Role of Serum Copper and Zinc in Pathogenesis of Psoriasis

[1.]Dr.Margit Gajjar, [2]. Dr.H.B.Sirajwala, [3].Dr.Dipti Gajjar,[4] .Dr.Ipsa Pandya

1(Tutor,Department of Biochemistry , Medical College Baroda,Gujarat, India)
2. (Associate Proffesor,Department of Biochemistry , Medical College Baroda,Gujarat, India)
3. (Tutor,Department of Biochemistry ,GMERS Medical College Gotri,Gujarat, India)
4 (Third year resident,Department of Skin and VD , Medical College Baroda,Gujarat, India)

I.   Introduction:

Psoriasis is a hyper proliferative cutaneous disease of multifactorial etiologies: genetic background, environmental factors, vascular and immune system disturbances [1.]Typical psoriatic lesions are erythomatous papules which form plaques characterized by sharp borders and increased scaling.

II.   Oxidative Stress, Trace Metals And Psoriasis

Oxidative stress has been implicated in the etiopathology of psoriasis. Significant abnormalities of antioxidant mechanisms have been demonstrated in the blood and plaques of psoriatic patients [2]. An insufficient antioxidant system, together with increased levels of reactive oxygen species (ROS) has been suggested to be important in the pathogenesis of this disease.Oxidative stress can result from deficiency of trace elements such as zinc, copper and selenium.The process of keratinization and melanin formation is enzyme-dependent and therefore influenced by Copper and Zinc deficiencies or excesses as trace elements are involved in enzymatic activities and immunologic reactions.

There is no comprehensive study on the levels of trace elements, oxidants and antioxidants defense mechanism and their inter-element relationships in psoriasis. In the present study, Serum Copper and Serum Zinc of Psoriasis patients were analyzed and Serum Copper and Zinc (Cu/Zn) ratio was calculated.

III.   Role Of Copper And Zinc In Psoriasis

Copper is associated with a number of mettaloproteins. Copper containing mettaloenzyme superoxide dismutase protects against random free radical damage.Both intracellular and extracellular SODs are copper and zinc containing enzymes, convert **super oxide radical** to **peroxide**, which can be removed subsequently by **Catalase** and other antioxidant defenses. The plasma protein ceruloplasmin bind to copper ions and prevents oxidative damage from free copper ions, which generate hydroxyl radicals [3].

Zn is second to iron as the most abundant trace element in the body. More than 300 metal enzyme occurs in all six categories of enzyme systems. In some enzymes, such as Cu and Zn superoxide dismutase, structural stability is ensured by zinc protein binding and catalytic activity of the enzyme by the active copper site. Sign and symptom of the zinc deficiency include growth retardation with stunting; increased incident of infection, possibly related to alteration in immune function; diarrhea; reproductive teratogenesis; skin lesions; alopecia; eyesight defect and other adverse clinical outcomes [3].

One the most common trace metal imbalances are elevated copper and depressed zinc. The ratio of copper to zinc is clinically more important than the concentration of the either of these trace metals. More than the concentration of Zn or Cu in the blood serum, it is more important the balance between them. The optimal plasma or serum ratio between these two elements is 0.70-1.00.

IV.   Aims And Objective

To study the role of serum COPPER (Cu) and ZINC (Zn) in pathogenesis of Psoriasis and as marker of severity of Psoriasis. To estimate serum COPPER and Serum ZINC level in Psoriasis patients and in Control groups. To correlate the values of serum COPPER and ZINC with the severity of Psoriasis.

