

ORIGINAL ARTICLE

Evaluation of the Serum Zinc Level in Adult Egyptian Patients with Melasma

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ABSTRACT

Background: Melasma is a pigmentary disorder. Zinc has anti oxidative and anti-inflammatory properties. Zinc also stops more activity of melanocytes and guard skin from ultraviolet rays. These mechanisms make zinc has a role in prevention of melasma. The aim was to assess the serum zinc level in adult Egyptian patients with melasma, and to correlate duration and severity of melasma with its level.

Methods: A Case- control study involved a total of 72 melasma patients and 72 healthy controls and carried in the outpatient clinic of Dermatology, Venereology & Andrology Department, Faculty of Medicine, Zagazig University Hospitals from February to august 2018. Melasma severity was assess by modified area and severity index (mMASI). Calorimetric method was used for measurement of the levels of serum zinc in each group. The statistical analysis was performed with SPSS software.

Results: The results revealed a significant decrease in levels of the serum zinc in all cases and a high important negative correlation between serum zinc level and both mMASI and duration of melasma in the studied cases.

Conclusions: Comparing melasma patients with age and sex matched control regarding serum zinc level there is a decrease in the level of the serum zinc in all cases. A negative correlation present between serum zinc level and melasma severity and its duration in all cases.

Keywords: Melasma; Zinc; Females; Egyptian; Severe



INTRODUCTION

Melasma is a localized hyperpigmentation of the sun bared areas of the skin characterized by brown macules and patches with geographic or ragged edges. it can commonly affect face on cheek, forehead, nose, upper lip or chin. It less commonly affects extra facial location such as the neck, arms and chest. Although melasma can affect all races and both sexes, it is more commonly seen in women of child-bearing period and in dark-skinned individuals living in areas with intense ultraviolet (UV) radiation [1]. The incidence of melasma range from 1.5% and 33.3%. Its incidence in pregnancy is about 50-70% [2]. Melasma often represents a mixture of three patterns: centrofacial, malar and mandibular patterns, according to clinical appearance [3]. The exact cause of melasma still unclear but many causes have been concerned in the pathophysiology of melasma as familial inheritance, sun exposure, female sex hormones, pregnancy, hormonal activity, oral contraceptives, thyroid dysfunction, antiepileptic drugs, and cosmetic products [4].

Zinc (Zn) is an essential trace mineral that is present in almost all body cells and it comes after iron which is a co-factor for most enzyme classes. It is important for the cell growth, development, and differentiation. zinc also is an intracellular regulator that regulates the expression and activation of biological molecules such as transcription factors, enzymes, adapters, channels, and growth factors, along with their receptors [5]. Zinc has anti oxidative and anti-inflammatory characteristics, which may help in skin rejuvenation. It can also prevent solar degeneration, and extra activity of melanocytes. These mechanisms make zinc has a role in prevention of melasma [6]. Zinc deficiency is a global problem affecting health of the developed and developing countries. Zinc deficiency was rated to be 17.3% and ranges from 11%-80% [7]. Zinc Deficiency causes many dermatological diseases including acne vulgaris [8] psoriasis [9], vitiligo [10], warts [11], alopecia areata [12]. Serum zinc level was estimated in many cutaneous disorders [13]. This is the first study in which the relation of serum zinc levels with melasma is

investigated in Egyptian patients. Deficiency of zinc participates in the pathogenesis of melasma so we expect better results with oral zinc supplements in these patients.

METHODS

A case control study was performed at the outpatient clinic of Dermatology, Venereology and Andrology Department, Faculty of Medicine, Hospitals of Zagazig University, after the approval of the Institutional Review Board (IRB) during the period from February 2018 till august 2018. IRB approval number is (4497). A written acceptance was taken from all cases before involvement in the study. Seventy-two female patients aged from (24-53y) matching the inclusion criteria were involved in the study as group1 (patients' group). Seventy-two apparently healthy females aged from (21-59y) were involved in the study as group2 (control group). The practical part of this study was completed in Clinical Pathology Department. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion Criteria was adult Egyptian patients with melasma. With exclusion of females taking zinc one month before diagnosis of melasma, Patients complain of persistent diarrhea, hepatic insufficiency, renal insufficiency, heart failure. History of considerable drug or alcohol misuse, History of malabsorption disorders, Pregnancy, active malignancy. Patients treated with immunosuppressive drugs. Patients with other pigmentation disorders, Patients using a topical or inhaled corticosteroid or systemic steroids within 1 month before the study, Patients using any treatment with isotretinoin, topical hydroquinone, or drugs that can cause hyperpigmentation within one month before the study.

