Biophysical properties of skin in pregnancy: A controlled study

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Abstract
Aim: It is well-known that there are some physiologic changes in the skin during pregnancy. In this study, we aimed to compare the biophysical changes in the skin of pregnant women with healthy non-pregnant women's skin.

Material and Methods: A total of 60 pregnant women in the third trimester and 30 age-matched healthy volunteers as a control group were included in our study. Stratum corneum hydration, erythema, melanin of forearm and sebum content of forehead of skin were measured with noninvasive cutometer and compared between groups with the use of IBM's SPSS software (SPSS version 17.0 for Windows).

Results: We found a moderate but significant disturbance of melanin and erythema on the forearm between pregnant women and healthy volunteer women. There was no significant correlation between baby gender and skin parameters of pregnant women.

Discussion: We conclude that even the clinically normal-appearing skin of pregnant women compared with healthy volunteers have increased melanin secretion and erythema properties.

Keywords
Erythema; Humidity; Melanin; Pregnancy; Sebum; Striae distensae

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Introduction
The period during which an organism experiences immunological, metabolic, endocrine and vascular changes in a complex but a perfect balance is called pregnancy [1,2]. In normal pregnancy, these are characterized by protein hormones such as high elevations of human chorionic gonadotropin (HCG), somatomammoprotein, chorionic thyrotropin, chorionic corticotropin as well as prolactin, progesterone, estrogen hormones and mediators that completely alter the body's functions [3]. Although pregnancy changes vary from person to person, many women find that their skin is one of the most noticeable affected areas [4]. However, it is not exactly known how pregnancy hormones affect the physiology, immunology and inflammatory response of the skin [5]. The skin constitutes the largest non-reproductive organ targeted by estrogen. Even if the effects of estrogen on the skin are still unclear, it is known that in women, declining estrogen levels are associated with a variety of cutaneous changes. Skin function and quality with various stages of life accompany the changes in estrogen production and it is clear that estrogen replacement can symptomatically treat many menopausal symptoms [6]. Evidence suggests that skin biophysical properties in predicting and developing of disease are important for appropriate skincare [7]. It is critical to consider the influence of genetic and environmental factors on most of the skin characteristics [8]. Physiological skin changes due to pregnancy are often ignored by health professionals [3]. There are few comprehensive studies on the physiological functions of the skin during pregnancy. In this study, we aimed to determine physiologic barrier changes of the skin, comprising melanin, stratum corneum (SC) hydration, erythema, surface sebum content at the pregnancy time period.

Material and Methods
Study subjects
This cross-sectional controlled clinical study was performed in our hospital and study protocol was approved by the ethics committee (2013/101) and was performed according to the Declaration of Helsinki principles. All of the participants were instructed about the investigation and informed consent was obtained from each one.
Sixty primiparous pregnant women whose ages ranged from 18 to 40 years and 30 healthy volunteers whose ages ranged from 20 to 38 years old were enrolled in the study. Pregnant women who were in the third trimester of their pregnancy, experienced pregnancy for the first time and single pregnancy were included in the study. This period was chosen because physiological changes in pregnancy were seen more in the 3rd trimester. Of the subjects, 55 had Fitzpatrick’s skin type III, three had II and two had IV.
Participants having the habit of smoking, alcohol etc., getting systemic and topical medicine treatment (except iron and vitamin supplements), suffering from systemic or dermatologic disease, applying oil (almond, olive oil, etc.) or moisturizers were excluded from the study. No skin care products had been applied to the measured sites for at least 24 hours prior to the measurement, and the measured sites had not been washed with a cleanser for at least 2 hours prior to the measurement. Skin biophysical measurements were performed at two different locations of the body, i.e. the right volar surface of the forearm (hydration, melanin, erythema) and in the middle of the forehead (sebum) by staff physician (RI). Detailed medical history of pregnant women who met the inclusion criteria of the study was taken, the data of these women such as dermatological examination, received total weight gain, waist circumference, the gender of their babies (depending on the results late USG) and striae distensae (SD) existence were recorded.

Noninvasive measurements of the stratum corneum
The epidermal barrier function was measured using the device MPA 580 (Courage & Khazaka, Germany) with respective probes of Sebumeter, Corneometer, Mexameter. The capacity of stratum corneum hydration was measured using the Corneometer 825, the measuring principle of which is based on the high degree of polarity of the water molecule because it uses the high dielectric constant of water for analyzing the water-related changes in the electrical capacitance of the skin. The measuring range of the device is 0 – 130 arbitrary units (a.u.). The amount of the targeted skin sebum secretion was measured using the Sebumeter 815; the measuring principle of which is based on the difference of light intensity through a plastic strip in contact with the skin for 30 seconds to indicate the amount of absorbed sebum. The measuring range of the device is 0 – 350 μg/cm2.

Erythema and skin pigmentation were measured using Mexameter 18 probe; the measurement of which is based on the absorption and reflection. The Mexameter shows that the melanin and erythema values range from 0 to 999. The mean value of three recordings for each participant was used for analysis. Measurements were obtained between 9:00 am and 12:00 am due to diurnal variations and measured in a room at a temperature of 20–25°C and relative humidity of 30–40%.