V.   Material And Method

Present study was carried out, at Clinical Chemistry Laboratory in S.S.G. Hospital and Medical College, Vadodara, to measure the level of Serum Copper, Serum Zinc and Serum Copper/Zinc ratio in patient with Mild and Severe Psoriasis. This case control study consisted of 100 subjects; 50 were patients with Psoriasis attending Skin & V.D. Department, S.S.G. Hospital and Medical College, Vadodara and 50 age and sex matched healthy controls were evaluated. They are divided in two groups depend upon Psoriasis Area and Severity Index score (PASI SCORE)

Group I (n=20) consist of patients with PASI SCORE <10(13 males and 7 females) and **Group II (n=30)** consist of patients with PASI SCORE >10(20 males and 10 females) and the rest 50 were controls **(Group III).** Patients and controls with diabetes mellitus, thyroid disease, autoimmune disorder or concomitant dermatological diseases, or had taken systemic or topical treatment within three months before the present study, or receiving any medication that could change serum levels of trace elements such as diuretics, psychologic drugs, anti-arrhythmic medications or supplements were excluded. All patients provided written informed consent.
.

PSORIASIS AREA AND SEVERITY INDEX (**PASI**) is the most widely used tool for the measurement of severity of psoriasis. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). PASI less than 10 considered as mild Psoriasis and PASI greater than 10 considered as moderate to severe Psoriasis.

Sample

All blood specimens were taken after 8-10 hours fast in the morning between 9- 12 hours in the collection Centre OPD, S.S.G. Hospital Vadodara. The blood from forearm vein was collected in a plain tube and allowed to clot at room temperature for 30 minutes and centrifuged for 10 minutes at 3500rpm. All the precautions were taken in accordance with the Clinical and Laboratory Standards Institute criteria [4] to eliminate metal contamination while collecting and storing the samplesand samples with signs of hemolysis were discarded
At the same time, the psoriasis area and severity index (PASI) scores of psoriatic patients were determined by a Dermatologist.
The serum was divided into proper aliquots and frozen at -20Ċ until used for measuring of Zn and Cu. Serum Zn and Cu concentrations were estimated in fully Automated Biochemistry Analyzer (Miura 300) at 578 nm. Standard Calibration graph was prepared using working Copper Standard concentrations 200 μg/dl,175 μg/dl, 150 μg/dl, 125 μg/dl, 100 μg/dl, 75 μg/dl, 50 μg/dl, 25 μg/dl results were calculated accordingly. Standards (prepared in deionized water) were run in the range of 25–200μg/dl for Cu and Zn.
This study is approved by Institutional Ethics Committee for Human Research (IECHR), Medical College and SSG Hospital Baroda,Gujarat, India
EC Reg.no.: ECR/85/Inst/GJ/2013

VI. Statistical Analysis
All data were given as mean ± standard deviation (SD). Statistical version-6 for windows was used for statistical analysis. Levels of Zn, Cu in sera of patients and control subjects were compared by paired student's *t*-test. The differences were considered to be significant when the *p* value was less than 0.05

VII. Result And Analysis
This case control study consisted of 100 subjects; 50 were patients with Psoriasis (age ranges: 25-60 years with mean age 42.22±12.0) including 33 males (66%) and 17 females (34%) and 50 controls (age ranges: 25-50 year with a mean age 32.5 ±8.3) including 32 males (64%) and 18 females (36%) were evaluated. (Table 1)

Table 2 show the mean values of trace elements (Zn and Cu), in both patients and controls.
Mean value of Serum Copper in Severe Psoriasis is significantly high (121.29 ± 42.75 μg/dl) compared to Controls (99.9 ± 23.1 μg/dl), which was significant (p<0.005).Mean value of Serum Zinc in Severe Psoriasis is significantly low (66.38 ± 24.33 μg/dl) compared to Controls (82.4 ± 15.9 μg/dl), which was significant (p<0.005).

