ORIGINAL ARTICLE

Estimation of serum ferritin levels in female patients with melasma

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Abstract

Background Melasma is a chronic acquired localized hypermelanosis, causing cosmetic problem for women and impairing their quality of life. The effect of low body iron stores on skin pigmentation is not exactly known.

Objectives To evaluate total body iron stores by assessing serum iron, ferritin, total iron binding capacity (TIBC) and hemoglobin levels among non-pregnant females with and without melasma, and to correlate between serum ferritin levels and severity of melasma.

Methods A cross-sectional case control study including 50 non-pregnant women with melasma and 50 age-matched non-pregnant women without melasma. Serum iron, ferritin, TIBC and hemoglobin levels in the two groups were measured and compared. Melasma Area and Severity Index (MASI) score used for assessing melasma severity.

Results The mean ± SD of serum iron levels in the patients with melasma (63.6 ± 33.8 mcg/dl) as compared to the control population (67.1 ± 33.3 mcg/dl) with *p* value (0.604). Low mean Serum ferritin levels found in the patients with melasma (26.9 ± 26.1 ng/ml) as compared to the control population (38.2 ± 31.4 ng/ml) and the difference was statistically significant with *p* value (0.05). The mean hemoglobin levels in the case group (11.8 ± 1.4 g/dl) in comparison to the control group (12.8 ± 1.1 g/dl) with a highly significant *p* value 0.0001.

Conclusions Our Patients with melasma had significant low serum ferritin and hemoglobin levels in comparison to the control group, and the severity of melasma as per MASI score showed a negative correlation with low serum ferritin levels.

Keywords: Melasma, ferritin, iron, total iron binding capacity, MASI.

Introduction

Melasma is a chronic acquired facial hypermelanosis with a characteristic pattern of symmetric light-to-dark brown hyperpigmented macules and patches, involving sun- exposed areas [(1)]. The condition is most commonly seen in women of childbearing age with Fitzpatrick skin types IV to VI (2). Three patterns of melasma are commonly seen: centrofacial, malar and mandibular pattern (3). The pathogenesis of melasma is not fully understood. However, genetic background, sunlight exposure and hormonal influences seem to be the most important etiological factors (4). The effect of body iron stores on melasma is not exactly known (5). Different studies have been considering the common dermatologic symptoms of iron overload (hemochromatosis) and the relationship between iron deficiency and melasma (4). Qazi, et al. found that hemoglobin, serum iron and ferritin levels were significantly low in patients with melasma as compared to control population, while the serum TIBC levels in the patients were higher than in the control population; indicating the presence of iron deficiency and low body iron stores in the patients with melasma (5). However, in a recent cross-sectional study Shahla, et al. Showed the prevalence of iron, folate and vitamin B12 deficiency among a group of patients with melasma (7).

The aim of our study was to evaluate total body iron stores by assessing serum iron, ferritin, total iron binding capacity (TIBC) and hemoglobin levels among non-pregnant females with and without melasma, and to correlate between serum ferritin levels and severity of melasma.

Materials and Methods

A group of 50 adult non-pregnant Libyan female patients with melasma recruited from dermatology outpatient clinics in Benghazi, compared with a group of 50 age-matched healthy females without melasma as a control group. A detailed medical history was obtained from each patient and the control subjects, and both patients and control subjects were exposed to dermatological examination, which aided by Wood's lamp examination to localize abnormal melanin pigmentation in the skin as a guide to clinical diagnosis of melasma. The diagnosis was based on clinical findings, and aided by examination under Wood's lamp. In our study Melasma Area and Severity Index

(MASI) score was calculated for assessment of melasma severity (8). Blood samples then were drawn from the patients and healthy subjects and tested for complete blood picture (CBP), serum ferritin, serum iron, and total iron binding capacity (TIBC). We considered serum iron levels 37-158 mcg/dl, ferritin 9-160 ng/dl, TIBC 249-412 mcg/dl, and hemoglobin (Hb) 12-15 g/dl, as normal among our patients. Data analyzed using Statistical Package for Social Science (SPSS) version 22, *p*-value was considered significant when ≤ 0.05.

