

## Serum Iron profile in Female patients of Melasma: A case control study

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### ABSTRACT

**Background:** Melasma is a common acquired pigmentary dermatosis characterized by presence of symmetric, hyperpigmented patches, most commonly seen on the face. It is most commonly seen in young to middle aged females. The exact cause of melasma is not known, however a number of factors have been implicated in its etiopathogenesis. The effect of body iron stores on melasma is not exactly known. Although iron overload has been seen to affect skin pigmentation, effect of low body iron stores on skin pigmentation is unknown. In this study, we evaluated total body iron stores by assessing serum iron, ferritin and total iron binding capacity (TIBC) level among nonpregnant females with and without melasma. **Materials and Methods:** A cross-sectional case control study was conducted in 2016 at Department of Dermatology, Government Medical College, Jammu for a period of one year. The study comprised of 70 non pregnant females with and without melasma. Serum iron level, TIBC and ferritin in the two groups were measured and compared. The severity of melasma was assessed on the basis of MASI score. The correlation between severity of melasma and derangements in iron profile were also assessed in the study. **Results:** Comparison of serum Iron levels in cases and controls showed lower levels in patients of melasma ( $58.84 \pm 29.17$ ) as compared to control population ( $82.26 \pm 45.83$ );  $p < 0.001$ . Serum ferritin levels were found to be lower in patients of melasma ( $20.06 \pm 18.64$ ) as compared to control population ( $42.29 \pm 30.08$ );  $p < 0.001$ . Comparison of serum TIBC between cases and controls showed higher values in cases ( $424 \pm 58.98.33$ ) compared to control population ( $384.45 \pm 74.55$ )  $p < 0.007$ . Also a positive correlation was found between severity of melasma as per MASI score and derangement in Iron profile. **Conclusion:** Serum Iron, ferritin levels were found to be significantly lower in patients of melasma compared to the control population whereas Total iron binding capacity (TIBC) was found to be higher in patients of melasma compared to the control population indicating low body iron stores in patients of melasma. The severity of melasma as per MASI score correlated well with the derangements in iron profile. Hence patients with melasma had low body Iron stores compared to control population indicating a possible role of iron deficiency in the etiopathogenesis of melasma.

**Key Words:** ferritin, MASI, Melasma, Total iron binding capacity

### Introduction

The word melasma is derived from a Greek word melas meaning black. Melasma is a relatively common, acquired facial melanosis with a characteristic pattern of symmetric, marginated, light-to-dark brown hyperpigmented macules and patches, involving sun-exposed areas mainly on face, occasionally affecting the forearms.

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The prevalence of melasma varies between 1.5% and 33.3% depending on the population.[1,2] The exact prevalence of melasma in India is not known, however, it is observed more frequently among individuals with skin type IV-VI, especially in women of Hispanic, Caribbean and Asian origin living in areas of intense ultraviolet radiation[3]. Melasma is commoner in women, especially in their reproductive years, but about 10% cases occur in men also.[4]

The exact cause of melasma is unknown. However, multiple factors are implicated in its etiopathogenesis, mainly sunlight, genetic predisposition, pregnancy, thyroid disorders, certain drugs and female hormonal activity[5,6,7]. Dermatopathic anemia has attracted the attention of clinicians because iron deficiency was

found to be a metabolic consequence of skin diseases such as erythroderma, exfoliative dermatitis, psoriasis, eczema, and many others. Iron, cobalt, magnesium, selenium, vitamin E and C are known to have effect on the progression of skin diseases, but little data about serum iron level and melasma are available. Recent studies in the past have shown a relation between iron deficiency and melasma. Hence, keeping in view the recent studies on the role of iron deficiency in melasma we plan to evaluate serum iron profile in patients of melasma.

**Materials and Methods**

The study was conducted in the Post Graduate Department of Dermatology, Venerology and Leprology of SMGS Hospital, Government Medical College Jammu, from November 2016 to October 2017. The study group comprised of 70 cases of melasma and 70 age and sex matched controls fulfilling the inclusion and exclusion criteria. The inclusion criteria involved clinically diagnosed female patients of melasma and non pregnant females. Pregnant females were not included in the study. Patients with cardiac or thyroid disease, patients on oral contraceptives, hormonal therapy, phototoxic or anticonvulsant drugs known to cause or aggravate melasma and patients with menstrual irregularities were also excluded from the study. A detailed history regarding the demographic profile, medical history and medical examination were performed in both cases and controls. Melasma was diagnosed on the basis of wood’s lamp examination.

