role of zinc has been reported in many dermatological conditions such as acrodermatitis enteropathica, chronic aphthous stomatitis, recurrent herpes labialis, cutaneous leishmaniasis and cutaneous viral warts.<sup>6,8</sup>

There are only few studies providing us data regarding serum level of zinc in patients with warts. According to a case control study conducted by Raza and Khan serum zinc levels were low in 56% patients with warts and 32% of age and sex matched controls (P = .0003).<sup>6</sup> Considering the role of zinc in immune-modulation, wart regression and paucity of data regarding serum level of zinc in patients with warts, this study was undertaken to determine the association of low serum zinc levels with multiple warts. By determining this association we can use oral zinc sulphate solely or as an adjuvant with other conventional therapeutic modalities available for warts.

## Methods

This comparative case-control study was conducted in Department of Dermatology, Services Hospital, Lahore for a period of six months. Patients 12-65 years of age, of either sex, having plantar, common, filiform and genital warts, 6-20 in number for

duration of 3-12 months and age and gender matched controls (attendants and relatives of patients) were selected.

The patients with chronic dermatological or systemic disorders (already diagnosed cases of diabetes mellitus, chronic liver disease), taking zinc supplements, immune deficiency congenital or acquired (on systemic steroids or immunosuppressants), pregnant and lactating females were excluded from the study. An informed consent was obtained for conducting the study and using their data for research purpose. A special questionnaire was completed through an interview and data were collected for analysis such as demographic characteristics (age, sex), number, type and duration of warts.

5ml of blood sample was taken from patients as well as controls after history and examination. Serum zinc analysis was carried out by atomic absorption spectrometry. Serum zinc level < 800µg/L was taken as low. Data was entered and results were analysed statistically using SPSS 12. Descriptive statistics were calculated. Mean and standard deviations were calculated for continuous variables i.e. age. Frequency and percentage were calculated for low serum zinc level and gender in both groups. Odds ratio (OR) was calculated for the association of low serum zinc level and multiple

viral warts. OR >2 was considered as significant.

### Results

Fifty five patients and an equal number of age and gender matched healthy controls were recruited in the study who fulfilled the inclusion and exclusion criteria.

While considering the descriptive statistic, age of the patients as well as the controls ranged from 12-65 years with a mean of 30.02+10.04 years. Most of the studied population (n=69, 62.7%) was in the age group 21-30 years.

In both studied groups 38 (69.1%) were males and 17 (30.9%) were females. Plantar warts(n = 28,50.9%) were the most common presentation followed by common warts (n = 13 ,23.6%), filiform warts (n = 8,14.5%) whereas genital warts (n= 06, 10.9%) were the least common. Among patients, the serum zinc level ranged from 680-1020 microgram / litre with a mean of 812.33 + 105.57 whereas the level ranged from 687-1020 microgram/litre with a mean of 848.96 + 113.68 microgram/litre among controls. The serum zinc level was low in 33 (60%) patients and 19 (34.5%) controls (**Table 1, 2**). Odds ratio (OR) for the association of low serum zinc levels with multiple viral warts was found to be 2.84 which is statistically significant as it is >2 (**Table 3**).

**Table-1:** Patients with low serum zinc Level .

		Frequency	Zinc Level of cases		
			Percent	Valid Percent	Cumulative Percent
	Low serum zinc	33	60.0	60.0	60.0
Valid	Normal ser zinc	22	40.0	40.0	100%
	Total	55	100	100	

**Table-2:** Patients with low serum zinc Level .

		Frequency	Zinc Level of controls		
			Percent	Valid Percent	Cumulative Percent
	Low serum zinc	19	34.5	34.5	34.5
Valid	Normal ser zinc	36	65.5	65.5	100%
	Total	55	100	100	

**Table-3:** Association between low serum zinc level and multiple viral warts.

Risk Estimate	Value	V95% Confidence Interval	
		Upper	Lower
Odds ratio zinc level (low serm zinc/normmal) serum zinc	2.842	1.310	6.166
For cohort Warts = Yes	1.673	1.134	2.467
For cohort Wants = No	.589	.390	.888

