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Original Research Article

Serum Estradiol Levels and Melasma Severity in Pregnant Women: A Cross-Sectional Study from North India

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Abstract:

Background: Melasma, a common dermatological concern, manifests as symmetrical hyperpigmented facial patches, posing cosmetic and psychological challenges, notably among pregnant women. Termed "chloasma gravidarum," it affects up to 50-70% of pregnant women, particularly those with darker skin tones. Hormonal fluctuations, notably elevated estrogen levels during pregnancy, are pivotal contributors to melasma's development. Despite extensive research, the precise mechanisms remain unclear. Our study analyzed serum estradiol levels in pregnant women with melasma to elucidate hormonal influences and improve clinical management.

Methods: This cross-sectional study conducted over two years recruited 97 pregnant women with melasma and 95 healthy pregnant controls from a tertiary care center in North India. Dermatologists conducted comprehensive clinical examinations, assessing hyperpigmented patches and quantifying melasma severity using the Melasma Area and Severity Index (MASI). Fasting venous blood samples were collected for serum estradiol level quantification using a competitive ELISA kit. Statistical analysis included Student's t-test for group comparisons, and Pearson correlation analysis to explore the relationship between serum estradiol levels and melasma severity.

Results: In our study, demographic characteristics were similar between the Melasma (n=97) and Control (n=95) groups, with no significant differences in age (29.5 ± 4.2 years vs. 30.1 ± 3.9 years, p = 0.306) and gestational age (25.8 ± 3.1 weeks vs. 26.5 ± 2.8 weeks, p = 0.102). Majority of melasma cases belonged to Fitzpatrick Skin Types IV (24.7%) and V (22.7%). Melasma severity varied, with 41.2% classified as Mild. Mean serum estradiol levels were significantly higher in the Melasma Group (125.6 pg/mL ± 20.3) than Controls (118.2 pg/mL ± 18.9) (p = 0.009). Positive correlation existed between melasma severity and serum estradiol levels (r = 0.29, p = 0.025).

Conclusion: Our study reveals a significant positive correlation between serum estradiol levels and melasma severity in pregnant women, indicating a potential role of elevated estradiol levels in melasma development or exacerbation. Future research should focus on elucidating underlying mechanisms and developing targeted interventions for melasma management.

Keywords: Melasma, Pregnancy, Estradiol Hormone, Hyperpigmentation, Dermatology.

Introduction

Melasma, a common dermatological concern characterized by symmetrical hyperpigmented patches predominantly on the face, poses a significant cosmetic and psychological burden, particularly among pregnant women. Termed "chloasma gravidarum" or "the mask of pregnancy," melasma affects up to 50-70% of pregnant women, with higher prevalence observed in individuals with darker skin types.

While melasma is generally considered a benign condition, its impact on self-esteem and quality of life can be profound [1,2,3]. The etiology of melasma is multifactorial, encompassing genetic predisposition, hormonal fluctuations, ultraviolet (UV) radiation exposure, and other environmental factors. Among these, hormonal influences, particularly the surge in estrogen levels during pregnancy, have long been recognized as pivotal contributors to the development and exacerbation of melasma. Estradiol, the predominant estrogen hormone, undergoes substantial elevation during pregnancy, reaching peak concentrations in the second and third trimesters. This surge in estrogen levels coincides with the onset and exacerbation of

melasma, suggesting a potential causal relationship [4,5,6]. The pathogenesis of melasma involves complex interactions between hormonal, genetic, and environmental factors. Estrogen, known for its melanogenic properties, is believed to stimulate melanocyte activity and melanin synthesis, leading to the characteristic hyperpigmentation observed in melasma. Furthermore, estrogen enhances the expression of melanogenic enzymes and receptors, amplifying the melanogenesis process [7].

Despite considerable research into the pathophysiology of melasma, the precise mechanisms by which estrogen influences melanocyte function and pigment production remain incompletely understood. Elucidating the role of estrogen, particularly estradiol, in the pathogenesis of melasma is crucial for developing targeted therapeutic approaches and improving clinical management strategies [8,9].

