original article

Altered Levels Of Serum Cu And Cu/zn Ratio In Psoriasis.

Akansha Singh, Jyoti Aggarwal, Tousief Irshad Ahmed, Sanjeev Gupta.

Abstract:

Introduction: Psoriasis is a cutaneous disorder caused by unregulated proliferation of keratinocytes. The underlying etiology is complex with disturbances in the modulation of immunity and inflammation, especially in the epidermis playing a prominent role. Certain trace elements are essential to modulate immunity, regulate inflammation and maintain a healthy pro-oxidant-antioxidant balance and among them, copper and zinc play a prominent role.

Methods: Eighty patients of psoriasis along with 50 age and sex matched healthy controls were selected. Venous blood samples were analyzed for serum copper and Zinc and Cu/Zn ratio was calculated. A comparison of serum Cu, Zn and Cu/Zn ratio was made in terms of receiver operating characteristic (ROC) curve.

Results: Mean value of serum copper was found to be significantly high as compared to controls, which was not the case with zinc. Statistically significant difference was found in the mean levels of Cu/Zn ratio among patients and controls. Receiver operating characteristic (ROC) curve analysis revealed marginally higher AUROC for Cu (0.987) as compared to Cu/Zn ratio (0.949).

Conclusion: Copper levels were higher as compared to controls while zinc levels showed no significant differences. The increased copper levels may play an etiopathogenic role in triggering the development of psoriasis by diverse mechanisms. The suitability of the Cu/Zn ratio in diagnosing psoriasis could not supersede that of solitary copper measurements as evidenced by the ROC curve.

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Introduction

Psoriasis is a dermatological affliction which is characterised by disturbances in the proliferation of epidermal keratinaocytes. The disorder is primarily immune mediated with other factors, such as genetic predisposition, environmental triggers and vascular perturbances playing major etiological and prognostic roles[1]. Anti-oxidant defense of the body appears to be strained or grossly compromised in samples taken from blood and skin lesions showing heightened levels of free radicals, primarily reactive oxygen species (ROS), suggesting insufficient or overwhelmed anti-oxidant defense[2].Trace elements such as zinc and copper are essential structural components of the ubiquitous enzyme Superoxide Dismutase (SOD), an enzyme catalysing the dismutation of the superoxide radicals[3]. They are involved in enzymatic regulation of the processes of keratinisation, concomitant melanisation[4] and as modulator of inflammatory pathways especially the nuclear factor (NF-κB) pathway[5]. Thus, any disturbances in homeostasis of Copper and Zinc may adversely impact the above-mentioned mechanisms of anti-oxidant defence, immunity modulation, and inflammation as well as keratinocyte proliferation. This convergence of multiple pathological mechanisms may be the trigger for the development of psoriasis[6].

The Cu/Zn ratio has been studied extensively especially with reference to nutrition[7], immunity[8], all-cause mortality[9] and inflammation[10]. There are

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variant views as to the effect of diseases such as psoriasis on this ratio. Some studies suggest that measuring Cu/Zn ratio may be advantageous over measuring either of these metals individually[4,11].

The aims of the present study were to evaluate the serum zinc and copper levels in patients of psoriasis in comparison to controls. As studies elucidating the role of this ratio are scarce and have divergent conclusions, we conducted this study to find the possible association of altered Cu/Zn ratio with psoriasis.

Methods

Present study was carried out in the Departments of Biochemistry and Dermatology, in a tertiary care centre of North India after the approval of institutional ethical committee. This was a case control study consisting of 80 subjects of psoriasis attending dermatology OPD. Fifty age and sex matched healthy volunteers without any sign of skin disease were taken as controls. Subjects with autoimmune disorders, metabolic disorders, malignancy, on diuretics, penicillamine, multivitamin minerals supplement containing Zn or Cu, any medications known to affect Zn, Cu levels and lactating and pregnant women were excluded from the study. Venous blood samples were collected and analyzed for serum copper and Zinc by using colorimetric technique with Erba 5 plus semi auto analyzer. Serum Cu/Zn ratio was calculated.

Statistical Analysis

Results were presented as mean + standard deviation. The unpaired't' test was used to compare the levels of the test and control group. A comparison of serum Cu, Zn and Cu/Zn ratio was made in terms of Receiver Operating Characteristic (ROC) curve. Area under the ROC (AUROC) and their 95% confidence interval (CI) were evaluated as a measure of diagnostic accuracy. The area under the ROC curve is considered a global performance indicator for a prognostic factor[12]. All p-values <0.05 were considered significant. All analyses were performed using the SPSS version 20.0.

Results

In this case control study, 80 patients of psoriasis (age ranges: 19-75 years with mean age 41.94 + 13.45) including 59 males (73.8%) and 21 females (26.2%) and 50 controls (age ranges: 21-69 year with a mean age 40.96 + 12.39) including 29 males (58%) and 21 females (42%) were evaluated.

The mean levels of trace elements were studied in both patients and controls Table 1. Serum copper was found to be significantly higher in patients as compared to controls but results were non-significant for serum zinc Figure 1. Statistically significant difference was found in the levels of Cu/Zn ratio among patients and controls Figure 2.

Parameter		N	Mean	Std. Deviation	t-value	p-value
Cu	Control	50	122.594	14.067	15.906	.0001**
	Patients	80	174.513	20.208		
Zn	Control	50	97.875	15.537	.213	.832
	Patients	80	98.669	23.299		
Ratio Cu/ Zn	Control	50	1.268	0.145	8.513	.0001**
	Patients	80	1.863	0.480		

Table 1: Mean levels of copper, zinc and copper/zinc ratio in control and patients.