On clinical examination patients were classified into three types: centrofacial, malar and mandibular type. Hb, serum Iron, Ferritin and TIBC levels were measured in both cases and controls. Also the severity of melasma was graded on the basis of MASI Scoring Serum iron level of 50-175 µg/dL, ferritin 4.6-204 ng/dL and TIBC 250-450 µg/dL and Hb 11-16 was considered as normal levels in our study.

**Statistical analysis**

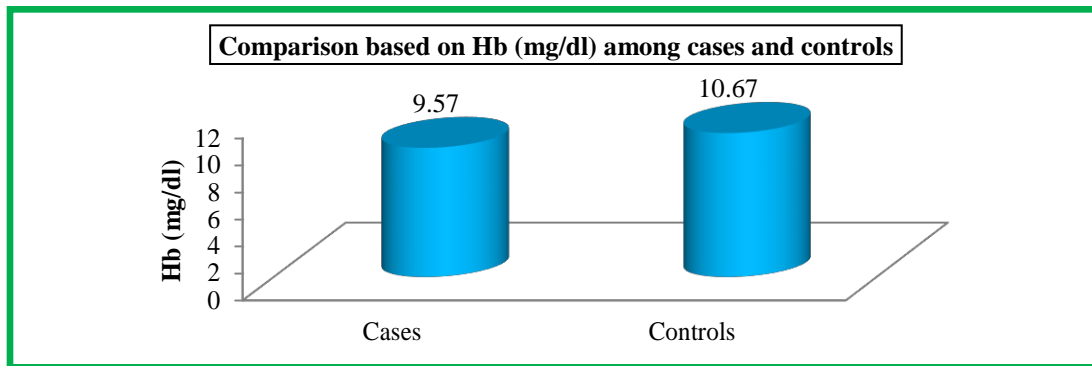
The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., (Chicago, Illinois, USA) by Kolmogorov Smirnov test. Student’s independent t-test was employed for comparison of continuous variables. Chi-square test or Fisher’s exact test, whichever appropriate, was used for comparison of categorical variables. Karl Pearson’s coefficient of correlation was applied to determine the correlation between MASI and iron profile among study cases.

**Results**

70 non pregnant patients clinically diagnosed as cases of melasma along with age and sex matched controlled were enrolled in the study during study period of 1 year. Case and control groups were matched for demographic variables (age, marital status and known related melasma disorder). Hemoglobin levels were found to be lower in patients of melasma (9.57± 1.16) as compared to the control population (10.67±1.10) and this difference was found to be statistically significant (p<0.001).

**Table 1: Comparison based on Hb among cases and controls**

Hb	Mean	SD	Range	P-value
Cases	9.57	1.16	6.4-13.9	<0.001*
Controls	10.67	1.10	7.8-14.5	

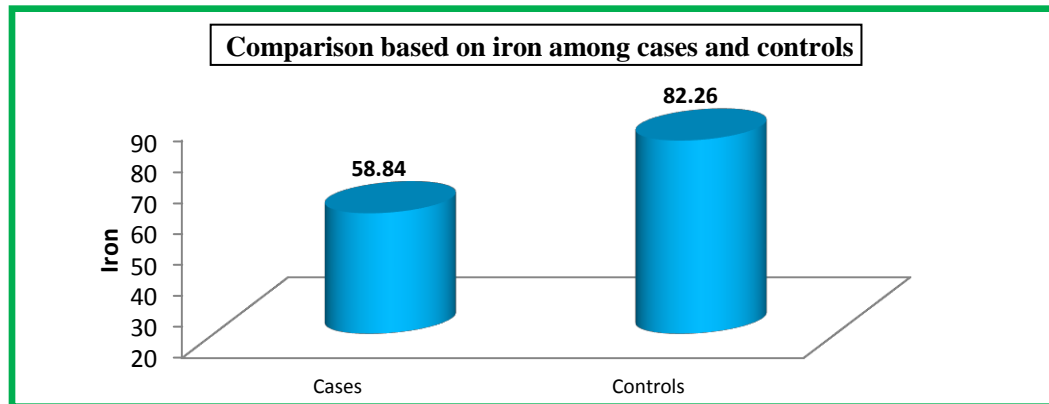


**Fig 1: Comparison based on Hb (mg/dl) among cases and controls**

**Table 2: Comparison based on iron among cases and controls**

Iron	Mean	SD	Range	P-value
Cases	58.84	29.17	10.8-142	<0.001*
Controls	82.26	45.83	20-359	

Comparison of serum iron levels in cases and controls showed lower levels in patients of melasma ranging between 10.8-142 (58.84± 29.17) as compared to control population where the serum iron levels ranged between 20-359 (82.26± 45.83) and this difference was found to be statistically significant (p <0.001).



