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Original Research Article

Association of serum iron profile in female patients with melasma

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ABSTRACT

Background: Melasma, an acquired pigmentary disorder, presents as symmetric, hyperpigmented macules and patches, primarily on the face. Its prevalence ranges from 1.5% to 33.3% and affects women more than men, impacting self-image and quality of life. Genetic predisposition, sun exposure, and hormonal factors significantly increase tyrosinase activity. The study aims to find an association between serum iron profile and melasma among female patients.
Methods: This hospital-based cross-sectional study occurred in the Department of Dermatology and Venereology at Dhaka Medical College Hospital, enrolling 100 women from July 2022 to June 2023. Participants were divided into groups: Group A (patients with melasma) and Group B (healthy respondents without melasma).
Results: The study compared two groups, finding no significant differences in age, marital status, occupation, or income. Group A had a higher percentage of patients with a family history of melasma (70% vs 28%) and significantly lower levels of hemoglobin, serum ferritin, iron, and transferrin saturation, but higher TIBC levels compared to Group B. Melasma was mainly central facial and symmetrical. Group A had a higher frequency of low haemoglobin, ferritin, iron, and transferrin saturation. The mMASI scores showed a negative correlation with hemoglobin, iron, ferritin, and transferrin saturation, and a positive correlation with TIBC, indicating more severe melasma with poorer iron profiles.
Conclusions: There was a significant inverse correlation between low body iron stores and the severity of melasma, indicating that iron deficiency may contribute to or aggravate melasma in females. Therefore, the findings suggest that iron supplementation could improve treatment outcomes for melasma.

Keywords: Association, Serum iron profile, Melasma

INTRODUCTION

Melasma is a common, acquired pigmentary disorder that manifests as symmetric, hyperpigmented macules and patches in sun-exposed areas, mostly over faces.[1] The prevalence of melasma varies between 1.5% and 33.3%, depending on the population.[2] Melasma is common in women, especially in their reproductive years, but about 10% of cases also occur in men.[3] Although this disorder has been considered a benign condition, which usually has only aesthetic implications, it may affect self-image and self-esteem, with a negative impact on a patient's

quality of life.[4] This disorder is an interplay of various internal and environmental factors. Genetic predisposition, sun exposure, and hormonal factors are the most important, as they significantly increase tyrosinase activity. Genetic predisposition has been suggested by the evidence of familial history and the association with particular races. Studies have shown that the genes related to lipid metabolism, such as PPARα, ALOX15B, DGAT2L3 and PPARGC1A, are less expressed in melasma. The role of the UVR has been well established in the development of melasma. The UVR increases melanocyte proliferation and activity, promotes the transfer of melanin pigments to keratinocytes, and causes peroxidation of lipids in the cellular membranes, which leads to the generation of free radicals and promotes melanocytes to produce excess melanin by upregulating expression of the melanogenic mediators from keratinocytes and dermal stem cells.

The female sex hormone's activity is vital in melasma's pathogenesis. The association of this disorder with pregnancy, oral contraceptive pills and hormone replacement therapies in post-menopausal women is well-known.[4] According to clinical manifestations, three patterns of melasma have been recognised over the face: centro facial, malar, mandibular, and extra facial. Melasma may also be found. Under Wood's light examination, four types of melasma, epidermal, dermal, mixed and indeterminate, have been identified.[4]

Iron is essential for various biological functions, including cellular respiration, energy production, DNA synthesis, and cell proliferation.[5] Dietary iron occurs in two forms: heme and non-heme. The average adult stores about 1-3 g of iron in his or her body. A balance between dietary uptake and loss maintains this balance.[6] Apart from the amount of available iron in the diet, the human body conserves iron stores by reutilising the iron derived from the breakdown of red cells and the retention of iron without an excretion mechanism. Serum ferritin concentration generally correlates with the tissue iron stores. Iron deficiency refers to reducing iron stores that precede overt iron-deficiency anaemia or persists without progression.[7] Poverty, malnutrition, famine, chronic blood loss, various diseases, and infections are different causes of anaemia in the multitude of people living with iron deficiency in developing countries, especially children and pregnant women.[7-9] The prevalence of anaemia was 41.8% in Bangladesh, and it remains a significant public health issue among 15–49-year-old women.[10] There have been few studies which have suggested a relationship between iron deficiency and melasma.[11]A few pieces of evidence have suggested that hyperpigmentation can occur as a result of iron deficiency, and patients with melasma have been reported to have lower serum levels of haemoglobin (Hb), iron, ferritin and total iron binding capacity (TIBC).[12-14] Hence, considering the recent studies on the role of iron deficiency in melasma, the serum iron profile in melasma patients in this department was planned to be evaluated.