Comparison of the values according to the type of psoriasis (Mild and Severe); we found no significant differences for all values studied

Table 1: Demographic Profile of Study Groups

	MALE	FEMALE	TOTAL	AGE(MEAN±SD)
GROUP :1 (PASI<10)	13	7	20	45.8±10.9
GROUP:2 (PASI>10)	20	10	30	41.5±12
GROUP:3 (CONTROL)	32	18	50	32.5±8.3

Table 2: Comparisons of Serum Copper, Serum Zinc

This table shows that Serum Copper is significantly high in Severe Psoriasis patients(Group II) and Serum Zinc is Significantly low in Severe Psoriasis(Group II)
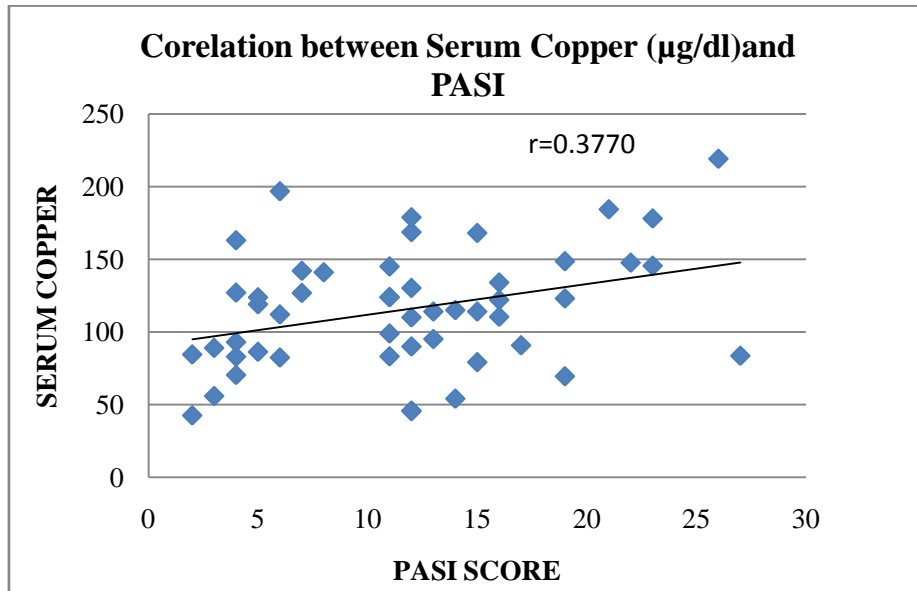
	GROUP : I (PASI SCORE<10) (mean±sd)	GROUP: II (PASI SCORE>10) (mean±sd)	GROUP : III (CONTROL) (mean±sd)	P VALUE of group I and II	P VALUE of group II and III	P VALUE of group III and I
S.COPPER (RANGE) 45-185 µg/dl	106.96±36.86	121.29±42.75	99.9±23.1	P=0.2265	P<0.05 (0.0049)	P=0.2773
S.ZINC µg/dl (35-110 µg/dl)	77.44±30.39	66.38±24.33	82.4±15.9	P=0.1607	P<0.05 (0.0006)	P=0.3747

**Comparison of Serum Copper and Serum Zinc in all three groups.**
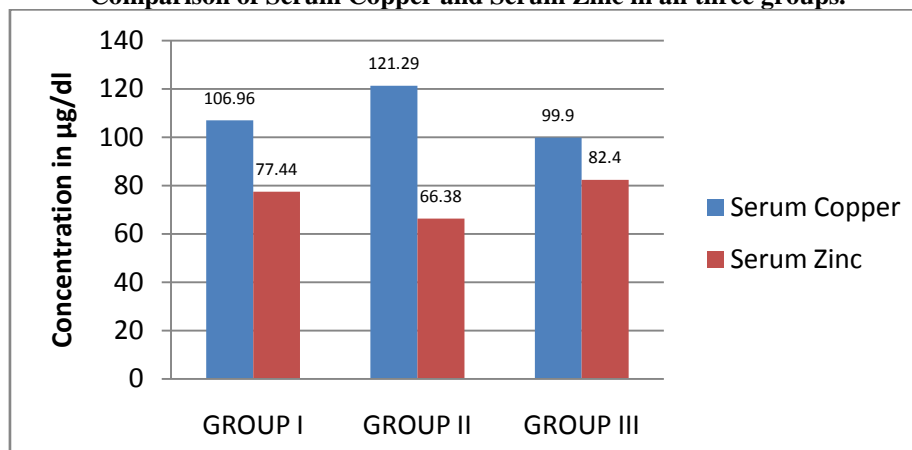
This graph shows that Serum Copper is significantly high in patients with severe Psoriasis (group II) than in control (group III),Serum Zn is significantly low in patients with severe Psoriasis (group II) than in control (group III)

Correlation between Serum Copper (µg/dl)and PASI

Corelation between Serum Copper (µg/dl)and PASI

N=30,r=0.3770 p=0.05
Weak positive correlation.