This study aimed to analyse the association between serum estradiol hormone levels and melasma in pregnant women. By analyzing serum estradiol levels in pregnant women with melasma compared to healthy controls, we seek to delineate the relationship between hormonal fluctuations and the development of melasma during pregnancy. Understanding the hormonal basis of melasma may offer valuable insights into its prevention, management, and treatment, ultimately alleviating the burden of this distressing condition on affected individuals.

Materials and Methods

Study Design and Participants: This study employed a cross-sectional design conducted over 2 years between May 2021 to April 2023and recruited pregnant women attending OPD of Obstetrics and Gynaecology of Tertiary care center, North India, for routine ANC check-up. Using convenient sampling techniqueA total of 97 pregnant women diagnosed with melasma and 95 healthy pregnant controls without melasma were enrolled. Inclusion criteria comprised pregnant women aged 18-35 years with singleton pregnancies in third trimester and without a history of dermatological disorders or hormonal therapy. Exclusion criteria included women with a history of photosensitivity disorders, autoimmune diseases, or endocrine disorders. Written informed consent was obtained from all participants before enrollment.

Clinical Examination: All participants underwent a comprehensive clinical examination conducted by dermatologists with expertise in pigmented lesions. The examination included meticulous visual inspection under both natural light and Wood's lamp examination using a handheld Wood's lamp emitting ultraviolet (UV) light with a wavelength of 365 nanometers. This dual examination technique allowed for the comprehensive evaluation of the extent and distribution of hyperpigmented patches on the face, forehead, cheeks, nose, upper lip, and chin.

Additionally, the severity of melasma was meticulously assessed using the Melasma Area and Severity Index (MASI). The MASI is a validated scoring system that quantifies the severity of melasma based on the extent and darkness of pigmented lesions in specific facial regions. Dermatologists used a standardized method to calculate the MASI score by assessing the percentage involvement and intensity of pigmentation in four facial regions: the forehead, cheeks, nose, and chin. Each region was assigned a numerical score based on the severity of pigmentation, with higher scores indicating more severe melasma. The total MASI score, derived from the sum of individual regional scores, provided an objective measure of the overall severity of melasma for each participant.

Measurement of Serum Estradiol Levels: Fasting venous blood samples were collected from each participant during their routine prenatal visits. Blood samples were drawn into vacutainer tubes without anticoagulants and allowed to clot for 30 minutes at room temperature. The samples were then centrifuged (RemiElektrotechnik Limited, India) at 3000 revolutions per minute (rpm) for 10 minutes to obtain serum, which was subsequently aliquoted into labeled cryovials and stored at -80°C until further analysis.

Serum estradiol levels were quantified using a QuicKey Pro Human E2(Estradiol) ELISA Kit (uses the Competitive-ELISA principle), following the manufacturer's instructions. In brief, serum samples were thawed at room temperature and mixed gently to ensure homogeneity. An enzyme-linked immunosorbent assay (ELISA, Elabscience®, United States) kit specific for estradiol was employed for hormone quantification. Standard curves were generated using known concentrations of estradiol standards provided with the kit. Absorbance readings were obtained using a microplate reader at the appropriate wavelength specified by the manufacturer. The concentration of estradiol in each serum sample was extrapolated from the standard curve and expressed in picograms per milliliter (pg/mL).

Statistical Analysis: Statistical analysis was performed using SPSS version 20.0. Descriptive statistics were calculated for demographic and clinical characteristics of the study participants. Continuous variables were expressed as means ± standard deviations (SD). Categorical variables were presented as frequencies and percentages.The Student's t-test was employed to compare serum estradiol levels between pregnant women with

melasma and healthy controls. Pearson correlation analysis was conducted to explore the relationship between serum estradiol levels and the severity of melasma, as assessed by the Melasma Area and Severity Index (MASI) [10]. Correlation coefficients (r) were calculated to determine the strength and significance of the association between these variables.A p-value <0.05 was considered statistically significant.

