

## Correlation of Estradiol and Estriol Serum Levels to Melasma Severity in Pregnant Women

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### ABSTRACT

Melasma is also known as chloasma or mask of pregnancy because it shows during pregnancy as a symmetrical hyperpigmented lesion. Melasma patients in Indonesia was estimated to be 0.2–4% of all dermatology patients. In Saiful Anwar General Hospital Malang, East Java, Indonesia, melasma was found in 338 of 9736 dermatology patients per year (3.4%) in 2014, and is the seventh most common diagnosis in dermatology clinic. In 2015, melasma incidence was declined to 226 of 8310 patients per year and not included in the top ten most common dermatology diagnoses. The current data from Saiful Anwar General Hospital dermatology clinic in 2016 stated that melasma patient was 185 of 7945 patients per year (2.3%). Melasma etiopathogenesis included the genetic factor, ultraviolet exposure, and hormonal activity. The most common aetiology was the combination of genetic, hormonal status and ultraviolet radiation. Hormonal factors were pregnancy, oral contraception of estrogen replacement therapy, ovarian cancer, thyroid or ovary dysfunction, cosmetics, nutrition, phototoxic and photoallergic drugs, hepatic diseases, parasitosis and antiepileptic drugs. Pregnancy was related to several characteristic skin changes, one of them being chloasma that was related to hormonal change. Estrogen surge was the critical factor that explained hyperpigmentation in melasma [7]. HLs was caused by the increase of  $\alpha$ -MSH (melanocyte stimulating hormone) expression in keratinocytes [8,9]. Estrogen is a steroid hormone with ten carbon atoms formed mainly by androstenedione. There are three types of estrogen with more than 400 functions in the body. The three estrogen types are estrone (E1), estradiol (E2) and estriol (E3). Biologically, estradiol is the most active form. The ratio of a biological effect of those three hormones are E2:E:E3=10:5:1. Estradiol potency is twelve times the potency of estrogen and eight times the

potency of estriol; therefore, estradiol is said to be the main estrogen. A study by Gopichandani et al. supported the hypothesis that the main pathogenesis of melasma was estradiol. HLs was proven by the high estradiol level in pregnant women with melasma compared to those without melasma. The other forms of estrogen such as estriol and estrone also affected the cytoplasm and the main estrogen receptor known to be expressed in the melanocyte. Especially in the third trimester, the high level of estriol and estradiol was related to the high level of MSH, which caused tyrosinase and dopachrome tautomerase production; this sequence led to melanogenesis and melasma. Melasma Area Severity Index (MASI), compiled by Handel et al. in 1994, was used to measure the clinical severity of melasma. The total score was related to the highest probability of clinical severity of melasma.

There were 25 pregnant women aged 15–49 years old with melasma included as study sample. The mean age of the sample was 32.5 years old (SD 7.77). Majority of the subjects came from age group 31–40 years old and in the third trimester. There were 21 subjects (84%) in the first trimester, three subjects (12%) in the second trimester and one subject (4%) in the first trimester. As much as 18 subjects (72%) were from Pasuruan and seven subjects (28%) were from Malang. Sun exposure was noted in 13 subjects (52%) with the positive family history of melasma and 12 subjects (48%) without the family history of melasma. Based on ethnic group, Javanese was the most common ethnic group in our study, which was 16 subjects (32%), followed by Madura (8 subjects, 16%) and Bugis (1 subject, 2%). Comorbidities found in the subjects were preeclampsia (4 subjects, 16%), hyperemesis gravidarum, ventricular septal defects, asthma, macrosomia, condyloma acuminata, anemia and hepatitis B. Epidermal melasma was

the most common type of melasma in our study (17 subjects, 68%), followed by dermal type (3 subjects, 12%) and mixed type (5 subjects, 20%). Table 1 showed that there was no statistical difference in age group, place of origin, ethnic group, pregnancy stage, sun exposure duration, positive family history, comorbidities, melasma type and melasma severity score ( $p > 0.05$ ) based on Chi-square test

Melasma lesion was categorized into two basic types, i.e. epidermal and dermal type. In epidermal type, there was melanin deposition in the basal and suprabasal layer of the epidermis, and melanocytes were pigmented with many dendrites. In dermal type, there was perivascular melanophages at the superficial dermal and deep dermal layer, with little pigmentation in the epidermal layer [18]. In our study, the most common melasma type was epidermal (68%), mixed (20%), and dermal (12%). The mean estradiol level, estradiol level and MASI score were highest in dermal type melasma, although it was statistically insignificant. This finding differed from a study result of Miranti et al. that reported mixed type was the most common type. The study explained that melasma type was correlated with the binding of estrogen receptor and estradiol.

In this study, there were several shortcomings that potentially caused bias. The study sample size was too small so that a bigger sample size for a future study will be needed. The method in measuring melasma severity was subjective and depended on the examiner; although, this risk was reduced by using three examiners. A more objective method to determine melasma severity was needed, such as a Mexameter or chroma meter. Besides, melasma was a localized hyperpigmentation disorder in the face, but the estradiol and estradiol measurement was taken from a blood sample. Therefore, histopathology studies may be needed. Subjectivity and study methods, including sample extraction, measurement, data gathering, and analysis, could affect the study validity.

Serum estradiol level was not correlated with melasma severity in pregnant women. This

correlation was not found with estradiol level. Estradiol and estradiol level had 24.4% impact on MASI score; the rest of 75.6% was the result of other variables not included in this study, such as genetic factor or sun exposure.