Correlation between Serum Zinc and PASI SCORE

COREELATION BETWEEN SERUM ZINC AND PASI SCORE
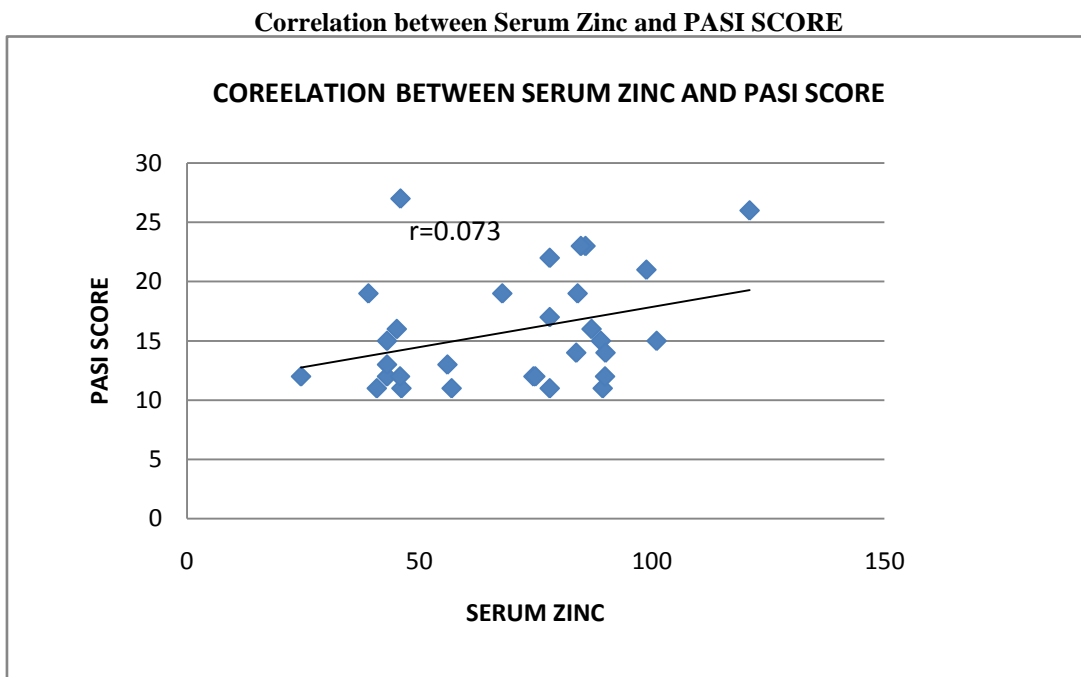
n=30 no correlation (r=0.073)

VIII.   Discussion:

The unique process of keratinization and melanin formation is enzyme-dependent and therefore could be influenced by trace element deficiencies or excesses as trace elements are involved in enzymatic activities and immunologic reactions[5].

Trace elements were measured in order to illuminate the possible role in the pathogenesis of psoriasis.

This study was conducted on 50 patients with psoriasis of different severity and 50 healthy volunteer. On measurement of serum trace elements it was found many abnormalities in dermis compared to healthy dermis [6].

There are contradictory reports regarding serum levels of trace elements in psoriasis. When serum levels of trace elements and Cu/Zn were compared against the PASI score and duration of the disease, the serum level of Cu/Zn ratio showed a statistically significant correlation with the PASI score. McMillan et al, reported that psoriatic patients with more extensive skin involvement had lower Zn levels than those with minimal involvement [7].