Results

A group of fifty non-pregnant females with melasma (case group) was recruited from dermatology outpatient clinics in Benghazi, and a group of fifty age-matched healthy non-pregnant females without melasma (control group), were included in the present study. The ages of the patients and healthy controls were ranged from 27 to 55 years, with a mean of age ± SD of 42.2 ± 6.1 years. A family history of melasma was positive in 42% of the patients with melasma. According to the clinical type of melasma, out of 50 melasma patients, 28 (56%) were with the malar type as shown in fig. 1 and 22 (44%) were with centrofacial type of melasma as shown in Fig. 2. Twenty patients with melasma, representing 40%, demonstrated that sun exposure is a contributing factor in the onset of melasma, and 29 (58%) patients acquired melasma during pregnancy, while only one (2%) patient believed that both sunlight exposure and pregnancy were the predisposing factors for melasma as shown in Tab. 2. A total score of MASI with ranges from zero to 48 were used to calculate the severity of melasma (9). A total score of 1.8 to 21 was observed in our patients. The mean of MASI score was 8.8 ± 4.9, and when we correlated MASI score with iron parameters, a negative correlation between low serum ferritin and MASI score was found, with *p* value 0.004 and correlation factor 0.405 as seen in Tab. 5.

Figure 6. shows a comparison between the hemoglobin levels in the cases and controls. The mean hemoglobin levels were found to be lower in melasma patients (11.8 ± 1.4 g/dl) as compared to control population (12.8 ± 1.1 g/dl) and this difference found to be statistically significant with *p* value 0.0001. In addition, the mean serum ferritin was lower in melasma patients (26.9 ± 26.1 ng/ml) as compared to the control group (38.2 ± 31.4 ng/dl) and this difference was found to be statistically significant with *p* value 0.05. About 26% of the cases had low serum ferritin levels. While, in 16% of the control subject were found to have low serum ferritin levels as shown in Fig. 4. The mean iron levels in the group of melasma patients was (63.6 ± 33.8 mcg/dl), while in the control group was (67.1 ± 33.3 mcg/dl) and the difference between the two groups was statistically not significant with *p* value 0.604 as

shown in Tab. 4. The mean of TIBC levels was found to be high in melasma patients (373.4 ± 115.8 mcg/dl) as compared to the control population (301 ± 81 mcg/dl) and the difference between the two groups was statistically significant with *p* value 0.0001. Figure 7 shows the distribution of case and control groups according to absence or presence of anemia. Anemia was found in 21 (42%) patients compared with 10 (20%) of the healthy subjects, and the difference was statistically significant with *p* value 0.031. Melasma has been classified into epidermal, dermal, and mixed subtypes (10). In our study, Wood's lamp examination shows that out of 50 (100%) patients with melasma 9 (18%) had epidermal melasma and 41(82%) had dermal melasma.

Discussion

Melasma is a common acquired facial hypermelanosis with a characteristic pattern of symmetric light-to-dark brown hyperpigmented macules and patches involving sun- exposed areas (1). However, the pathogenesis of melasma is not fully understood, Ortonne et al, in a recent global survey reported that a combination of hormonal factors such as pregnancy or OCP intake, and sunlight exposure are involved in their patients with melasma (11). Iron overload has been reported to effect skin pigmentation, however the effect of body iron stores on melasma is not clear (5). Ferritin is predominantly utilized as a serum marker of total body iron stores. In cases of iron deficiency and overload, serum ferritin serves a critical role in both diagnosis and management (12). In our study, a low serum ferritin level was reported in 26% of the patients and 16% of the control subject, the difference was statistically significant (*p* value = 0.05). This finding was in agreement with the result reported by Qazi et al (5) as they found that serum ferritin levels were significantly low in melasma patients as compared to control population. In a cross-sectional case study conducted in 2012 on 33-non-pregnant women, Behrangi et al found that serum ferritin levels were non significantly low in melasma patients compared to their control population (6). We found that the mean serum iron levels in our patients (63.6 ± 33.8 mcg/dl), was lower than the mean iron levels in control group (67.1 ± 33.3 mcg/dl) and the difference between the two groups was statistically not-significant (*p* value = 0.604). Similar finding were reported by Behrangi et al (6). But Jie et al (13) found high serum iron levels in melasma patients in comparison with their control group.