Ethical Considerations: This study was conducted following the principles outlined in the Declaration of Helsinki and approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment, and measures were taken to ensure confidentiality and anonymity throughout the study.

Results

In our study, the demographic characteristics of the study participants were comparable between the Melasma (n=97) and Control (n=95) groups.

No significant differences were observed in age (29.5 ± 4.2 years vs. 30.1 ± 3.9 years, p = 0.306) and gestational age (25.8 ± 3.1 weeks vs. 26.5 ± 2.8 weeks, p = 0.102). Residence (urban vs. rural) and parity also showed no significant differences between the groups (p = 0.368 and p = 0.230, respectively) (Table 1).

Table 1: Demographic Characteristics of Study Participants

Characteristic	Melasma Group (n=97)	Control Group (n=95)	p-value
	Number (%), Mean ± SD		
Age (years)	29.5 ± 4.2	30.1 ± 3.9	0.306
Gestational Age (weeks)	25.8 ± 3.1	26.5 ± 2.8	0.102
Residence			
Rural	44 (45.4%)	37 (38.9%)	0.368
Urban	53 (54.6%)	58 (61.1%)	
Parity	2.7 ± 1.1	2.9 ± 1.2	0.230

In our study, among the melasma cases, the majority belonged to Fitzpatrick Skin Type IV (24.7%), followed by Type V (22.7%) and Type III (18.6%). Type II accounted for 12.4% of the participants, while Types I and VI constituted 8.2% and 13.4%, respectively. These findings reflect a diverse representation of skin types within the study population, ranging from very fair to dark brown to black skin tones (Table 2).

Table 2: Distribution of Fitzpatrick Skin Types in cases (N=97)

Fitzpatrick Skin Type	Description	Number (%)
Type I	Very fair skin, always burns easily, never tans.	8 (8.2%)
Type II	Fair skin, burns easily, tans minimally.	12 (12.4%)
Type III	Fair to medium skin, sometimes burns, gradually tans.	18 (18.6%)
Type IV	Medium skin, rarely burns, tans with ease.	24 (24.7%)
Type V	Darker skin, very rarely burns, tans easily and substantially.	22 (22.7%)
Type VI	Dark brown to black skin, never burns, deeply pigmented.	13 (13.4%)

In our study, among the melasma group, the majority of participants (41.2%) fell into the Mild category, with MASI scores below 8. Moderate melasma was observed in 36.1% of participants, with MASI scores ranging from 8 to 12. Severe melasma, characterized by MASI scores between 13 and 20, was present in 18.5% of participants. A smaller proportion of participants (4.1%) had Very Severe melasma, with MASI scores exceeding 20. The mean MASI score was 18.7 ± 4.7 (Table 3).

Table 3: Classification of Melasma Severity Based on MASI Score

MASI Score Range	Melasma Severity Classification	Number (%)
<8	Mild	40 (41.2%)
8 to 12	Moderate	35 (36.1%)
13 to 20	Severe	18 (18.5%)
> 20	Very Severe	4 (4.1%)

In the Melasma Group (n=97), the mean serum estradiol level was 125.6 pg/mL (±20.3), significantly higher compared to the Control Group (n=95) with a mean of 118.2 pg/mL (±18.9) (p = 0.009).When considering melasma severity, participants with Very Severe melasma (n=4) exhibited the highest mean serum estradiol level of 140.5 pg/mL (±23.2), followed by those with Severe melasma (n=18) with a mean of 125.8 pg/mL (±20.1), and Moderate melasma (n=35) with a mean of 120.3 pg/mL (±19.5). Participants with Mild melasma (n=40) had the lowest mean serum estradiol level of 110.7 pg/mL (±18.8). The differences in serum estradiol levels across the melasma severity classifications were statistically significant (p = 0.004) (Table 4).

