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# Estimation of Serum Trace Elements Levels in Libyan Patients with Psoriasis Vulgaris: A Case Control Study

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**Abstract:** Background: Psoriasis is a chronic autoimmune skin disease with a worldwide prevalence of 2–3%. Psoriasis is caused by a complex interplay among the immune system, genetic background, auto-antigens, and environmental factors. Trace elements are required for the normal functioning of many enzymes and play a significant role in the development of many diseases. Objective: To assess the serum levels of zinc, copper, magnesium, iron and folate in patients with psoriasis compared to healthy controls. Patients and Methods: A total of 41 patients with psoriasis vulgaris were compared with 50 age and sex matched healthy subjects. Serum levels of zinc (Zn), copper (Cu), magnesium (Mg), iron (Fe) and folate were measured in both groups and compared. Psoriasis Area and Severity Index (PASI) were used to measure the severity of the disease. Results: The mean serum level of Zn was 142.2±52 in patients compared to 90.2±18.9 in the controls (P=.000), serum level of Cu was 161.1±58.5 in patients versus 156.3±42.8 in control group (P=.650). Serum Mg was 2.4±0.5 in patients and 1.9±0.2 in control subjects (P=.000). Serum Fe was 90.8±50 in patients as compared to 116.9±32.4 in control subjects (P=.004), whereas, serum folate was 6.6±3.9 in patients and 9.5±5.3 in control subjects (P=.005). There was no significant direct correlation between levels of trace elements under study and PASI scoring. Conclusions: Trace elements particularly Zn, Cu, and Mg appear to be elevated in psoriasis patients, while Fe and folate were low in psoriatic patients, however, they can't serve as biomarkers for disease activity.

**Keywords:** Psoriasis Vulgaris, Trace Elements, PASI

## 1. Introduction

Psoriasis is a common, chronic inflammatory skin disease, which affects approximately 2–3% of the world population [1]. It is characterized by well demarcated erythematous scaly papules and plaques [1, 2]. The pathogenesis of psoriasis is still poorly understood. It results from the interactions between genetic predisposition and a large spectrum of environmental risk factors [3]. Furthermore, psoriasis is an immune-mediated disease characterized by the production of reactive oxygen species due to the overexpression of pro-inflammatory cytokines [4].

Trace elements are essential to biochemical processes in the body and are involved in immunological and inflammatory reactions. The keratinization and melanin formation are enzyme-dependent processes and could be influenced by imbalance between trace elements [4]. Previous studies have shown different interplay between essential trace elements and nonessential toxic elements resulting in the production of reactive oxygen species; like superoxide ion, hydrogen peroxide, and hydroxyl radical [3]. Trace elements metabolism has already been extensively studied in various medical fields [5]. The present study aimed to assess the serum levels zinc, copper, magnesium, iron and folate in patients with psoriasis vulgaris compared to healthy controls, and their role as a biomarker of psoriasis severity.

# 2. Methods

### *2.1. Patients and Control Subjects*

A case-control study was carried out in El-Jumhoria teaching Hospital in Benghazi, Libya, enrolling 41 psoriasis patients, 20 males and 21 females, attending the dermatology clinic of the hospital, and 50 age and sex matched healthy subjects with no history of chronic, inflammatory or autoimmune skin or systemic diseases were included as control group. Inclusion criteria were diagnosis of psoriasis vulgaris according to a reliable history findings and physical examination. Patients with concomitant chronic, inflammatory and autoimmune diseases were excluded from the study. Patients with severe psoriasis and those under any type of treatment were also excluded. Disease severity was determined according to the Psoriasis Area and Severity Index (PASI), patients with PASI <3 were mild, PASI=3.1-10 moderate and PASI >10 were severe.

### *2.2. Blood Collection for Analysis of Trace Element*

Blood samples were drawn from each patients and control subjects for measurement of serum levels of zinc (Zn), copper (Cu), magnesium (Mg), iron (Fe) and folate.

Informed consent has been obtained from each patient and control subject and manuscript is according to declaration of Helsinki.

### *2.3. Statistical Analysis*

All statistical analyses were performed using SPSS software for Windows (Version 16.0). Results are presented as mean±standard deviations for continuous variables and as a number (%) for categorical variables. The Chi-square test and independent t-test were used for statistical analysis. Differences were considered as statistically significant with P values < 0.05.