## Discussion

Warts are a common dermatological problem in our society. These are small tumors of the skin and other epithelial surfaces caused by a virus called the human papillomavirus.<sup>1</sup> Their appearance can differ depending on the type and location on the body. Most cases occur between ages 12-16 years.<sup>9</sup> Despite viral immune evasion, the immune system effectively clears most HPV infections, which resolve without any medical intervention. It is basically the cell-mediated immunity that plays a role in regressing viral warts. However, sometimes, the infection remains persistent, progressive or recurrent probably because of some defect in immunity against the virus.<sup>10,11</sup>

Deficiency of zinc is said to have an adverse effect on cell mediated immunity. It has been suggested that it affects mainly the functions of Th1 cells. Even a mild deficiency in humans may be accompanied by an imbalance of Th1 and Th2 cells, decreased serum thymulin activity, decreased recruitment of T naive cells, a decreased percentage of T cytolytic cells, and decreased NK cell lytic activity. It is crucial to the normal development of immune cells, and it plays an important role in maintaining the activity of a range of immune cells, including neutrophils, monocytes, B and T cells, natural killer cells and macro-phages.<sup>7,12,15</sup>

The use of immune modulation as a treatment of viral warts is a relatively newer concept. Zinc sulphate has been used successfully for the treatment of viral warts. It has been stated that local irritation which is produced by topical zinc application may trigger immune response. However, it may be due to replacement of zinc deficiency or by immunomodulatory functions of the zinc. The possibility that low 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>14</sup>

In our study mean age of patients and healthy controls was  $30.02 \pm 10.045$  while age range was 12-65 years. Most of the patients and controls were in the age group 21-30 years ( $n=69, 62.7\%$ ). In the previous study done by Raza and Khan sample size was large, 75 patients with the similar inclusion criteria for age were included in the study. Mean age and standard deviation in this study was  $25.8 \pm 8.90$  years.<sup>6</sup>

This shows that in spite of differences in sample size of two studies mean age is not very far away

from each other. In our study 69.1% were males and 30.9% were females in both studied groups. In the study conducted by Raza and Khan 69.3% were males and 30.7% were females.<sup>6</sup> In a similar study conducted by Shahbaz, et al. in Iran 47% were males in both studied groups.<sup>1</sup>

This observation shows that there was slightly more male predominance in our and other studies. This could be due to easy approach of males to health facilities due to cultural reasons.

Significant difference in serum zinc concentration was found between the two groups in our study. 34.5% healthy controls and 60% patients having viral warts had serum zinc levels below the normal range which clearly indicates that although a considerable proportion of our population is deficient in zinc, this deficiency is present in a higher number of patients with multiple viral warts as the difference was statistically significant (odds ratio = 2.84). Our results are consistent with other studies such as 56% of patients with viral warts and 32% healthy controls had low serum zinc levels in a study by Raza and Khan.<sup>6</sup>

The serum zinc level of patients in our study was 680-1020 microgram/litre with a mean of  $812.33 \pm 105.57$ . In a similar study by Raza and Khan serum zinc level of patients with viral warts ranged from 695-1090 microgram/litre with a mean of  $804.38 \pm 100.60$  was statistically lower than the level of serum zinc in the healthy control group 690-1100 microgram/litre with a mean of  $836 \pm 91.04$ , whereas Yaghoobi, et al reported a mean serum zinc level of  $550.9 \pm 100.7$  micro-gram/litre in patients with recalcitrant multiple viral warts.<sup>14</sup> Also in another study by Al-Gurairi, et al mean serum zinc level of all patients with viral warts  $625 \pm 100.7$  microgram/litre was significantly lower than at baseline in comparison with the level of serum zinc in healthy controls  $878 \pm 100$  microgram/litre.<sup>15</sup> Although mean serum zinc levels in patients in these studies were lower, this difference may be due to different standards or techniques used or because of other nutritional deficiencies. An estimation of serum zinc levels by the photometric method is less accurate whereas an estimation by atomic absorption, the method we employed in this study, is a fairly accurate method for estimation of metals including zinc.