Table 4: Serum Estradiol Levels in Study Participants

Variables	Serum Estradiol Level (pg/mL)Mean ± SD	p-value
Group		
Melasma Group (n=97)	125.6± 20.3	0.009
Control Group (n=95)	118.2± 18.9	
Melasma Severity Classification		
Very Severe (n=4)	140.5±23.2	0.004
Severe (n=18)	125.8± 20.1	
Moderate (n=35)	120.3±19.5	
Mild (n=40)	110.7±18.8	

Correlation analysis showed that there is a positive correlation between age and serum estradiol levels ($r = 0.24$, $p = 0.032$), suggesting that older individuals tend to have higher serum estradiol levels. While there is a positive correlation between gestational age and serum estradiol levels, it is not statistically significant ($r = 0.18$, $p = 0.101$). The correlation between parity and serum estradiol levels is very weak and not statistically significant ($r = 0.05$, $p = 0.502$), indicating that parity does not significantly influence serum estradiol levels in this study population. However, there is a moderate positive correlation between melasma severity and serum estradiol levels ($r = 0.29$, $p = 0.025$), suggesting that individuals with more severe melasma tend to have higher serum estradiol levels (Table 5).

Table 5: Correlation analysis Between Serum Estradiol Levels, and other variables

Variables	Serum Estradiol Levels	P value
	Pearson correlationcoefficient (r)	
Age (n=192)	0.24	0.032
Gestational age (n=192)	0.18	0.101
Parity (n=192)	0.05	0.502
Melasma severity (n=97)	0.29	0.025

Discussion

Melasma, a common hyperpigmentation disorder affecting pregnant women, has been linked to hormonal fluctuations, particularly elevated levels of estradiol [11]. Our study aimed to investigate the relationship between serum estradiol levels and melasma severity in pregnant women, along with exploring potential associations with demographic and clinical factors.

Our findings revealed a significant positive correlation between serum estradiol levels and melasma severity, indicating that higher estradiol levels may contribute to the development or exacerbation of melasma during pregnancy. This is consistent with previous studiesby Gopichandani et al., and Goglia et al., highlighting the role of estrogen in melanogenesis and pigmentation regulation [12,13]. Estradiol stimulates melanocyte activity and melanin production, which can lead to hyperpigmentation, including the characteristic brown patches seen in melasma.

Interestingly, we observed significant differences in serum estradiol levels between the Melasma Group and Control Group, with the former exhibiting higher estradiol levels. This suggests a potential association between elevated estradiol levels and the presence of melasma and was also observed in the studies by Moin et al., and Miranti et al., [14,15]. However, the causal relationship between estradiol and melasma remains complex and multifactorial, involving interactions with other hormones, genetic predisposition, and environmental factors such as sun exposure [16,17].

Our study also explored the influence of demographic and clinical factors on serum estradiol levels and melasma severity. While age showed a significant positive correlation with serum estradiol levels, gestational age and parity did not exhibit statistically significant correlations. These findings suggest that age-related hormonal changes may play a role in modulating serum estradiol levels, but the impact of pregnancy-related factors such as gestational age and parity may be less pronounced in this context [18,19,20]. The distribution of Fitzpatrick Skin Types in our study population reflects the diversity of skin tones among pregnant women with melasma. This underscores the importance of considering individual skin characteristics in melasma management and treatment approaches [21].

Limitations

Despite the valuable insights provided by our study, several limitations should be acknowledged. The cross-sectional design limits our ability to establish causal relationships between estradiol levels and melasma severity. Longitudinal studies are needed to elucidate the temporal dynamics of hormonal

changes and melasma development throughout pregnancy. Additionally, factors such as dietary habits, skincare practices, and genetic predisposition were not fully explored in our study and warrant further investigation.