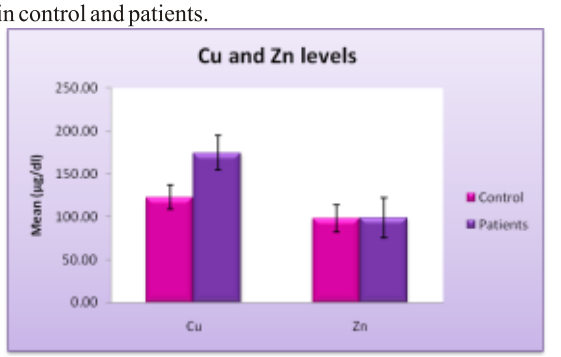

Figure 1: Mean levels of copper and zinc in control and patients.

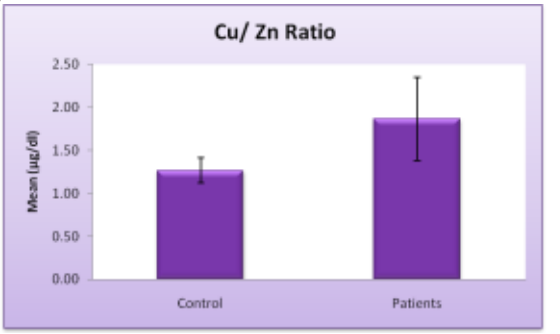

Figure 2: Mean levels of copper/zinc ratio in control and patients.

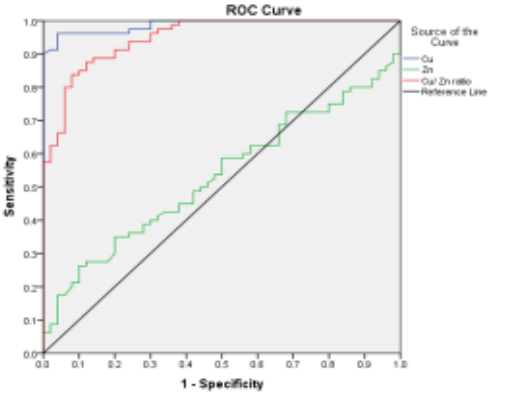

Figure 3: Receiver Operating Characteristic curve for Cu, Zinc and Cu/Zn in psoriasis patients. AUROC is

marginally higher for Cu (0.987) than for Cu/Zn (0.949).

The parameters were compared in terms of AUROC and it was found to be > 0.7, for both serum Cu and Cu/Zn ratio Figure 3, thus suggesting that these parameters can be used to evaluate the risk of psoriasis. Sensitivity and specificity of each parameter at a particular cut off point has been shown Table 2.

Area Under the Curve							
Variable(s)	Area	Std. Error	p-value	95% Confidence Interval		Sensitivity	Specificity
				Lower Bound	Upper Bound		
Cu	.987	.007	.0001**	.974	1.000	.963	.960
Zn	.531	.050	.551	.433	.630	.538	.520
Cu/ Zn ratio	.949	.017	.0001**	.914	.983	.875	.880

Table 2: Specificity and sensitivity of each parameter

DISCUSSION

Trace elements were measured in order to elucidate their possible roles in the pathogenesis of psoriasis. Zn and Cu are important cofactors and modulators of many clinical and biological functions in skin disorders, including psoriasis[13]. The protective role of Zn and modulatory role of Cu in combating oxidative stress is of prime importance, therefore alterations in their serum levels could be responsible for the changes in proxidant- antioxidant balance observed in psoriasis[14].

The altered levels of zinc and copper in psoriasis have been variously reported in different studies[15,16]. In studies conducted by Zackheim et al[17], Lipkin et al[18], Basavaraj et al[19], Abdel-Khalek et al[20] serum copper levels were found to be higher in psoriatic patients as compared to controls. This was corroborated by our findings as well. However, the measurement of plasma zinc in psoriasis resulted in conflicting data; both reduced and normal levels have been reported. Some studies conducted by Butnaru et al[21], Najat Sadeq Hasan et al[22] and Elhaddad et al[23] showed higher zinc levels in sufferers of psoriasis while some other studies, as those of Ala et al[24], Kreft et al[25] and Ozturk et al[26] observed insignificant results. Our study appears to be in accordance with the results of the latter studies as zinc levels showed no significant difference between the study group and control group.

Limited studies are available in regard to Cu/Zn ratio in psoriasis. So far, to best of our knowledge no study has been conducted in this region correlating Cu/Zn ratio with psoriasis. The present study observed significant increase in the levels of Cu/Zn ratio in patients as compared to healthy controls, comparable to the studies conducted by Shahidi Dadras et al[27], Sirajwala et al[28], and Wacewicz et al[29]. However, apart from comparing the parameters in terms of unpaired 't' test, this study has also compared the parameters in terms of AUROC curve, which revealed marginally higher AUROC for Cu alone (0.987) as compared to Cu/Zn ratio (0.949), thus belittling any diagnostic benefit of the latter vis-a-vis the former. This raised Cu/Zn ratio in our view is attributable mostly to raised copper rather than reduced zinc which played only a static role as the denominator in the ratio. The suitability of this ratio in diagnosing psoriasis could not supersede that of solitary copper measurements as evidenced by the AUROC curve.

The increased Copper levels observed in psoriatic patients in our study may etiologically explain the development of events triggering underlying psoriasis, particularly the compromise in free-radical defense, failure to modulate immunity and the resultant inflammation and haphazard keratinocyte proliferation.

Our study was limited to a small number of patients and further studies utilising larger sample sizes are needed on a large numbers of patients to understand the role of altered copper levels in the pathogenesis of psoriasis.

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Conflict of interests: None.

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