Relationship between plasma adiponectin levels and cellulite

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INTRODUCTION
Cellulite is a local anatomic and metabolic disorder of the subcutaneous tissue, causing changes in body contours to become unesthetic so that it looks like an orange peel.1,2 Cellulite occurs in about 85–90% of women over 20 years. Cellulite can occur in all races but is more common in Caucasians than Asians.3 The causes of cellulite are multifactorial, but there are several hypotheses that cellulite can occur due to genetic factors, differences in sex, age, race, diet and hormones.4-6 The pathophysiology of cellulite is a complex process caused by the dysfunction of microcirculation, local fat accumulation, and changes in lymphatic drainage.5-8

Adiponectin is a hormone produced by adipose tissue which influences metabolism, endothelial function, inflammation and extracellular matrix deposition. The endocrine function of adiponectin can affect subcutaneous vascularization, which is the pathophysiology of cellulite.4,9-11 Histologically the appearance of cellulite was found to be in the extracellular matrix with enlarged fibrocollagenous fibers that lined the subcutaneous tissue.9,12,13 Adiponectin produced by adipose tissue accumulates in the extracellular matrix, and an increase in adiponectin levels can suppress the process of sclerotic fibrosis which is the pathophysiology of cellulite by inhibiting TGF-β signaling.5,14,25

However, research on this matter is still limited. Therefore, this study aims to determine the relationship between plasma adiponectin levels and cellulite.

METHODS
This study is an analytic observational study with a cross-sectional design involving 40 cellulite patients and 40 controls. Each patient underwent a history and dermatological examination. Then proceeded to assess plasma adiponectin levels from blood samples by ELISA test. These data were analyzed statistically using the Chi-square test.

RESULTS
In this study, the highest demographic characteristic of cellulite patients were considered a significant result. The exclusion criteria are pregnant and lactating women, hypertension, coronary heart disease, dyslipidemia and type 2 diabetes mellitus.

The ethical license was granted by the Health Research Ethics Committee, Faculty of Medicine, University of North Sumatra. History, clinical examination, and blood sample tests to check plasma adiponectin.

Plasma adiponectin levels were measured by using Human Adiponectin Elisa Kit Bioassay®, which determined the optical density of adiponectin using a spectrophotometer (Multiskan Thermo Scientific TM). Analysis in descriptive analysis, Chi-square test to determine the relationship between plasma adiponectin levels with cellulite where p < 0.05 was considered a significant result.

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ABSTRACT
Background: Decreased adiponectin levels as a humoral vasodilator in subcutaneous adipose tissue in the cellulite area are thought to cause microcirculation disorders and tissue hypoxia, ultimately a local fibrotic response and collagen strands (septa) resulting in the appearance of cellulite. Adiponectin accumulates in the extracellular matrix. It is suspected that an increase in adiponectin levels can suppress the process of sclerotic fibrosis, thereby inhibiting the formation of cellulite. This study aimed to determine the relationship between plasma adiponectin levels and cellulite.

Methods: This study is an analytic observational study with a cross-sectional design involving 40 cellulite patients and 40 controls. Each patient underwent a history and dermatological examination. Then proceeded to assess plasma adiponectin levels from blood samples by ELISA test. These data were analyzed statistically using the Chi-square test.

Results: In this study, both cellulite and control patients were 20–30 years with the average plasma adiponectin level in cellulite was 8.07±3.94 µg/ml. The highest cellulite location in the femoral and gluteus areas was 62.5%. The results of this study showed that there was a statistically significant relationship between plasma adiponectin levels and cellulite (p = 0.025 < 0.05).

Conclusion: There is a significant relationship between low plasma adiponectin levels and the risk of cellulite.

Keywords: Cellulite, plasma adiponectin levels, risk.


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in 20-30 years (62.5%). The demographic characteristics of the subjects based on age are presented in Table 1.

In this study, the subjects were divided into cellulite and control groups (with no cellulite). In the cellulite group, 25 (62.5%) subjects were in the age range 20-30 years, with 12 (30.0%) in the 31-40 years age group (Table 1). A minority of the subjects were included in the 41-50 years of age. The control group had a roughly similar distribution, but no subjects were observed in the 41-50 year age group. According to the location, we observed that 25 (62.5%) subjects had their cellulite in the gluteus and femoral areas, while 11 (27.5%) subjects had it only in the femoral area (Table 2).