Measurement of TIBC levels has been used in the diagnosis of iron deficiency anemia, iron overload, and chronic inflammatory disorders (14). The higher TIBC level in women with melasma indicates lower iron storage (15). We found the mean ± SD of TIBC levels in case group (373 ± 115.8 mcg/dl) is higher than that of the control group (301 ± 81 mcg/dl). These results were in good agreement with the results obtained by Qazi et al (5) and Behrangi et al (6), indicating the presence of iron deficiency and low body iron stores in the patients with melasma. We applied MASI score proposed by Kimbrough-green et al (8), in order to clinically quantify the severity of facial melasma in our patients, in whom all blood parameters tested for association with MASI score. We found a negative correlation between low serum ferritin levels and MASI score with *p* value 0.004. These results were in agreement with the results reported by Qazi et al (5), as they found a negative correlation between MASI score and serum ferritin, but also they found a negative correlation between MASI score and both serum iron and hemoglobin levels (5). However, Goodarzi et al (15) tested all blood parameters in relation to MASI, but no correlation was found. In our study a low hemoglobin level was reported in 42% of the patients with melasma and 20% of the control subjects, and the mean hemoglobin levels found to be lower in melasma patients (11.8 ± 1.4) g/dl as compared to the control population (12.8 ± 1.1) g/dl and this difference was found to be statistically significant (*p* value 0.0001). These results were in good agreement with the results reported by Qazi et al (5), as they found the mean hemoglobin levels were lower in patients with melasma when compared with the control population. However, our results differ from those obtained by Goodarzi et al (15), as they found no statistically significant difference in the mean serum hemoglobin levels between the melasma patients and control groups. In our patients with melasma, the iron profile of women with melasma was different from that of the control subjects. Anemia was reported in 42% of our patients with melasma in comparison to the healthy control group (20%), and the difference was statistically significant with *p* value 0.03. This may indicate a possible association of melasma with iron deficiency anemia (5). However, Behrangi et al (6), reported low serum iron, ferritin and TIBC levels in 33 non-pregnant females with melasma compared to 33 non-pregnant females without melasma and the difference was not statistically significant, suggesting that iron deficiency anemia is a prevalent problem among young women. Moreover, Kiayani et al (16) found no association of melasma with iron deficiency anemia. Low mean of serum ferritin, serum iron and hemoglobin levels,

and increased TIBC levels in our patients with melasma indicate low iron levels and storage, and may suggest a possible role for iron deficiency anemia in melasma.

Limitations

The present study had some potential limitations among them: A small sample of population and the patients were limited to female gender.

Conclusions

Our Patients with melasma had significant low serum ferritin, serum iron and hemoglobin levels, and increased TIBC levels in comparison to the control group, and the severity of melasma as per MASI score showed a negative correlation with low serum ferritin levels. These findings indicate low serum iron levels and storage, and may suggest a possible role for iron deficiency anemia in melasma. However, further studies with large sample sizes should be considered.

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Fig. 1. Malar type of melasma

Fig. 2. Centrofacial type of melasma.