Numerous studies have shown the relationship of zinc deficiency with infections and the benefits of zinc with respect to these diseases in human.<sup>14,16,17</sup> A study has revealed that viral warts completely disappeared in more than 78.1% of the patients treated with oral zinc sulphate for 2 months.<sup>14</sup>

Zinc deficiency was found in 60% of the patients in our study; the remaining patients had serum zinc levels within normal limits. This finding probably suggests that factors other than serum zinc deficiency like other nutritional deficiencies may also be operative in immunity failure against clearance and development of multiple viral warts.

## Conclusion

The present concludes that there is an association

between the low serum zinc level and multiple viral warts. So, low serum zinc level can be considered a risk factor for the multiple viral warts.

*Department of Dermatology  
SIMS/Services Hospital, Lahore  
[www.esculapio.pk](http://www.esculapio.pk)*

## References

1. Naseri M, Shahbaz S, Handjani F, Ghariheh A. Serum zinc levels in patients with multiple warts. *J Pak Assoc Dermatol* 2009;19:4-8.
2. Sterling JC. Virus infections. In: Burn T, Breatnach S, Cox N, Griffith C. *Rook's text book of dermatology*. 8th ed. Oxford: Wiley-Blackwell 2010;33.1-81.
3. Nanette B. Silverberg. Human papilloma virus infections in children. In: Schrotten H, Wirth S. *Pediatric infectious diseases revisited*. 1st ed. USA: Birkhäuser Basel 2007;365-90.
4. Stanley M. Immune response to human papilloma virus. *Vaccine* 2006; 24 (suppl 1):16-22.
5. Frazer IH. Interaction of human papilloma viruses with host immune system: a well evolved relationship. *Virology* 2009;384:410-4.
6. Raza N, Khan DA. Zinc deficiency in patients with persistent viral warts. *J Coll Physicians Surg Pak* 2010;20(2):83-6.
7. Prasad AS. Zinc mechanism of host defence. *J Nutr* 2007 ;137(5):1345-9.
8. Prasad AS. Zinc in human health: effect of zinc on immune cells. *Mol Med* 2008 ;14(6):353-7.
9. Mulhem E, Pinelis S. Treatment of nongenital cutaneous warts. *Am Fam Physician* 2011;84(3):288-93.
9. Stanley MA. Immune responses to human papilloma viruses. *Indian J Med Res* 2009;130: 266-7
10. Khurshid K, Pal SS. Role of Candida antigen in treatment of viral warts: a placebo-controlled study. *J Pak Assoc Dermatol* 2009;19:146-50
11. Lazarczyk M, Cassonnet P, Pons C, Jacob Y, Favre M. The EVER Proteins as a Natural Barrier against Papillomaviruses: a New Insight into the Pathogenesis of Human Papillomavirus Infections. *Microbiol Mol Biol Rev* 2009;73(2):348-70.
12. Maggini S, Wenzlaff S, Hornig D. Essential role of vitamin C and zinc in child immunity and health. *J Int Med Res* 2010;38(2):386-414.
13. Yaghoobi R, Sadighha A. Evaluation of oral zinc sulfate effect on recalcitrant multiple viral warts: A randomized placebo-controlled clinical trial. *J Am Acad Dermatol* 2009;60(4):706-8.
1. Al-Gurairi FT, Al-Waiz M, Sharquie KE. Oral zinc sulphate in the treatment of recalcitrant viral warts: randomized placebo-controlled trial. *Br J Dermatol* 2002;146:423-31.
15. Bagherani N, Yaghoobi R, Omidian M. Hypothesis: Zinc can be effective in treatment of vitiligo. *Indian J Dermatol* 2011;56(5):480-4.
16. Sadighha A. Oral zinc sulphate in recalcitrant multiple viral warts: a pilot study. *J Eur Acad Dermatol Venereol* 2009 ;23(6):715-6.