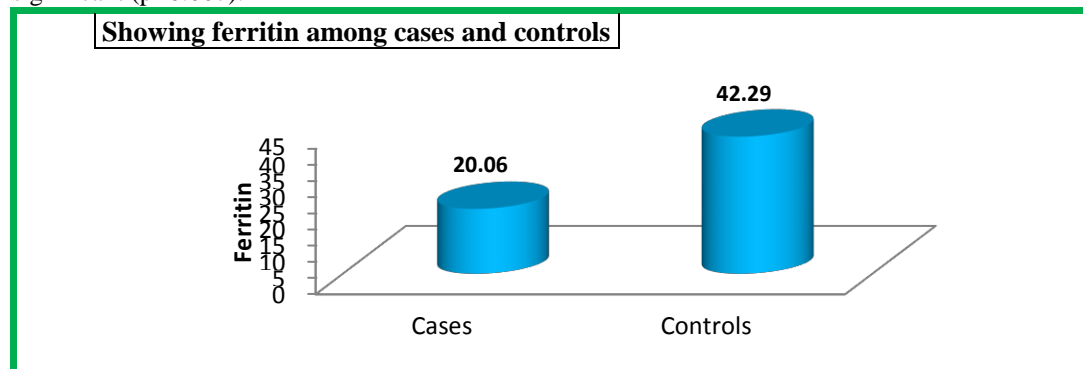
**Fig 2: Comparison based on iron among cases and controls**

Serum ferritin levels were found to be lower in patients of melasma ranging between 4.1-100.8 (20.06±18.64) whereas the serum ferritin levels ranged between 3.9-207.3 (42.29±30.08).The difference was found to be statistically significant between cases and controls (p<0.001).

**Table 3: Comparison based on ferritin among cases and controls**

Ferritin	Mean	SD	Range	P-value
Cases	20.06	18.64	4.1-100.8	<0.001*
Controls	42.29	30.08	3.9-207.3	

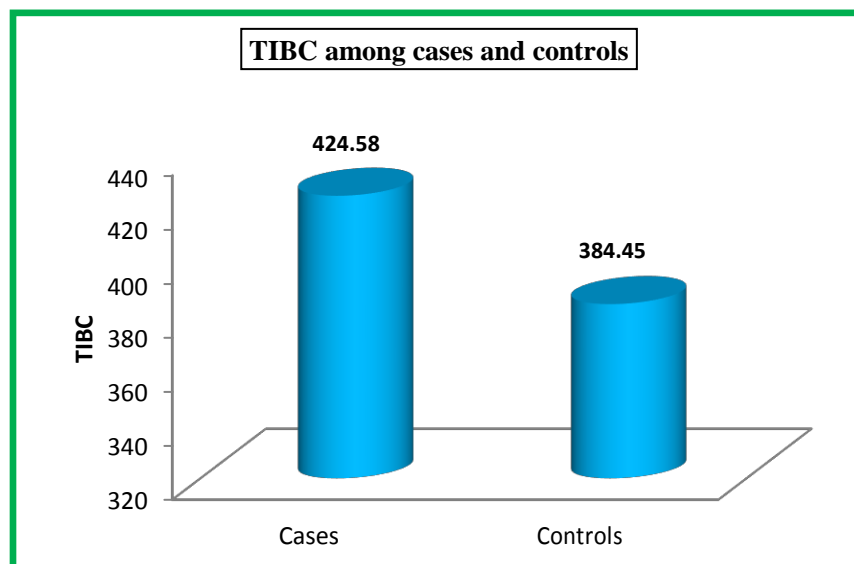
Comparison of serum TIBC between cases and controls showed higher values in cases ranging between 124-666 (424.58± 98.33) compared to control population ranging between 208-556 (384.45± 74.55) and this difference was found to be statistically significant (p=0.007).