Statistical Methods
Categorical variables were described in frequencies and percentages; numerical variables were described in means and standard deviations or medians and IQRs (interquartile range). The Shapiro-Wilk test was used to check the normality distribution of numerical variables. Two independent means were compared with the Student’s t-test, and two independent medians were compared using the Mann-Whitney U test in pregnant women and controls. The relationship between numeric parameters was tested by the Spearman Correlation Analyses. A p-value less than 0.05 was accepted statistically significant. All analysis was conducted by SPSS17.0 statistical software.

Results
The baseline characteristics of the 60 pregnant women included in this study are shown in Table 1. A significant relation between pregnant women and a control group was determined in terms of the value of melanin and erythema (P<0.05). Erythema increase in pregnant women led to an increase in the level of melanin. No significant impairment in the skin sebum secretion and capacity of stratum corneum hydration were detected between pregnant and non-pregnant women (p >0.05) (Table 2). Overall, the Spearman’s rank test showed a positive linear correlation between skin melanin and erythema (r=0.586, p=0.002) (Figure 1), although linear correlation between skin
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The correlation between melanin and erythema in pregnant women:

Table 1. Characteristics of pregnant women

<table>
<thead>
<tr>
<th>Pregnant women (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (Median, IQR)</td>
</tr>
<tr>
<td>Weight gain (Median, IQR)</td>
</tr>
<tr>
<td>Waist circumference (Median, IQR)</td>
</tr>
<tr>
<td>Fetus sex (n, %)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Striae distensae(SD)(n, %)</td>
</tr>
<tr>
<td>Absent</td>
</tr>
<tr>
<td>Present</td>
</tr>
<tr>
<td>IQR: Interquartile range</td>
</tr>
</tbody>
</table>

Table 2. Comparison of age and index values between pregnant women and control group

| Age(Median, IQR) | 28(7.0) | 26(9.0) | 0.558 |
| Melanin index(Median, IQR) | 125.5(53.25) | 108.5(45.0) | 0.048 |
| Erythema index(Mean±SD) | 238.4±60.3 | 195.9±50.5 | 0.001 |
| Skin hydration index(Mean±SD) | 33.4±8.4 | 35.2±5.4 | 0.224 |
| Sebum index(Median, IQR) | 162.5(94.0) | 156.5(94.0) | 0.485 |
| SD:Standart deviation Skin hydration index:a.u Sebum index:μg/cm2 |

Table 3. Comparison of index values between pregnant women with and without SD

<table>
<thead>
<tr>
<th>Pregnant woman with SD(n=20)</th>
<th>Pregnant woman w/o SD (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanin index(Median, IQR)</td>
<td>124(51.5)</td>
</tr>
<tr>
<td>Erythema index(Mean±SD)</td>
<td>242.4±77.7</td>
</tr>
<tr>
<td>Skin hydration index(Mean±SD)</td>
<td>36.7±9.8</td>
</tr>
<tr>
<td>Sebum index(Median, IQR)</td>
<td>165(85.25)</td>
</tr>
</tbody>
</table>

Figure 1. The correlation between melanin and erythema in pregnant women

Figure 2. The correlation between melanin and skin hydration in pregnant women

melanin and hydration was negative (r = -0.414, p=0.001) (Figure2). SC hydration on the forearm in the pregnant women with SD was significantly different from that in the pregnant women without SD (p<0.05) (Table 3). When comparing index values between pregnant women with male and female fetus, this difference was not statistically significant.

Discussion

During pregnancy, physiologic skin changes are often markedly revealed because of the numerous metabolic, mechanical, and hormonal adjustments of this state. The most common physiologic changes are seen more in the 3rd quarter [3]. Physiologic changes in the skin during pregnancy can be complex and confusing [2].

In the present study, we found that physiological state of pregnancy had a significant effect on changes in basal skin physiology parameters especially melanin and erythema in the pregnant women at the third trimester rather than in non-pregnant healthy volunteer. These changes, especially melanin content are correlated with erythema and skin hydration. Hyperpigmentation in pregnancy is attributed to the increased output of some combination of pituitary, and ovarian hormones (melanocyte-stimulating hormone, estrogen, progesterone), and bioactive sphingolipids derived from the placenta. These hormones were thus suggested to be strong stimulants of melanogenesis [9]. Seite S et al. found 177±37 on the forehead, 193±34 on chine, 147±28 on the right malar area, 150±27 on the left malar area in pregnant women [10]. However, we found melanin value as 133.07±44.30 on the right inner forearm. Although we identify lower melanin value in our pregnant women, it was significantly higher than the control group. In this study, the average age of the group was younger (26 years) and all of them were having their first baby, single pregnancy, measured from forearm. These reasons may explain the low melanin level occurrence rate noticed in the study. Vascular changes during pregnancy frequently occur to a variable extent in all women. They are thought to be caused by high levels of circulating estrogens, angiogenesis factors associated with hyperkinetic circulation, the marked rise in blood volume, and genetic predisposition [9]. Vascular endothelial growth factor (VEGF) could have a direct influence on melanocyte behavior through its receptor on them [11]. Similarly, we found that skin parameters increased significantly especially erythema index and melanin index in pregnant women. Interestingly, we
found that the average erythema index of forearm is higher in the pregnant women with SD. Also, it may be explained that striae formation could be associated with erythema increase. We demonstrated that the skin erythema index was higher in pregnant women than control group but was not significantly different among pregnant groups.