Conclusion

Our study reveals a significant positive correlation between serum estradiol levels and melasma severity in pregnant women, indicating a potential role of elevated estradiol levels in melasma development or exacerbation. While age correlates significantly with serum estradiol levels, gestational age and parity do not show significant associations. The diverse presentation of melasma across different skin tones underscores the importance of personalized treatment strategies. Despite limitations such as the cross-sectional design, our findings contribute to understanding the complex relationship between hormonal fluctuations and melasma severity during pregnancy. Future research should focus on elucidating underlying mechanisms and developing targeted interventions for melasma management.

References

1. Bolanca I, Bolanca Z, Kuna K, et al. Chloasma-the mask of pregnancy. Coll Antropol. 2008;32:139–41.
2. Purim KS, Avelar MF. Photoprotection, melasma and quality of life in pregnant women. Rev Bras Ginecol Obstet. 2012;34:228–34.
3. Tzouveka E. Epidemiology and Risk Factors of Melasma. J Pigment Disord. 2014;2:1-3.
4. Verma K, Kumre K, Sharma H, Singh U. A Study of Various Etiological Factors in the Causation of Melasma. Indian J Clin Exp Dermatol. 2015;1:28-32.
5. Watson CS, Jeng YJ, Kochukov MY. Non-genomic actions of estradiol compared with estrone and estriol in pituitary tumor cell signaling and proliferation. Federat Am Soc Exp Biol J. 2008;22:3328-36.
6. Prossnitz ER, Barton M. Estrogen biology: New insights into GPER function and clinical opportunities. Mol Cell Endocrinol. 2014;389:71-83.
7. Ortonne JP, Arellano I, Berneburg M, et al. A global survey of the role of ultraviolet radiation and hormonal influences in the development of melasma. J EurAcad Dermatol Venereol. 2009;23:1254–62.
8. Damevska K. New Aspects of Melasma. Serbian JDermatol Venereol. 2014;6:5-18.
9. Falah N. Estriol review: Clinical applications and potential biomedical importance. Clin Res Trials. 2015;1:29-33.
10. Rodrigues M, Ayala-Cortés AS, Rodríguez-Arámbula A, Hynan LS, Pandya AG. Interpretability of the Modified Melasma Area and Severity Index (mMASI). JAMA Dermatology. 2016;152:1051-2.
11. Kumar S, Mahajan BB, Kamra N. Melasma in North Indians: A clinical, epidemiological and etiological study. Pigment Int. 2014;1:95-99.
12. Gopichandani K, Arora P, Garga U, et al. Hormone Profile of Melasma in Indian Females. Pigment Int. 2015;:85-90.
13. Goglia L, Bernacchi G, Melasma GS. A Cosmetic Stigma During Pregnancy. J Pigment Disord. 2014;1:1–4.
14. Moin A, Jabery Z, Fallah N. Prevalence and awareness of melasma during pregnancy. Int J Dermatol. 2006;45:285–8.
15. Miranti A, Anwar A, Djawad K, Pattelongi I, Wahab S, Abdullah N. Analysis Level of Serum Estradiol Hormone of Pregnant Women with Melasma. Am J Clin Exp Med. 2016;4(2):26-29.
16. Damevska K. New aspects of melasma. Serb J Dermatol Venereol. 2014;6:5-18.
17. Jadotte YT, Schwartz RA. Melasma: Insights and Perspectives. Acta Dermatovenerol Croat. 2010;18:124-9.
18. Hexsel D, Rodrigues TC, Dal'Forno T, Zechmeister-Prado D, Lima MM. Melasma and pregnancy in southern Brazil. J EurAcad Dermatol Venereol. 2009;23:367–8.
19. Lakhdar H, Zouhair K, Khadir K, et al. Evaluation of the effectiveness of a broad-spectrum sunscreen in the prevention of chloasma in pregnant women. J EurAcad Dermatol Venereol. 2007;21:738–42.
20. Handel AC, Lima PB, Tonolli VM, Miot LD, Miot HA. Risk factors for facial melasma in women: a case-control study. Br J Dermatol. 2014;171:588-94.
21. Handel AC, Miot LDB, Miot HA. Melasma: a clinical and epidemiological review. An Bras Dermatol. 2014;89:771-82.