# 3. Results

A total of 41patients with psoriasis vulgaris were enrolled in this study and compared with 50 age and sex matched healthy control subjects. Table 1. Show the demographic data of patients and control subjects. None of the patients had severe psoriasis, and no significance difference between male and female patients regarding PASI score.

Serum Zn and serum Mg were significantly higher in patients compare to control subjects, whereas, serum Fe and serum folate were significantly lower in patients than control subjects. However, serum Cu was higher in patients as compare to control subjects but this difference was statistically insignificant (Table 2).

Serum Zn was significantly lower in patients with moderate PASI, however, no significant correlation was found between PASI score and serum levels of other trace elements (Table 3). Also, there was no association between duration of disease and serum levels of trace elements under study. Serum Fe was significantly lower in female patients as compare to male patients, however, no statistically significant difference was seen in serum levels of other trace elements between female and male psoriasis patients (Table 4).

***Table 1.*** *Demographic characteristics of patients and controls.*

| Demographic data | Patients | Control subjects | P value |
|---|---|---|---|
| Number | 41 | 50 | |
| Age (mean±SD yrs.) | 32.5±9 yrs. | 31.8±9 yrs. | .699 |
| Sex<br>Male (%) | 20 (48.8%) | 23 (46%) | .479 |
| Female (%) | 21 (51.2%) | 27 (54%) | |
| PASI<br>Mild PASI<3 | 13 (32%) | NA | NA |
| Moderate PASI=3.1-10 | 28 (68%) | | |

***Table 2.*** *Serum levels of trace elements in patients and control.*

| Mean±SD | Psoriasis patients | Control subjects | P value |
|---|---|---|---|
| Zinc (µg/dl) | 142.2±52.2 | 90.2±18.9 | .000* |
| Copper (µg/dl) | 161.1±58.5 | 156.3±42.8 | .650 |
| Magnesium (mg/dl) | 2.4±.5 | 1.9±.2 | .000* |
| Iron (µg/dl) | 90.8±50 | 116.9±32.4 | .004* |
| Folate (ng/ml) | 6.6±3.9 | 9.5±5.3 | .005* |

***Table 3.*** *Serum levels of trace elements in psoriasis patients according to their PASI scoring.*

| Mean±SD | PASI score Mild | PASI score Moderate | P value |
|---|---|---|---|
| Zinc (µg/dl) | 171±49 | 124±46 | .004* |
| Copper (µg/dl) | 163.4±63 | 159.7±57 | .849 |
| Magnesium (mg/dl) | 2.5±.5 | 2.4±.5 | .443 |
| Iron (µg/dl) | 82±40 | 97±56 | .363 |
| Folate (ng/ml) | 6.2±4.3 | 6.9±3.8 | .616 |

***Table 4.*** *Serum levels of trace elements in psoriasis patients according to their gender.*

| Trace elements | Female | Male | P value |
|---|---|---|---|
| Zinc (µg/dl) | 130±56 | 155±47 | .129 |
| Copper (µg/dl) | 160±71 | 162±42 | .907 |
| Magnesium (mg/dl) | 2.5±.6 | 2.4±.5 | .362 |
| Iron (µg/dl) | 65±33 | 118.4±51 | .000* |
| Folate (ng/ml) | 6±3 | 7.5±5 | .187 |

# 4. Discussion

Psoriasis is a chronic autoimmune inflammatory skin disease. It is characterized by well-demarcated, scaly plaques mainly on extensor surfaces of the body. These lesions highlight the fundamental processes underlying its pathogenesis which are an increase proliferation of keratinocytes, shortened cell cycle, prolonged desquamation process and inflammation [1]. It results from the interactions between genetic predisposition and a large spectrum of environmental risk factors [2]. Despite multiple previous studies on the pathogenesis of psoriasis, there is controversial evidence regarding the role of epidermal barrier disturbances and oxidative stress in the pathophysiology of psoriasis [6].