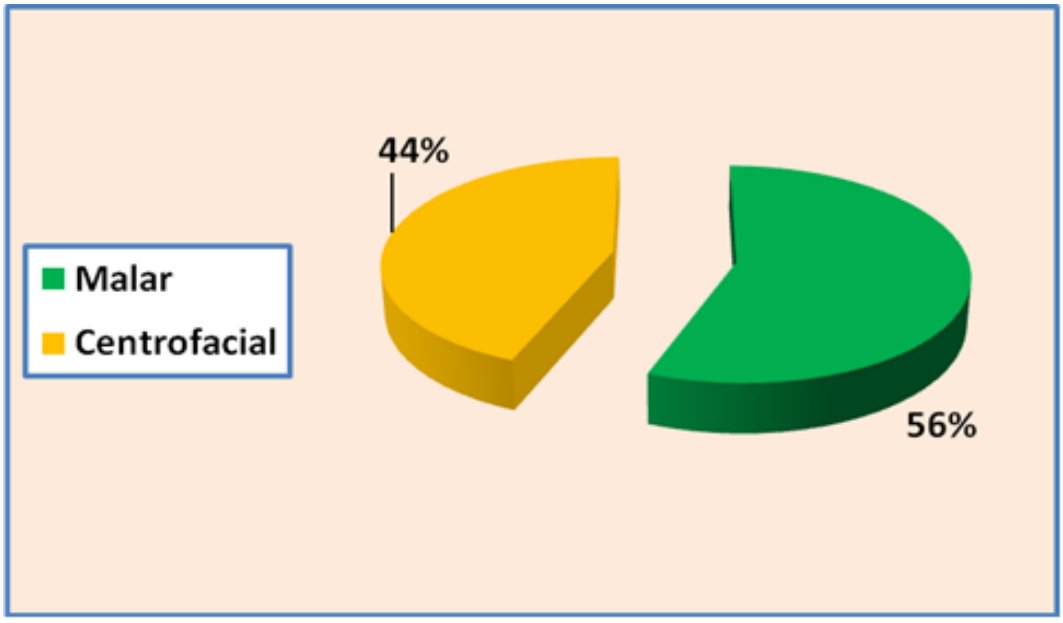

Fig. 3. Distribution of patients according to type of melasma.