Then the adiponectin level was measured using ELISA. The ELISA showed that adiponectin concentration in the cellulite group was lower than in the control group (8.07 ± 3.94 µg/ml vs. 8.23 ± 3.16 µg/ml) (Table 3). Assessing the effect of adiponectin with cellulite, we found that the OR value at 2.7 (p = 0.025) means that subjects with lower plasma adiponectin have a 2.7 times higher risk of cellulite than those who have a higher level of adiponectin (Table 4).

**DISCUSSION**

The incidence of cellulite is more common in women. This disorder is rarely found in men; only about 2% are affected, especially men with androgen deficiency, such as Klinefelter’s syndrome, hypogonadism and post-castration. This study found that most of the research subjects in both the cellulite and control groups were in the 20-30 year age range of 62.5% and the control group of 67.5%. The results of this study are in line with Gulec et al. that cellulite is more common in women with an age range of 26-62 years, with the results of the average age of cellulite patients being 43.2 ± 10.4 years. Studies conducted by Putri et al. also reported a similar condition that most cellulite patients were in the age range of 20-29 years by 46%. Hexel et al. stated that cellulite occurs around 85-90% in women aged over 20 years. Cellulite can be found around 85-90% in postadolescent women. In women aged 30 years, the dermis has reached its maximum thickness, which continues to decrease with age. In addition, with age, the connective tissue in the dermis begins to loosen due to the aging process of collagen and elastin fibers. This allows more adipose cells to protrude into the dermis area to give the appearance of cellulite.

This study found that the most cellulite found in the cellulite patient group was in the femoral and gluteus locations, amounting to 25 people (62.5%). This result is different from Uebel et al., found that the most cellulite was found on the thighs at 88.8%. Meanwhile, Lauren et al. found that 52% of cellulite was located in the buttocks area. Cellulite can be found in body areas containing subcutaneous adipose tissue. However, certain areas such as the thighs and buttocks are more prone to the occurrence of cellulite.

In this study, the most common locations for cellulite were found on the thighs and buttocks. Women generally have a higher percentage of body fat than men. A greater percentage of body fat is stored in the thighs and buttocks in women. This type of fat deposition is typically called the gynoid. Cellulite can also be found on the breasts, lower abdomen, upper arms and nape of the neck, i.e., in all areas where the adipose distribution pattern is female.

Table 3 shows the mean plasma adiponectin levels in the cellulite group were 8.07 ± 3.94 µg/ml and 8.23 ± 3.16 µg/ml in the control group. These results are in line with the research conducted by Emanuele et al., the results of adiponectin levels in subcutaneous tissue in cellulite women with a mean value of 12.6 ± 3.1 µg/ml. Meanwhile, the mean plasma adiponectin level was 20.3 ± 7.3 µg/ml. This is different from the findings above;
and tissue hypoxia, which in turn leads to impaired vascular microcirculation and the formation of tissue complexes subcutaneous fibrous.\textsuperscript{5,26}

Cellulite is more common in women. In addition to the presence of the hormone estrogen, there are also anatomical differences in connective tissue in the skin, which has a thicker dermis, and fat lobe septa in women have a presentation of perpendicular septa to the skin surface, an important role in the ethio-pathophysiology of cellulite is increasing.\textsuperscript{27,28}

**CONCLUSION**

The patients with cellulite have lower plasma adiponectin than those without cellulite. Low plasma adiponectin is also related to an increased risk of having cellulite.

**AUTHOR CONTRIBUTION**

All authors have contributed to this research process, including preparation, data gathering, analysis, drafting, and approval to publish this manuscript.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest regarding the publication of this article.

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4. Tokarska et al., suspected a possible relationship between low adiponectin levels and the development of cellulite.\textsuperscript{4}
5. Based on research conducted by Emanuele et al., it was found that cellulite is associated with the ACE-1 gene and hypoxia-inducible factor-1-a (HIF1-a). In the female gene that carries the ACE-1 and HIF1-a alleles, it is said to increase the risk of cellulite due to increased production of angiotensin II in subcutaneous adipose tissue, causing dysregulation of blood flow and tissue hypoxia, which in turn leads to impaired vascular microcirculation and the formation of tissue complexes subcutaneous fibrous.\textsuperscript{5,26}