Oxidative stress is defined as the imbalance between the formation of oxidants, i.e. free radicals, reactive oxygen species (ROS) and reactive nitrogen species, and the anti-oxidant defense systems such as the enzymes superoxide

dismutase, catalase, and glutathione peroxidase [6]. Trace elements like selenium, zinc and copper are involved in the destruction of free radicals through cascading enzyme systems [2-4]. Zn and Cu are an integral part of many metalloenzymes, including superoxide dismutase [2]. Trace elements are essential to biochemical processes in the body and are involved in immunological and inflammatory reactions. Moreover, the keratinization is an enzyme-dependent processes and could be influenced by the deficiencies and excesses of trace elements [6]. Recent studies on the role of trace elements in the etiopathogenesis and treatment of psoriasis have shown controversial findings and are still limited [2].

The serum level of zinc was significantly higher in patients under study, however serum zinc was significantly higher in patients with mild psoriasis. These results are consistent with previous study [5]. In study of Elhaddad et al, the serum zinc level was a statistically highly significant increase in all psoriatic patients (mild, moderate and severe) as compared to healthy controls [7]. However, previous studies showing decreased levels of serum zinc in patients with severe psoriasis [3, 8]. While study of Wacewicz et al. found no statistically significant difference in the serum zinc levels among psoriatic and the normal population [4]. This difference in serum zinc between our study and others may be because none of our patients had severe psoriasis.

Serum copper level was statistically insignificantly raised among the patients as compare to control subjects with no correlation between Cu levels and psoriasis severity was detected in our study, these results are consistent with previous studies [9, 10]. However, Basavaraj et al. and Elhaddad et al, found a significant increase in the serum Cu level of both mild and severe psoriasis patients [3, 7]. Moreover, Ala et al reported a significantly higher serum Cu in psoriatic patients than in healthy volunteers and they suggested copper-chelating agents, such as penicillamine as treatment option for those patients [11]. Serum copper is an important trace metal, largely reflects serum ceruloplasmin which levels are known to increase under physical stress, inflammation, or disease. It is not known whether psoriasis accelerates the release of ceruloplasmin into the blood or whether the synthesizing capacity is enhanced, or both. In spite of many efforts, no definite mechanism has been established which accounts for this increasing level of serum Cu in psoriasis patients [7]. Furthermore, high concentrations of Cu may cause increased oxidative damage to lipids, proteins and DNA, which may contribute to inflammatory skin disorders [12].

The magnesium serum levels in psoriatic patients under study showed a significant increase in comparison to that in healthy controls with no significant correlation between magnesium levels and PASI scoring in psoriatic patients. Basavaraj et al, reported that serum Mg mean value was significantly higher in Psoriasis patients as than in control [3]. However, other study reported a reduction in serum magnesium mean value as compared to control [13].

For the serum Fe and folate levels both were significantly lower in our patients, in agreement with previous studies that reported low serum Fe among their psoriasis patients [3, 14]. Moreover, Shahidi-Dadras et al and Elhaddad et al, reported a significant decrease in the Fe concentration in psoriatic patients regardless of its severity [7, 9]. Iron deficiency was found to be a metabolic consequence of many skin diseases such as psoriasis [15]. Accelerated loss of nutrients from the hyperproliferation and desquamation of the epidermal layer of skin in psoriasis and increased utilization and consumption of Fe and folate by the proliferating cells leading to low serum Fe and folate in psoriasis [14]. Moreover, psoriasis is associated with deranged iron status characterized by depleted iron stores with concomitant unmet cellular iron requirements [14].

Many studies have demonstrated that plasma levels of folic acid are lower in psoriatic patients than in controls [16, 17]. Decreased serum folate in psoriasis may associated with inflammatory changes in intestinal mucosa, which causes reduced absorption of dietary folate [18]. Moreover, folic acid is required for re-methylation reaction of homocysteine to form methionine, studies have demonstrated that serum homocysteine level inversely correlate with serum folic acid levels in psoriatic patients [17, 18]. Furthermore, patients with psoriasis have a tendency to hyperhomocysteinaemia, which may predisposing them to higher cardiovascular risk and comorbidities [17-19].

## 5. Conclusions and Recommendations

Although the importance of measurement of trace elements in psoriasis is evident from our results, the levels of these trace elements did not prove to be useful in assessing severity of psoriasis. Moreover, whether these serum levels of trace elements are the cause or the result of the disease process needs further studies for interpretation. Future studies must assess larger population with the aim of measuring these elements not only in serum but also in the tissue.

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