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Original Article

Evaluation of Serum Estrogen, Progesterone, Prolactin and Testosterone in Patients of Melasma

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ABSTRACT

Objective: To evaluate the estrogen, progesterone, Prolactin and testosterone serum levels in melasma patients.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Dermatology Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Jul to Dec 2020.
Methodology: A total of 40 patients with melasma and 40 without melasma were included in this study. The study comprised female melasma patients aged 20 to 50 years old. All participants were tested for serum estrogen, progesterone, Prolactin and testosterone levels using immunoassay in the follicular phase (9th day) of the menstrual cycle.
Results: The statistically significant increase in serum progesterone (p=0.001) was found in patients with melasma. A significant decrease in prolactin levels (p=0.0001) was found in patients with melasma. No association was found between Group-1 and Group-2 regarding serum estradiol and testosterone (p=0.070 and p=0.461 respectively)
Conclusion: Patients with melasma have increased progesterone levels and decreased serum prolactin levels.

Keywords: Estrogen, Melasma, Progesterone, Prolactin, Testosterone.

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INTRODUCTION

Melasma (chloasma) is an acquired hyperpigmentation identified by patchy or confluent grey to brown macules occurring commonly over the face.[1] Females and darker skin types are more frequently affected. The overall prevalence of melasma ranges widely from 1-50%.[2,3] Three facial patterns of melasma include centrofacial, malar and mandibular. Centrofacial pattern comprises 50-80% of cases, and it is present over the upper lip, nose and forehead, exclu-ding the chin and cheeks.[4] The malar pattern is present over the cheeks; on the other hand, the mandibular pattern is present over the chin and jawline. There are four types of melasma based on the depth of pigment deposition as determined by wood lamp examination.[5,6]

The fact that melasma is more common in women suggests that female sex hormones may play a role in the pathogenesis of melasma.[7] Both estrogen receptors Alpha (ER-α) and Beta (ER-β) are expressed in human skin. Immunohistochemistry reveals higher estrogen and progesterone receptor expression in hyperpigmented lesions than in normally pigmented skin. Both estrogen and progesterone increase the number of melanocytes and their tyrosinase activity.[8] Progesterone, on the other hand, has also been shown to have considerable inhibitory effects on the proliferation of melanocytes in monoculture.[9] So far, it has conflicting reports on the development of melasma. The role of testosterone and Prolactin in the pathogenesis of melasma in female patients is unknown. However, low testosterone levels with increased luteinising hormone are associated with melasma in male patients suggesting testicular resistance.[10] The study is aimed to evaluate levels of serum estrogen, progesterone, Prolactin and testosterone in patients of melasma and address their role in treatment.

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METHODOLOGY

The comparative cross-sectional was conducted at the Dermatology Outpatient Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from July and December 2020 after approval by the Ethical Committee of Fauji Foundation Hospital, Rawalpindi (Ref No 496/RC/FFH/RWP). The sample size was calculated using the WHO sample size calculator, keeping the population proportion of melasma at 6%.[3]

Inclusion criteria: Females from 20-50 years of age with melasma, diagnosed based on clinical examination.

Exclusion criteria: Pregnant, lactating and postmenopausal females, patients on treatment for melasma, medications that affect pigmentation (combined oral contraceptives, hormone replacement therapy), systemic diseases causing melasma (thyroid disorders, diabetes, Cushing's syndrome etc.).

The study comprised two Groups, 40 with melasma (Group-1) and 40 without (Group-2). In addition, non-probability consecutive sampling was carried out for data collection. and informed written consent was taken from all participants. The participants' complete medical history and clinical examination were carried out. Personal data like onset, duration and family history of melasma, marital status, onset in pregnancy, use of cosmetics and veil, history of diseases and drugs that affect hormonal blood levels, and length and frequency of sun exposure were recorded. The type of skin and pattern was noted. The depth of melasma was examined using a wood lamp.

Serum estradiol, progesterone, Prolactin and testosterone levels were tested in the Fauji Foundation Hospital laboratory using VITROS ECIQ immunodiagnostic system and CHEMILUMINESCENCE immunoassay after four cc of venous blood was obtained under aseptic conditions. Tests performed were free of cost. The sample was taken during the follicular phase (9th day) of the menstrual cycle. Normal values of hormones in the follicular phase of the menstrual cycle in females are Estradiol: 147-1285 pmol/l, Progesterone: 0.318-3.18 nmol/l, Prolactin < 3ng/ml, Total testosterone: 0.198-2.67 nmol/l.[11,12]

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

In our study, 12(30%) patients had low, and 28(70%) had normal estradiol levels in Group-1 while 2(5%) had low and 38(95%) had normal estradiol levels in Group 2.