**Fig 3: Ferritin among cases and control**

**Table 4: Comparison based on TIBC among cases and controls**

TIBC	Mean	SD	Range	P-value
Cases	424.58	98.33	124-666	0.007*
Controls	384.45	74.55	208-556	

**Fig 4:TIBC among cases and controls**

We also studied the correlation between the severity of melasma as per MASI with the hemoglobin and iron profile of the melasma patients. Results showed a negative correlation between the severity of MASI and serum HB levels. ( $r = -0.367$ ;  $p = 0.002$ ). Regarding serum iron levels a negative correlation was found between serum iron levels and severity of melasma as per the MASI score ( $r = -0.46$ ;  $p < 0.001$ ). A negative correlation was also found between serum ferritin levels and severity of melasma as per MASI score ( $r = -0.283$ ;  $p = 0.017$ ).

**Table 5: Showing correlation between MASI and iron profile among study cases**

Parameter	Pearson Correlation	Sig. (2-tailed)
Hb	-0.367	0.002*
Iron	-0.461	<0.001*
Ferritin	-0.283	0.017*
TIBC	0.673	<0.001*

Regarding total iron binding capacity a positive correlation was found between serum total iron binding capacity and severity of melasma as per MASI score ( $r = 0.673$ ;  $p < 0.001$ ).

## Discussion

In our study, mean hemoglobin levels were lower in cases as compared to the control population. Also serum iron and ferritin levels were found to be lower as compared to the control population and this difference

was found to be statistically significant ( $p < .001$ ). Mean TIBC was found to be higher in the cases compared to the control population. The above findings are consistent with low body iron stores. Hence patients of melasma were found to have iron deficiency with lower body iron stores compared to the control

population. Also a significant correlation was found between severities of melasma as per the MASI score with the iron derangements. Hence patient with a higher score of MASI representing more severe melasma had more derangement in the iron profile compared to the patients with lower MASI score with less severe disease. Keeping in view the above results, several studies regarding iron and other micronutrients in patients of melasma have been conducted in the past. A study conducted by Ping et al, 1997[8] to assess the serum levels of trace elements in 46 non pregnant women with melasma showed higher amounts of iron, magnesium, copper and zinc among the study population. Another case control study conducted by Jie et al, 1999[9] on female patients of melasma to evaluate the serum levels of trace elements showed higher levels of iron and copper in female patients of melasma as compared to the controls. Sarkar R et al, 2010[10] conducted a study to assess the clinical, etiological and histological features of melasma in men. Laboratory investigations revealed anemia in 12.2% patients. Najad SB et al, 2012[11] conducted a cross-sectional descriptive study to evaluate the prevalence of iron deficiency anemia, folate and vitamin B12 deficiency in patients of melasma on 70 female patients diagnosed with melasma. The hemoglobin, hematocrit, serum iron and ferritin levels, folate and vitamin B12 were measured in all of them. Results showed mean hemoglobin level of  $11.2 \pm 1.63$  g/dl. 14.3% had low serum iron levels, 8.6% of patients had abnormal ferritin levels. Low levels of serum folate and serum vitamin B12 were observed in 3 patients and 1 patient respectively. Behrangi E et al, 2015[12] conducted a cross sectional case control study to evaluate serum iron level, ferritin and total iron binding capacity (TIBC) level among non pregnant women with and without melasma. The study included 33 non pregnant women with and without melasma. Serum iron, ferritin and TIBC were evaluated in both cases and controls. In case group, 27% had a lower level of serum iron, and 10% had higher serum iron level. In the control group, 15% were in the lower level and 10% upper level of serum iron ( $P > 0.05$ ). About 23% of patients in the case group had low ferritin level compared with 12% in the control group, but not statistically significant.

### Conclusion

Hemoglobin, serum iron and ferritin levels were found to be significantly lower in patients of melasma as compared to control population while as serum TIBC levels in cases were higher as compared to the control population indicating the presence of iron deficiency

and low body iron stores in the patients of melasma. Also low levels of iron stores correlated well with the severity of melasma. Hence, we suggest that iron deficiency may be one of the factors involved in the etiopathogenesis of melasma or may possibly act as an aggravating factor of melasma. Also considering the fact that the treatment of melasma tends to be prolonged and unconvincing, adding iron supplements may improve the clinical outcome of melasma and hence may prove to be a cost effective treatment in the management of melasma. However further studies with a larger sample size are required to validate our findings. Similar studies on male patients are also required so as to further confirm the role of iron deficiency in melasma. Also follow up studies to evaluate the effect of iron supplements in improvement of severity of melasma are required.

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**Abbreviations**

Hb- Hemoglobin

MASI- Melasma Area and Severity Index

**Conflict of Interest: None**

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