Data Collection and Clinical Examination

A questionnaire was fulfilled for all cases, which included information about demographic class, familial background of melasma, medical and drug intake, presence of melasma, and. Full dermatological assessment for melasma and other skin problems. The clinical diagnosis of the cases was made through the inspection of the affected area (light to gray brown macules and patches in the sun-exposed areas of the skin), and wood's lamp examination. The assessment of the size and severity of melasma was made by modified melasma area and severity index (mMASI). The mMASI score is calculated by subjective assessment of 2 factors: area (A) of involvement and darkness (D), with the forehead (F), right malar region (RM), left malar region (LM), and chin (C) corresponding to 30%, 30%, 30%, and 10% of the

total face, respectively. Area and darkness are scored as follows: area of involvement: 0 = absent, 1 = 10%, 2 = 10%-29%, 3 = 30%-49%, 4 = 50%-69%, 5 = 70%-89%, and 6 = 90%-100%; darkness: 0 = absent, 1 = slight, 2 = mild, 3 = marked, and 4 = severe.

$mMASI = .3A(f)D(f) + .3A(lm)D(lm) + .3A(rm)D(rm) + .1A(c)D(c)$. The total score range is 0 to 24 [14].

Measurement of serum zinc level
After obtaining consent. Using plastic syringes free of zinc, 5 milliliters of venous blood were taken from antecubital vein in complete aseptic conditions. Blood was allowed to clot. Supernatant serums will be centrifuged for ten minutes at 1700g and stored at -4°C until time of analysis. We use calimetric method to asses zinc levels in the serum of patients [15]. Normally in adults' serum zinc level was received as 70-140 $\mu\text{g/dL}$. Zinc considered to be deficient if a serum zinc level lower than 70.

STATISTICAL ANALYSIS

Statistical Package of Social Services version 21 (SPSS Inc., Chicago, IL, USA) was used to analyses the collected data. Data were represented in tables. The results were considered statistically significant when the significant probability was less than 0.05 ($P < 0.05$). P -value < 0.001 was considered highly statistically significant (HS), and P -value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The mean age of the cases was 37.24 ± 6.25 years, and the mean age of the controls was 33.92 ± 7.88 years. There were no significant differences in age or sex as shown in table (1).

Based on the wood's light examination, cases were also classified as Epidermal melasma ($n=38$, 52.8%), Mixed melasma ($n=16$, 22.2%), Dermal melasma ($n=18$, 25%) as shown in table (2).

Half of the studied cases (59.7%) have no family history. About $\frac{3}{4}$ of the studied melasma cases were not exposed to sun, taking hormonal contraceptive pills (CCPS) and no relation to past pregnancy. All of them have no other diseases and don't take any drugs (table 3).

The two studied groups show a highly statistically significant difference regarding zinc level. There is a significant decrease in serum zinc level in cases with melasma (mean 83.47 ± 22.28 SD) when compared with control (mean 92.63 ± 13.63 SD) as shown in table (4).

There is a high significant negative relationship between serum zinc level and mMASI ($r = -0.791$, p -value $< 0.001^*$) and between serum zinc level and duration of melasma as shown in table (5).

Table (1): Demographic data of the studied cases and control group (N=144).

Demographic data	Melasma patients (N=72)		Healthy control(N=72)		P- value
	No.	%	No.	%	
Age (years)					
Mean ± SD	37.24±6.25		33.92± 7.88		0.628 (NS)
Median (Range)	36 (24-53)		10 (21-59)		

* Mann Whitney U test.
P < 0.05 is significant.

Chi-square test.
NS: Not significant.

Table (2): Melasma type among of the studied patients (N=72).

Melasma type	Studied patients (N=72)	
	No.	%
Epidermal melasma	38	52.8
Mixed melasma	16	22.2
Dermal melasma	18	25.0

Table (3): History among the studied Melasma patients (N=72).

Item	Studied Melasma (N=72)	
	No.	%
Sun exposure		
• No	53	73.6
• Yes	19	26.4
Family History		
• Negative	43	59.7
• Positive	29	40.3
History of hormonal CCPs		
• Absent	15	20.8
• Present	57	79.2
Relation to past pregnancy		
• Negative	57	79.2
• Positive	15	20.8
No drugs	72	100.0
No diseases	72	100.0

Table (4): Serum zinc level in the studied cases and control group (N=144).