The mean age of onset was 29.98±6.553 years. The duration of melasma ranged from 1-10 years. The mean duration of melasma was 4.28±2.572 years. Twenty-four patients (60%) had the onset of melasma in pregnancy. 23(57.5%) had a positive family history of melasma. Twenty-one patients (52.5%) had dentofacial melasma, whereas 17(42.5%) had a malar type, 2(5%) had a mandibular pattern, 20(50%) had dermal melasma, 17(42.5%) had an epidermal type, and 3(7.5%) patients had mixed types of melasma. A significant difference was found between Group-1 and Group-2 for Prolactin and progesterone (*p*=0.0001 & 0.001, respectively). No significant difference was found between Group-1 and Group-2 regarding estradiol and testosterone (*p*=0.070 & 0.461, respectively) shown in Table.

Table: Comparison of Serum Estradiol, Progesterone, Prolactin and Total Testosterone Between the Study Groups (n=80)

Parameters	Study Groups		*p*-value
	Group-1 (n=40)	Group-2 (n=40)	
Serum Estradiol (pmol/L), n(%)			
Low	12(30%)	2(5%)	0.070
Normal	28(70%)	38(95%)	
High	0(0%)	0(0%)	
Serum Progesterone (nmol/L) n(%)			
Low	0(0%)	0(0%)	0.001
Normal	25(62.5%)	40(100%)	
High	15(37.5%)	0(0%)	
Serum Prolactin (ngm/ml) n(%)			
Low	19(47.5%)	0(0%)	0.0001
Normal	20(50%)	40(100%)	
High	1(2.5%)	0(0%)	
Serum Total Testosterone (nmol/L) n(%)			
Low	32(80%)	2(5%)	0.461
Normal	8(20%)	34(85%)	
High	0(0%)	4(10%)	

DISCUSSION

This study showed that patients with melasma had increased progesterone levels and decreased serum prolactin levels. In addition, there was a significant difference in melasma patients regarding onset in pregnancy. 60% of patients had onset in pregnancy in our study. Ortonne *et al.*[11] also reported the onset of melasma in pregnancy in 68% of patients during the global survey. Similarly, a previous study.[12] also reported that the most common triggering factors for melasma were pregnancy (36.4%) and oral contraceptives (16.2%).

The mean age of onset in this study was 29.98±6.553 years which complies with other studies done in the past.[3] The average age of onset of melasma among Brazilian females was 27.5±7.8 years, according to a study.[12] In our study, 57.5% of patients had a positive family history of melasma, consistent with a previous study.[13] in which 50% had a positive family history of melasma. The most common pattern in our study was centrofacial, however, another study conducted in Pakistan.[14] reported the malar pattern as the most common melasma pattern. Estradiol has conflicting results in the development of melasma. In studies conducted in India.[15] and Puerto Rico.[16] female melasma patients had significantly lower levels of estradiol which supports the theory that mild ovarian

dysfunction is a major contributor to the development of melasma. Handa *et al.*[17] did not observe an association between serum estradiol levels and melasma in male patients. Similarly, Hassan *et al.*[18] reported no association. There was a significant decrease in serum levels of progesterone in patients with melasma in a study conducted in India.[15] Our study showed a significant increase in progesterone in patients with melasma. Progesterone is a key factor in the development of melasma because it can develop in postmenopausal women who are administered progesterone but not in those who are given estrogen alone.[19]

A study on females in India showed decreased levels of total testosterone in melasma. However, our study showed no difference between serum testosterone levels and melasma. A study conducted in India ,[15] and Pakistan,[14] reported no association between serum prolactin and melasma. However, our study showed significantly decreased prolactin levels in patients of melasma which is consistent with the study by Hasan *et al.*[18] who found decreased levels of Prolactin in patients of melasma.

Our study showed the role of progesterone in the etiopathogenesis of melasma, as shown in previous study,[17] which reported the development of melasma in postmenopausal females who were administered progesterone but not in those who were only given estrogen. Although estrogen is important in the pathogenesis of melasma, our study showed no association between estrogen levels and the development of melasma.[19] Estrogen receptor sensitivity in both the hypothalami pituitary and the melanocytes in the target region may have a role in the development of melasma, according to the findings.[18] However, more research is required to validate estrogen's role in melasma fully.

Serum progesterone and Prolactin play a vital role in melasma, but more research on a broader scale is needed. Furthermore, larger sample size studies are required to corroborate the findings and monitor hormone levels in different menstrual cycle phases.

Our study showed that increased serum progesterone and decreased serum prolactin contribute to the development of melasma. Therefore, it can be used as a basis for future research into the effects of Prolactin and anti-progesterone therapies in treating melasma.

LIMITATIONS OF STUDY

The limited patient follow-up, COVID-19 OPD restrictions and tests were only conducted during the follicular phase of the menstrual cycle. To analyse the relationship between hormonal levels and melanogenesis, serum levels of melanocortin-stimulating hormones and adrenocorticotropic hormone should also be measured; however, this could not be done due to financial constraints.

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CONCLUSION

Patients with melasma have increased levels of serum progesterone and decreased levels of serum prolactin, while normal levels of estradiol and total testosterone.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SK & FUR: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SWQ & RNK: Conception, study design, drafting the manuscript, approval of the final version to be published.

AJ & MJY: Critical review, interpretation of data, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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