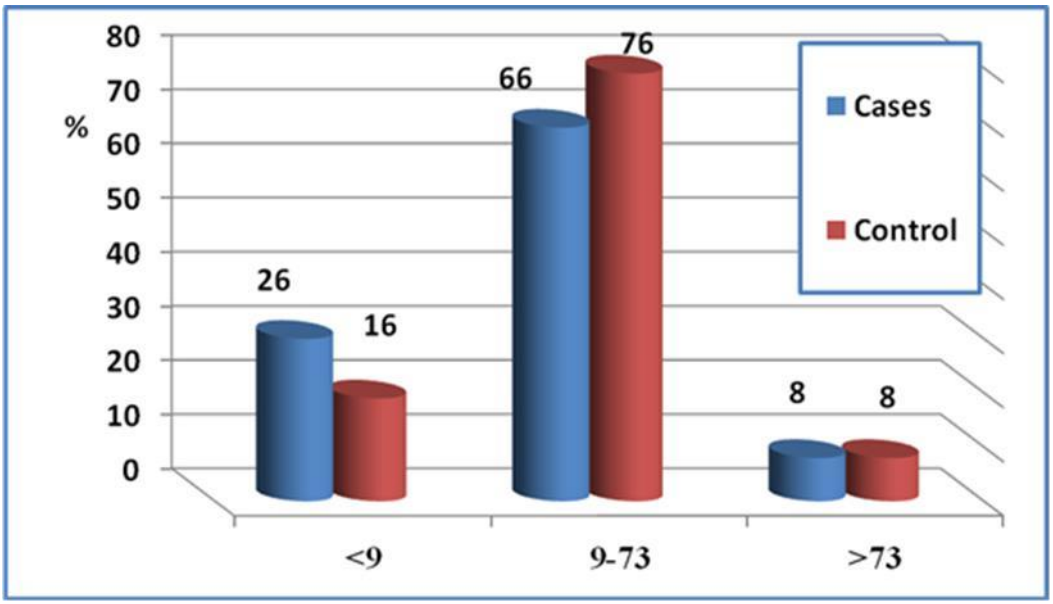

Fig. 4. Distribution of cases and control according to serum ferritin levels

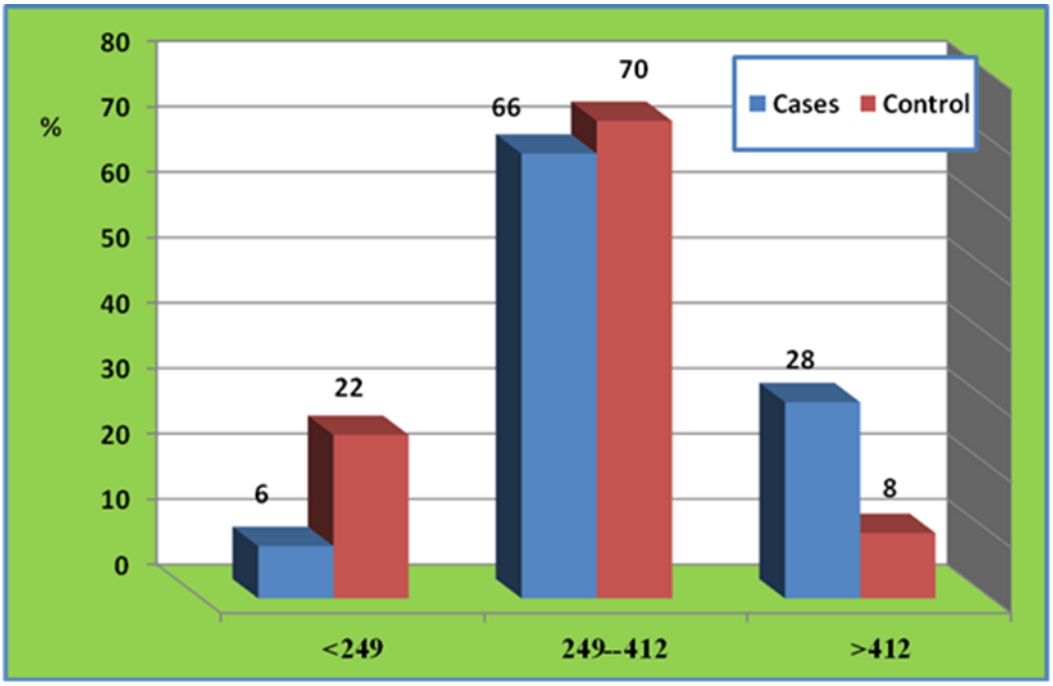

Fig. 5. Distribution of cases and control according to levels of total iron binding capacity (TIBC).

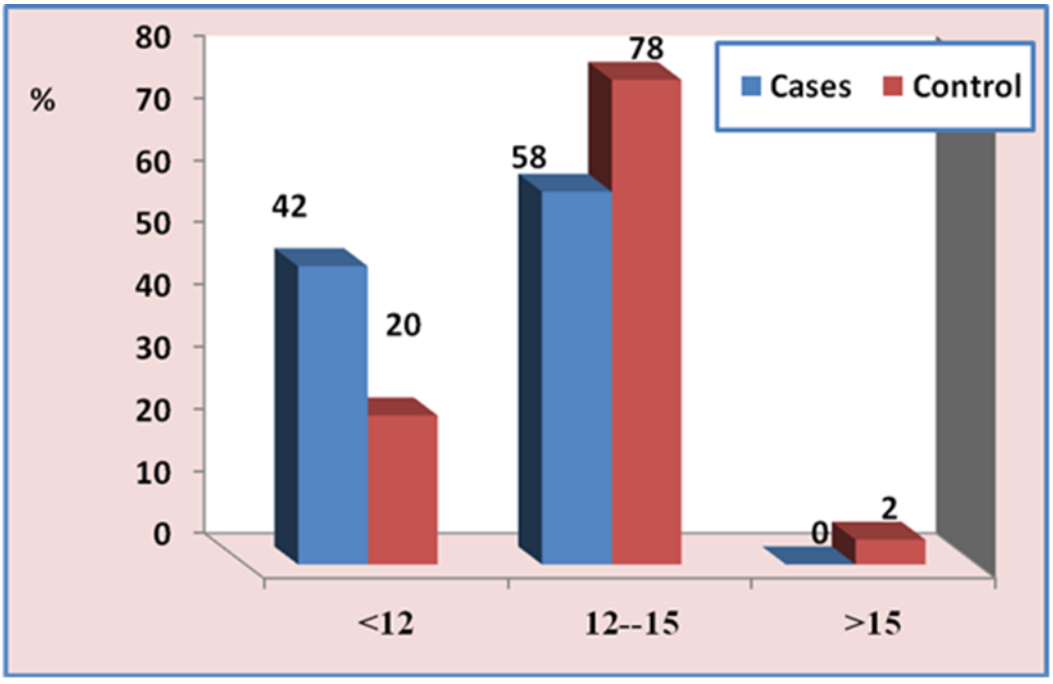

Fig. 6. Distribution of cases and controls according to hemoglobin Levels.