Our results indicated that there was no statically significant difference between serum levels of Zn in psoriasis patients with mild and severe disease, while the Cu/Zn ratio was significantly higher in patients.Some investigators have reported increased Zn concentrations in psoriasis scales, serum, urine and uninvolved skin of psoriasis patients [8]. This explained by that zinc used in rapid turnover of the skin and loss of zinc through exfoliation. And zinc deficiency may be the original cause of psoriasis. Some studies noted that psoriatic lesions retain a high content of zinc compared with the uninvolved skin, suggesting an imbalance in zinc distribution between serum and psoriatic lesions [11]. In fact zinc is a co-factor for DNA- and RNA polymerases required for protein synthesis in involved skin. Lowered level of serum protein or albumin which results from peeling off of a large quantity of scales from the body surface, may be also attributable to decreasing zinc level.

Basavaraj et al, found decreased Zn concentrations in both mild and severe psoriasis patients consistent with some studies[1-2] and increased Cu concentrations in both mild and severe psoriasis groups[9] While **Bhatnagar et al**, in their study on active and remissive phases of psoriasis, reported an increase in serum Zn and reduced Cu levels [11].

These inconsistent results may arise from different study designs. Our study was limited to a small number of the patients and many studies are needed on a larger numbers of patients to prove the role of trace elements in the pathogenesis of psoriasis

IX.   Conclusion

The finding of present study indicates that patients with severe psoriasis have higher mean Serum Copper, lower mean Serum Zinc and higher mean Serum Copper/Zinc ratio than with mild psoriasis and controls. Serum Copper/Zinc ratio correlate with Psoriasis Area Severity Index (PASI) and can be used as marker for assessing severity of disease. Serum Copper/Zinc ratio is the better marker for assessing severity of the psoriasis than Serum Copper and Zinc alone. Correction of trace elements imbalance may help in treatment and outcome of Psoriasis

Reference

[1].   Nagat Sobhy Mohamad: Trace elements homeostatic imbalance in mild and severe psoriasis: a new insight in biomarker diagnostic value for psoriasis. Our Dermatol Online. 2013; 4(4): 449-452

[2].   Estabraq ARK Alwasiti, Wasan T Al-Rubayee, Tammimy:Serum Copper, Zinc and Oxidative Stress in Patients with Psoriasis, Al-Nahrain College of Medicine ISSN 1681-6579, IRAQI J MED SCI, 2011; VOL.9 (2).

[3].   Carl A Burtis, Edward Ashwood, David E Burns: Teitz Textbook of Clinical Chemistry and Molecular diagnostics;Fifth edition, Chapter 31:Vitamin and trace elements;948-964.

[4].   National committee for Clinical Laboratory Standards Approved guidelines: Control of pre-analytical variation in trace element determination 1997; 17:1-30.

[5].   Siva ME, Subramanian KN: Kinetic models of trace element and mineral metabolism during development. CRC, 1995, Boca Raton, pp 159–70.

[6].   Nacim B, Ayvaz A, Hasan D: Trace metals in treatment of psoriasis. J Islamic AcadScienc.   1989;2:226-9

[7].   McMillan EM, Rowe D. Plasma zinc in psoriasis: relation to surface area involvement. Br J Dermatol 1983; 108: 301-5.

[8].   Voorhees JJ, Chakrabarti SG, Botero F, et al. Zinc therapyand distribution in psoriasis. Arch Dermatol 1969; 100:669-73.

[9].   Basavaraj KH, Darshan MS, Shanmugavelu P, et al.Study on the levels of trace elements in mild and severe psoriasis. ClinChimActa 2009; 405: 66-70.

[10].   Mohammad Shahidi-Dadras, MD,NastaranNamazi, MD,SaraKhalilazar,

[11].   MD,ShimaYounespour:Trace elements status in psoriasis and their relationship with the severity of the disease. Iran J Dermatol 2012; 15: 38-41.

[12].   Bhatnagar M, Bapna A, Khare A. Serum proteins, tracemetals and phosphatases in psoriasis. Indian J DermatolVenereolLeprol 1994; 60: 18.