METHODS

This hospital-based cross-sectional study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Dhaka, Bangladesh. A hundred women were enrolled in this study from July 2022 to June 2023 after obtaining ethical approval from the Ethics Committee of DMC. They were included in this study according to the inclusion and exclusion criteria and categorized into two groups:

Group A

Group A included the patients with melasma.

Group B

Group B included the healthy respondents without melasma.

The study included female patients aged 18 to 50 years, clinically diagnosed with melasma by Wood's lamp examination and confirmed by faculty members. Healthy individuals without melasma and those who provided written informed consent were also included. Exclusion criteria comprised pregnancy, lactation, systemic diseases (e.g., CKD, CLD, cardiac disease, pernicious anemia, Crohn's disease, celiac disease, leukemia, malignancy), endocrine diseases (e.g., thyroid disease, Addison's disease), known bleeding disorders, use of oral contraceptives, hormonal therapy, phototoxic or anticonvulsant drugs, iron, blood transfusions, and those who had received melasma treatment in the last six months.

Before collecting data, informed consent was obtained from all participants. Data were collected from the patients on variables of interest using the semi-structured questionnaire designed for an interview, observation, clinical examination, and hematological investigations of the patients. A separate data collection sheet was used for every subject. Melasma was diagnosed clinically and confirmed by the certified dermatologist. The types of melasma were graded using Wood's lamp examination. A modified Melasma Area and Severity Index (mMASI) score was used to assess the severity of melasma separately for each side of the face. For laboratory evaluation, Hb%, serum iron, serum ferritin, and total iron binding capacity (TIBC) were measured in both group and groups in the Hematology and Biochemistry department of BSMMU, Dhaka. Blood samples (5 ml) were drawn from the antecubital vein (in an arm without intravenous infusion ongoing) with aseptic precaution in an empty stomach by venipuncture in each participant.

Data analysis

All statistical analyses were performed using the statistical package for social science (SPSS) program, version 24.0 for Windows. Continuous parameters were

expressed as mean±SD and categorical parameters as frequency and percentage. The student's t-test made comparisons between groups (continuous parameters). Where applicable, categorical parameters were compared using the Chi-Square and Fisher exact tests. The correlation coefficient test was done using Pearson's correlation coefficient test. The significance of the results was determined in a 95.0% confidence interval, and the value of $p<0.05$ was considered statistically significant.

RESULTS

In this cross-sectional study of 100 patients, two groups (Group A and Group B) were compared. Table 1 presents the demographic and historical data of the female participants. The mean ages for Groups A and B were 38.84±8.0 years and 37.28±9.33 years, respectively, with no significant difference in age distribution ($p>0.05$). In Group A, 35(70%) patients with melasma had a positive family history of melasma, compared to 14(28%) in Group B, a statistically significant difference ($p<0.05$). Most participants worked less than 2.5 hours in the sun (64% in Group A vs. 70% in Group B), with no significant difference in sun exposure duration between groups ($p>0.05$). In Group A, 56.00% of females had melasma in the centro-facial area, and only 2 (4.00%) had it in the mandibular area. Symmetrical melasma was observed in 39(78.00%) cases, while 11 (22.00%) were asymmetrical (Table 2).

Table 3 shows that participants in Group A had significantly lower levels of haemoglobin (10.86±2.36 g/dl vs. 12.14±1.59 g/dl, $p=0.002$), serum ferritin (44.86±36.30 ng/ml vs. 88.96±28.19 ng/ml, $p<0.001$), iron (59.32±29.88 µg/dl vs. 96.74±36.51 µg/dl, $p<0.001$), and transferrin saturation (14.44±8.81% vs. 29.44±13.17%, $p<0.001$), but a higher level of TIBC (488.96±209.23 µg/dl vs. 361.96±175.56 µg/dl, $p=0.001$). Low haemoglobin (70% vs. 46%), low ferritin (30% vs. 4%), low iron (40% vs. 6%), and low transferrin saturation (56% vs. 12%) were significantly more frequent in Group A compared to Group B. Additionally, Group A exhibited a significantly higher TIBC (46% vs. 14%) level than Group B ($p<0.05$). Regarding mMASI scores, 20%, 68%, and 12% of patients had mild, moderate, and severe melasma, respectively, with a mean score of 12.02±4.31 among participants with melasma (Table 4).

The relationship between melasma severity, determined by the mMASI score, and haemoglobin and iron profiles was analyzed. There was a negative correlation between the mMASI score and haemoglobin ($r=-0.371$, $p=0.008$), serum iron levels ($r=-0.622$, $p<0.001$), serum ferritin levels ($r=-0.342$, $p=0.015$), and transferrin saturation ($r=-0.515$, $p<0.001$). Conversely, a positive correlation was found between total iron-binding capacity and melasma severity ($r=0.306$, $p=0.031$) (Table 5).