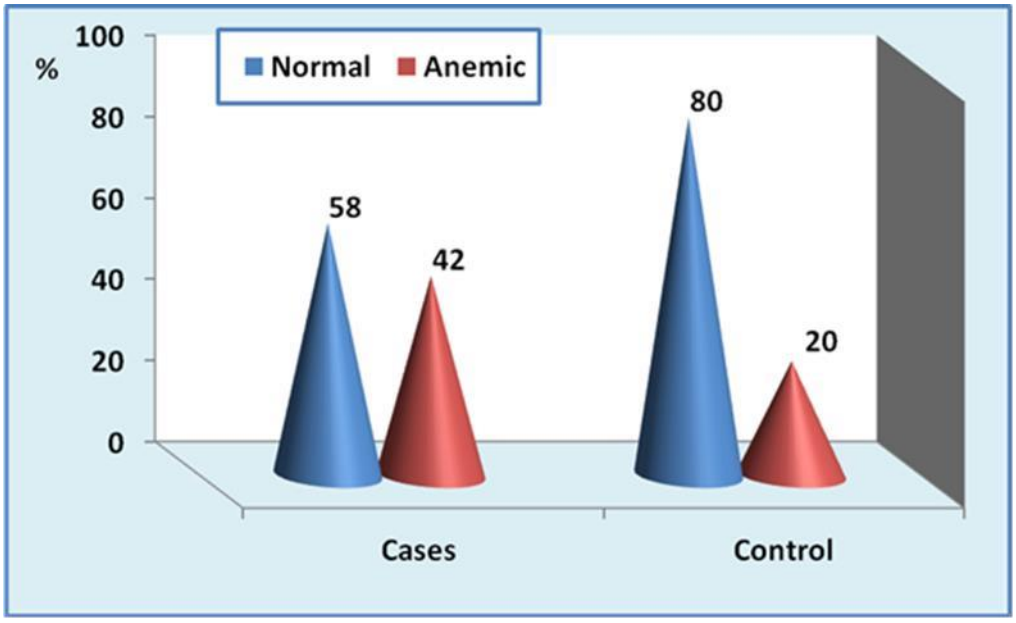

Fig. 7. Distribution of cases and controls according to anemia

Table1. Distribution of patients with melasma and controls according to age.

Age /year	Patients No. (%)	Controls No. (%)
≤30	1 (2%)	1 (2%)
31-40	17 (34)	17 (34%)
41-50	28 (56%)	28 (56%)
>50	4 (8%)	4 (8%)
Total	50 (100%)	50 (100%)

Table 2. Distribution of patients with melasma based on predisposing factors.

Predisposing factors	No. of patients (%)
Sun	20 (40%)
Pregnancy	29 (58%)
Sun + pregnancy	1 (2%)
Total	50 (100%)

Table 3. Serum iron levels in patients with melasma versus controls

Serum iron	Patients No. (%)	Controls No. (%)
> 37 mcg/dl	11 (22%)	8 (16%)
37-158 mcg/dl	39 (78%)	42 (84%)
Total	50 (100%)	50 (100%)

p value = 0.604 (Not significant)

Table 4. Iron parameters in patients with melasma versus controls.

Iron parameters	Patients (Mean ± SD)	Controls (Mean ± SD)	*p* value
Ferritin (ng/ml)	26.9 ± 26.1	38.32 ± 31.4	0.05
Iron (mcg/dl)	63.6 ± 33.8	67.1 ± 33.3	0.604
Hb (g/dl)	11.8 ± 1.4	12.8 ± 1.1	0.0001
TIBC (mcg/dl)	373.4 ± 115.8	301 ± 81	0.0001

Table 5. Correlation between Melasma Area Severity Index (MASI) in melasma patients and blood parameters.

Parameters	R	P- value
Hemoglobin level (g/dl)	-0.013	0.931
Serum ferritin level (ng/ml)	0.405	0.004**
Serum iron level (mcg/dl)	0.179	0.214
Total iron binding capacity (mcg/dl)	-0.038	0.791
MCV (fl)	0.096	0.509
MCH (pg)	0.025	0.863
MCHC (g/dl)	-0.158	0.274