

## Relationship between plasma adiponectin levels and cellulite



Sari Indriyani<sup>1\*</sup>, Imam Budi Putra<sup>2</sup>, Nelva Karmila Jusuf<sup>2</sup>

<sup>1</sup>Postgraduate Master of Clinical Medicine Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Medan, Indonesia

<sup>2</sup>Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Medan, Indonesia

\*Correspondence:

Sari Indriyani; Postgraduate Master of Clinical Medicine Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Medan, Indonesia; Phone : +628136.155.2462  
[sariindriyani220411@gmail.com](mailto:sariindriyani220411@gmail.com)

Received: 2022-02-10  
Accepted: 2022-04-22  
Published: 2022-04-30

### 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  $8.07 \pm 3.94$   $\mu\text{g/ml}$ . 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.

**Cite This Article:** Indriyani, S., Putra, I.B., Jusuf, N.K. 2022. Relationship between plasma adiponectin levels and cellulite. *Bali Medical Journal* 11(1): 434-437. DOI: 10.15562/bmj.v11i1.3466

## INTRODUCTION

Cellulite is a local anatomic and metabolic disorder of the subcutaneous tissue, causing changes in body contours to become unaesthetic so that it looks like an orange peel.<sup>1,2</sup> 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.<sup>3</sup> 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.<sup>4-6</sup> The pathophysiology of cellulite is a complex process caused by the dysfunction of microcirculation, local fat accumulation, and changes in lymphatic drainage.<sup>6-8</sup>

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.<sup>4,9-11</sup>

Histologically the appearance of cellulite was found to be in the extracellular matrix with enlarged fibrosclerotic fibers that lined the subcutaneous tissue.<sup>9,12,13</sup> 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- signaling.<sup>5,14,15</sup>

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 20-50 years old of 40 cellulite patients and 40 controls at the Dermatology and Venereology polyclinic in North Sumatra University, Medan. Every research subject who informed consent was included in this

study. 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<sup>®</sup>, 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.

## RESULTS

In this study, the highest demographic characteristics of cellulite patients were

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 ( $8.07 \pm 3.94$  g/ml vs.  $8.23 \pm 3.16$  g/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.<sup>16</sup> 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.<sup>13</sup> 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  $43.2 \pm 10.4$  years.<sup>17</sup> 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%.<sup>18</sup> Hexel *et al.* stated that cellulite occurs around 85-90% in women aged over 20 years.<sup>3</sup> Cellulite can be found around 85 -90% in postadolescent women.<sup>16</sup> In women aged 30 years, the dermis has reached its maximum thickness, which continues

**Table 1. Distribution of research subjects by age**

Age (years)	Cellulite patients		Control	
	n	%	n	%
20-30	25	62.5	27	67.5
31-40	12	30.0	13	32.5
41-50	3	7.5	0	0.0
Total	40	100	40	100

**Table 2. Distribution of research subjects based on the location of cellulite**

Location of Cellulite	Cellulite patients	
	n	%
Femoralis	11	27.5
Gluteus	1	2.5
Femoralis, gluteus	25	62.5
Femoralis, gluteus and abdomen	3	7.5
Total	40	100

**Table 3. Average plasma adiponectin levels in study subjects**

Group	Plasma adiponectin levels		
	n	Mean ( $\mu$ g/ml)	SD ( $\mu$ g/ml)
Cellulite	40	8.07	3.94
Control	40	8.23	3.16

**Table 4. Relationship between plasma adiponectin levels and cellulite.**

Plasma adiponectin levels	Group				
	Cellulite	Control	Total	OR	p value
Low	25(62.5%)	15(37.5%)	40 (50%)		0.025
Hight	15(37.5%)	25(62.5%)	40 (50%)	2.7	

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.<sup>19,20</sup>

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%.<sup>2</sup> Meanwhile, Lauren *et al.* found that 52% of cellulite was located in the buttocks area.<sup>21</sup> Cellulite can be found in body areas containing subcutaneous adipose tissue.<sup>22</sup> However, certain areas such as the thighs and buttocks are more prone to the occurrence of cellulite.<sup>19</sup>

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*.<sup>23</sup> 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.<sup>19</sup>

**Table 3** shows the mean plasma adiponectin levels in the cellulite group were  $8.07 \pm 3.94$   $\mu$ g/ml and  $8.23 \pm 3.16$   $\mu$ g/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  $12.6 \pm 3.1$   $\mu$ g/ml. Meanwhile, the mean plasma adiponectin level was  $20.3 \pm 7.3$   $\mu$ g/ml. This is different from the findings above;

according to the researchers, the difference in the average value of plasma adiponectin levels is due to related variations in each study. Factors that affect adiponectin levels in the blood can be influenced by various things, such as a high-fat diet and physical activity.<sup>24</sup> Examination of plasma adiponectin levels in other skin diseases has never been done. Examination of plasma adiponectin levels is generally used to determine the risk of a metabolic disease such as in obese people.<sup>25</sup>

Table 4 shows the subjects with low plasma adiponectin levels in the cellulite group as many as 25 people (62.5%) and high adiponectin levels in the cellulite group as many as 15 people (37.5%). Based on the Chi-square test, the p-value = 0.025 < 0.05, which means a statistically significant relationship between plasma adiponectin levels and cellulite. With the value of Odds Ratio (OR) = 2.7 CI. The results of this study are in line with studies conducted by Emanuele *et al.*, who found a significantly lower adiponectin mRNA expression in subcutaneous adipose tissue of women with cellulite than in controls.

According to Friedman *et al.* and Emanuele *et al.*, adiponectin expressed by adipose tissue may play a role in the pathophysiology of cellulite. However, the study in this area is still very limited. The exact cause of cellulite is still not clearly understood and is multifactorial, but several hypotheses state that cellulite can occur due to genetic factors, differences in sex, age, race, diet and hormones, supporting factors for the occurrence of cellulite, such as obesity, hormone intake, and metabolic changes.<sup>7,8</sup>

The results of this study indicate a significant relationship with OR = 2.7, which means that low plasma adiponectin levels cause a 2.7 times risk of cellulite. Tokarska *et al.* suspected a possible relationship between low adiponectin levels and the development of cellulite.<sup>4</sup>

Based on research conducted by Emanuele *et al.*, it was found that cellulite is associated with the ACE-1 gene and hypoxia-inducible factor1-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.<sup>5,26</sup>

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.<sup>27,28</sup>

## 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.

## FUNDING

The authors are responsible for all study funding without a grant or any external funding source.

## CONFLICT OF INTEREST

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

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