Table 1: Demography and history of the study female (n=100).

Variables	Group A		Group B		P value
	N	%	N	%	
Age in years					
Mean±SD	38.84±8.04		37.28±9.33		0.373
Family history					
Yes	35	70	14	28	<0.002*
No	15	30	36	72	
Duration of sun exposure					
>2.5 hours	18	36	15	30	0.523*
<2.5 hours	32	64	35	70	

*Statistically significant.

Table 2: Distribution of Group A participants by clinical findings of melasma (n=50).

Variables	Frequency (N)	Percentage (%)
Location of melasma		
Centro-facial	28	56.00
Malar	20	40.00
Mandibular	2	4.00
Symmetry of distribution		
Symmetrical	39	78.00
Asymmetrical	11	22.00

Table 3: Laboratory findings among the study participants (n=100).

Variables	Group A (n=50)		Group B (n=50)		P value
	N	%	N	%	
Haemoglobin					
Low	35	70	23	46	0.025*
Normal	15	30	27	54	
Mean±SD	10.86±2.36		12.14±1.59		
Serum ferritin					
Low	15	30	2	4	0.001*
Normal	35	70	48	96	
Mean±SD	44.86±36.30		88.96±28.19		
Serum Iron					
Low	20	40	3	6	<0.001**
Normal	30	60	44	88	
High	0	0	3	6	
Mean±SD	59.32±29.88		96.74±36.51		
Transferrin saturation					
Low	28	56	6	12	<0.001**
Normal	22	44	41	82	
High	0	0	3	6	
Mean±SD	14.44±8.81		29.44±13.17		
TIBC					
Low	0	0	3	6	<0.001**
Normal	27	54	40	80	
High	23	46	7	14	
Mean±SD	488.96±209.23		361.96±175.56		

*Statistically significant.

Table 4: mMASI score of melasma patients (Group A).

mMASI score	Frequency (N)	Percentage (%)
Mild (0<8)	10	20
Moderate (8<16)	34	68
Severe (16-24)	6	12
Mean±SD	12.02 ± 4.31	
Range	6-22	

Table 5: Correlation between mMASI and iron profile among melasma patients (Group B).

Variables	Correlation coefficient	P value
Haemoglobin	-0.371	0.008
Serum iron	-0.622	<0.001
Serum ferritin	-0.342	0.015
Transferrin saturation	-0.515	<0.001
TIBC	0.306	0.031

DISCUSSION

Melasma is a common hypermelanotic condition characterized by light to dark brown, irregular macules and patches on sun-exposed areas of the skin, particularly on the face.[15] It is more prevalent in women, especially during their reproductive years and in individuals with darker skin types. The etiopathogenesis of melasma is complex and not fully understood, involving a combination of genetic influences, exposure to sunlight, hormonal activities, and certain medications.[16] Although nutritional factors like zinc, iron, copper, magnesium, selenium, and vitamins E and C affect skin hyperpigmentation, there is limited evidence regarding the relationship between serum iron levels and melasma.[14,17] Iron deficiency anaemia, which has the highest prevalence among women of reproductive age, is also a common concern in the same population susceptible to melasma.[17] Building on these concepts, the current study aimed to determine the association between