Serum zinc level	Melasma patients (N=72)	Healthy control(N=72)	Test	P-value
Mean ± SD	83.47± 22.28	92.63 ± 13.63	1581	<0.001* (HS)
Median (Range)	72.29(55-144.58)	91.56(68.9-130)		

Mann- Whitney test
P < 0.05 is significant.

Table (5): Correlation between Serum zinc level and Modified Melasma area severity index (mMASI) and duration among the studied Melasma cases.

Item	Serum Zinc level	
	Correlation coefficient (r)	p- value
Modified Melasma area severity index (mMASI)	-0.791	<0.001* (HS)
Duration of melasma (years)	-0.257	0.030* (S)

Correlation is significant at the 0.05 level

DISCUSSION

Melasma is a symmetrical acquired hyperpigmented macules and patches appear on the sun-exposed areas of the skin of the face. It is widespread among women in their third or fourth decades of life especially Indian and Hispanic. There are three forms of melasma according to the appearance of the hyperpigmentation on the face, namely, the centrofacial, malar, and mandibular patterns. However, melasma often presents as a combination of these forms [16].

Modification of melanogenesis by zinc still uncertain. Also, it inhibits tyrosinase *in vitro*, but it also activates dopachrome tautomerase (Trp2). It is accepted that oral ingestion of zinc affects the amount of pigmentation and the melanosome configuration. High doses of zinc sulfate inhibit eumelanogenesis and cause severe murine hair hypopigmentation. Low zinc diets make irregular huge melanosomes in choroidal melanocytes of adult pigs resulting in abnormal and irregular melanin distribution [17].

Our study was considered to assess serum Zn levels in cases with melasma compared to age and sex matched controls.

The average age of our patients was (37.24±6.25) compared to those reported in India (38.5±7.8 years) [18]., Brazil (38.43±6.75 years) [18].

This study showed a high statistically significant decline in zinc level in patients with melasma. Zn deficiency was found in (48.6%) of the patients. Serum Zn level in patients' group was (83.47 ± 22.28 µg/dl) and in control group was (92.63 ± 13.63 µg/dl). This result is in agreement with Mogaddam et al [20]. who reported equal decrease in Zn levels in serum of cases compared to controls with mean serum level of zinc in melasma patients and controls was 77.4±23.2 µg/dL and 82.2±23.9 µg/dL, respectively (P-value=.0001)?

In this study, there was statistically important negative association between level of serum Zn and duration of melasma. The value in our study showed statistically high significance inverse correlation between serum zinc level and severity of melasma assessed by modified melasma area and severity index.

In agreement with Kaur et al [21]. The most common type was epidermal melasma 52.8% of the patients then dermal melasma 25% of the patients, while its mixed melasma in 22.2 % of patients. In our study, there was no statistically significant difference in serum Zn level in patients as regards type of melasma.

Taking of oral contraceptive pills considered as a reason for melasma in agreement with the results of Sheth and Pandya [22] as this study showed that about 79.2 percent of cases use this pill, this is due

to the increase in the estrogen receptors sensitivity due to zinc deficiency and oral zinc supplement may reverse this cycle.

In this study genetic background was observed in 40.3% in contrast to Kaur et al [21] who reported only 17% . Jagannathan et al [24] reported a familial tendency of 33% and KrupaShankar et al [24] reported it to be 31.1%.

In our study 26.4% of patients exposed to sun but 22 % reported to be exposed to sun in a study by Jagannathan et al [23].

In our study 20.8% of patients give history of occurrence of melasma during pregnancy but Kaur et al [21] reported 84% and Jagannathan et al [23] reported 28.7% female patients during pregnancy.

CONCLUSIONS

The results derived from this study, showed that serum zinc level decreases in patients with melasma compared to sex- and age-matched controls. Also, in comparison with recent cases with melasma and old cases, old cases have lower mean serum zinc levels. Highly significant inverse correlations were found between serum zinc level and disease severity and its duration in all patients with melasma. Therefore, serum zinc level may be a helpful marker of disease severity and duration in melasma, and zinc supplements may have useful therapeutic outcome. Additional studies are therefore required to assess the role of zinc supplements in patients with melasma, especially those with long standing, severe, or resistant lesions.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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