SC hydration was essential to maintain the properties of cutaneous functions such as regulating epidermal proliferation, differentiation or inflammation [12]. The SC hydration status is known to be regulated mainly by water-soluble natural moisturizing factors chiefly consisting of amino acids, intercellular lipids and sebum lipids in the SC [13,14]. One study reported that elevated endogenous estrogen increased dermal hydroscopic qualities. The dermis contributes to the water-holding capacity through its content of hydrophilic glycosaminoglycans [15]. However, we found that the hydration status of the SC decreased in pregnant women. There may be several factors contributing to the reduced SC hydration in the pregnancy group. The increase of eccrine gland activity as a result of the hormonal effects of pregnancy can cause hyperhidrosis. Vasomotor change and hyperhidrosis in pregnancy may cause increased transepidermal water loss (TEWL) in our patients. Higher TEWL values are believed to indicate a compromised barrier function and increased dry skin [16]. Our study revealed a reduction in the degree of stratum corneum hydration in all pregnant women. Disruption of the epidermal barrier consisting in reducing humidity and increasing TEWL value and reductions of these natural moisturizers values may be responsible for the skin dryness are confirmed by pregnant women. Hydration of the skin is also influenced by ethnicity and environmental variations [17,18]. In this study, environmental factors can influence humidity, certain personal and habitual factors, such as the increased hyperhidrosis, wearing closed clothes, frequent bathing, frequent soaping of face and forearm. In spite of some contradictions, it is estimated that sebaceous gland function increases in the last period of pregnancy [9]. Normally, the effect of estrogen on the sebaceous gland secretion is blocked, but it suggested that the sebum excretion rate is in fact increases in pregnancy. It may be explained by the presence of unknown powerful sebotrophic factors [19]. Some factors such as hormones, age, sex, and ethnicity (race) could affect the sebum secretion [20]. In one study including 10 pregnant women, sebum excretion rates from forehead skin were measured during and after pregnancy. They have been determined minor fluctuations during the middle and last trimesters of pregnancy [19]. We found that sebum secretion increased in pregnant women compared to control groups, but it was not significant. Cunliff et al. reported that sebum excretion increases by 10% as local temperature increases by one degree Celsius [21]. There are regional differences in the skin parameters. Sebum secretion is especially higher on the forehead [22]. The resulting increase of sebum secretion due to increased metabolism with high temperature in pregnancy can be the cause of this situation. Overall, both our pregnant women and control group had higher sebum value. The difference may be due to measurement of the forehead, environmental factors and/or our subjects’ ethnicities. Undoubtedly, SC surface change in pregnancy may disrupt skin function and structure. Fluctuation in hormone levels in pregnancy will be reflected in the physiology of the skin, but it is impossible to predict precisely how individuals will react. The decrease in the SC hydration induced by pregnancy may be more serious in pregnant women without SD than in pregnant women with SD. The cause of SD in pregnancy is still unknown, but it is a combination of distension and adrenocortical activity, genetic factors. Skin distension may lead to excessive mast cell degranulation with subsequent damage of collagen and elastin [23]. In the study by Stamatas et al., SD sites were very slightly more hydrated compared to control skin [24]. Our pregnant women with SD showed an increased SC hydration, sebum, and erythema status, but it was only correlated with SC hydration. This, moisture and other unknown reasons may affect formation of collagen and elastin. Notably, pregnant women with SD showed also significantly positive correlation by increasing the waist circumference.

To our knowledge, this is the first study of its kind to provide evidence that physiological skin changes encompassed melanin, erythema, and skin surface lipids caused by pregnancy at the third trimester. These findings suggest that pregnancy is required for the exclusive homeostasis of the skin biophysical properties. The main limitation of this study is the limited number of subjects and it is not comparing the environmental and ethnic factors.

Conclusion
Our present study demonstrated that erythema and melanin content of the skin in pregnant women were statistically different from non-pregnant women. Moreover, these results suggest that special care should be given to the skin in pregnant women, particularly with hyperpigmentation prone skin. The use of regular sun blocking cream containing higher protection factor on sun-exposed part of body and moisturizers with lower water-based content may be more appropriate in pregnancy. Regarding skin sensitivity in pregnancy, in order to avoid striae distensae, formulation of oily skincare products should be recommended. Future research will hopefully shed light affecting on the skin function and structure of hormonal and physiologic changes during pregnancy.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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