melasma and serum iron profiles. The study enrolled 100 female patients into two groups: 50 with melasma (Group A) and 50 without melasma (Group B). The mean age of participants in Group A was 38.84±8.04 years, while in Group B, it was 37.28±9.33 years. Most participants were between 37 and 46 years old (48% in Group A vs 38% in Group B), indicating that melasma is more prevalent among middle-aged women. The groups had no significant age difference (p>0.05). The age distribution in this study aligns with previous research. Goodarzi et al. reported a mean age of 36.89±8.88 years for women with melasma and 32.33±8.86 years for the control group, comparable to the current study.[17] Similarly, Prakash et al found that females comprised 85.7% of melasma cases compared to 14.3% of males, with the common age group being between 41 and 50 years.[11] These findings suggest that melasma is a common disorder among young to middle-aged women. Most patients with melasma had a positive family history (70% vs 28%), a significant finding (p<0.05). However, the duration of outdoor work in the sun, which was less than 2.5 hours for most subjects (64% vs 70%), was not significant (p>0.05). Goodarzi et al. observed similar results regarding family history and sun exposure duration.[17] This study's clinical characteristics of melasma showed that the centro-facial area was the most commonly affected site (56%), and a symmetrical distribution was predominant (78%). These findings align with typical melasma presentations, where the central facial region is a primary area of involvement. Symmetrical distribution is a hallmark of melasma, and these results reinforce this observation. Prakash et al. reported similar patterns, with the malar type accounting for 68.8%, followed by the centro-facial type (29.1%) and the mandibular type (2.1%).[11] Comparisons of hemoglobin (10.86±2.36 g/dl vs 12.14±1.59 g/dl), ferritin (44.86±36.30 ng/ml vs 88.96±28.19 ng/ml), iron (59.32±29.88 µg/dl vs 96.74±36.51 µg/dl), transferrin saturation (T-sat) (14.44±8.81% vs 29.44±13.17%), and TIBC (488.96±209.23 µg/dl vs 361.96±175.56 µg/dl) revealed that all iron profile parameters were significantly lower in melasma patients than in controls. The hemoglobin levels were significantly lower in the melasma group (p=0.002). Other iron profile parameters, including serum iron and ferritin, were significantly lower in melasma patients than controls (p<0.001). The mean mMASI score among melasma patients was 12.02±4.31. This study found a significant correlation between iron deficiency and melasma. Qazi and colleagues reported mean values for haemoglobin (9.57 g/dl vs 10.67 g/dl, p<0.001), serum iron (58.84 µg/dl vs 82.26 µg/dl, p<0.001), serum ferritin (20.06 ng/dl vs 42 ng/dl, p<0.001), and TIBC (424 µg/dl vs 384 µg/dl, p<0.05), which align with the findings of this study.[14] Goodarzi et al. also found significantly low serum ferritin and iron levels.[17] These findings suggest a potential association between iron metabolism and melasma. Lower hemoglobin levels in melasma patients could indicate anaemia, potentially contributing to the development or exacerbation of melasma. Similarly, lower serum ferritin and serum iron levels may indicate altered iron metabolism in melasma patients. Since iron is involved in various physiological processes, including melanin synthesis, disturbances in iron homeostasis could influence melanin production. Our study observed a negative correlation between the mMASI score and hemoglobin (r=-0.371, p=0.008), serum iron (r=-0.622, p<0.001), serum ferritin levels (r=-0.342, p=0.015), and transferrin saturation (r=-0.515, p<0.001) in melasma patients, suggesting that lower iron levels may be associated with increased melasma severity. This correlation supports the hypothesis that iron metabolism plays a role in melasma pathogenesis. Additionally, the positive correlation between TIBC and melasma severity (r=0.306, p=0.031) warrants further investigation into the role of iron-binding capacity in melasma. Studies have been conducted to establish the relationship between melasma and iron levels, though results have varied widely. For instance, Prakash et al. observed that mean ferritin levels in the melasma group were lower than in the group without melasma, with mean serum iron levels at 28.585 µg/dl in the melasma group compared to 135.018 µg/dl in the non-melasma group.[11] Other iron parameters also indicated significant iron deficiency in melasma patients, suggesting that iron deficiency is an important etiological factor. Hence, treating iron deficiency may be a novel therapeutic approach for patients with refractory melasma.[11] Qazi et al, in their case-control study on 140 females, found a clear link between melasma and iron levels but recommended using a larger sample size for future studies.[14] Qazi et al reported mean values for haemoglobin (9.57 g/dl vs 10.67 g/dl, p<0.001), serum iron (58.84 µg/dl vs 82.26 µg/dl, p<0.001), serum ferritin (20.06 ng/dl vs 42 ng/dl, p<0.001), and TIBC (424 µg/dl vs 384 µg/dl, p<0.05), which align with the findings of this study.[14] Goodarzi et al also found significantly low serum ferritin and iron levels.[17] These findings suggest a potential association between iron metabolism and melasma. Lower hemoglobin levels in melasma patients could indicate anaemia, potentially contributing to the development or exacerbation of melasma. Similarly, lower serum ferritin and serum iron levels may indicate altered iron metabolism in melasma patients. 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Limitations of the study

The study population was selected from a single tertiary center in Dhaka city, limiting the generalizability of the results to the entire country. Additionally, the sample size was not representative, further hindering the findings' generalisation. Time and resource constraints were also factors, and the sample was chosen purposively, introducing potential bias into the results.

CONCLUSION

This study revealed that haemoglobin, serum iron, and serum ferritin were significantly lower. In contrast, total iron binding capacity (TIBC) was higher in patients with melasma than in the comparison group participants. There was also a significant inverse correlation between low body iron stores and the severity of melasma. Hence, iron deficiency is one of the factors involved in the etiopathogenesis of melasma or may act as an aggravating factor of melasma in females. So, the study findings suggest that adding iron supplements will have a better therapeutic role in improving treatment outcomes.

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