

## The Correlation Between Body Mass Index And Leptin Levels In Users Of Depo Medroxy Progesterone Acetate (Dmpa)

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### Abstract

**Background:** Indonesia is the fourth most populous country in the world with the high rate of population growth and maternal mortality. To overcome this problem, Indonesian government implemented a program of "Family Planning". According to BKKBN 2007, 55.5% of women used contraceptive injections and the majority had a high BMI. BMI that increases is associated with an increase in the number of adipose cells in body that affects the leptin level.

**Objective:** To determine the correlation between body mass index (BMI) and leptin levels in contraceptive users of Depo Medroxy Progesterone Acetate.

**Methods:** the research method used in this research is cross sectional. The research was conducted at Department of Obstetrics and Gynecology, Faculty of Medicine, University of Sumatera Utara, General Hospital of H. Adam Malik and the health center of Helvetia in August 2017 with consecutive sampling. After the participant agreed with the informed consent, BMI was measured and 3 cc of blood was taken from the median cubital vein at 07.00-08.00 when fasting. Data were analyzed by Spearman correlation test with  $p$  value  $< 0,05$ .

**Results:** From 95 participants, 42 participants (44,2%), had an age interval between 30-39 years and 79 participants (83,2%) had leptin levels  $> 5$ . Most users of DMPA hormonal contraceptive were overweight at months 0 and 12, which 42 participants (44,2%) and 33 participants (34,7%) at 24 months, 46 participants (48,4%) had obesity level I.

**Conclusion:** There is a strong and significant correlation between body mass index and leptin levels in DMPA hormonal contraceptive users ( $r = 0,70$ ,  $p = 0,0001$ ).

**Keywords:** Depo Medroxy Progesterone Acetate, Body Mass Index, Leptin Levels.

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### I. Background

Indonesia is the fourth most populous country in the world and its growth rate is still high. The rate of population growth in Indonesia from 2000 to 2010 was 1,49% per year. Based on Indonesia Demographic and Health Survey 2012, maternal mortality rate in Indonesia was still high at 359 per 100.000 live births. The third Global Goal of SDG (Sustainable Development Goals) is to reduce Maternal Mortality rate (MMR) to 70 per 100.000 live births by 2030. MMR in Indonesia is still relatively higher compared with other ASEAN member countries. The risk of maternal mortality due to childbirth in Indonesia is 1:65 birth.<sup>1-4</sup> To overcome this problem, strategic intervention is needed in the form of business pillar of Safe Motherhood, and one of the enforcement efforts of safe motherhood pillar is to implement the Family Planning (KB) program. One of the methods of contraception used in Family Planning (FP) program is the injecting hormonal contraceptive method. Injectable contraceptive (combination or progesterone only) is a contraceptive that is safe and effective and reversible, does not require daily use, simple, cheap, and can be accepted by many people. Injectable contraceptives consist of two types of combined hormonal injectable contraceptives (consisting of medroxyprogesterone and estradiol cypionate) and progesterone injections (consisting of Depo Medroxy Progesterone Acetate (DMPA) or Norethisterone Enantate (NET-EN)).<sup>5,6</sup> DMPA is a microcrystalline suspension of synthetic progestin, injected intramuscularly every 3 months for contraception. DMPA is a derivative of hydroxyprogesterone 17 $\alpha$ . DMPA is a strong inhibitor of gonadotropin by a progestin effect. The function of progestin is to inhibit LH-surge (LH-surge) to prevent ovulation. The progestin level in the circulation is high enough to inhibit the occurrence of LH-surges that plays during ovulation so that LH in circulation will decrease as a result will inhibit the occurrence of fertilization.<sup>6-9</sup> DMPA injection has several side effects. An increase in

body mass index is a side effect of hormonal contraceptive use. Many researches have shown a significant increase in body mass index to the use of progestin hormonal contraceptives. DMPA has an increased effect of body fat composition compared to non-hormonal contraceptives after 6 months of use. Other researches are similar to the increase in body mass index after the use of DMPA in one, two, and three years of use compared with the group of IUD (Intra Uterine Device).<sup>10</sup>DMPA can bind to glucocorticoid receptors. High dose of DMPA is associated with glucocorticoids that affect the composition of body fat (including visceral fat). DMPA alters the neurohormonal regulation of appetite. Based on research there is an increase in leptin that is directly related to increased appetite. In the study of Batista et al., an increase in body mass index (3,01 kg) and BMI was significant after DMPA use for 12 months.<sup>11,12</sup>Based on the research results, there are several mechanisms that allegedly play a role in causing an increase of body mass index on DMPA acceptor. First, DMPA has glucocorticoid-like activity, which is associated with an increased of fat including visceral fat. Second, the hypogestrogenism caused by DMPA injection causes an increase of visceral fat and subcutaneous fat seen from increased waist circumference. Third, DMPA alters the neurohormonal regulation of appetite.<sup>13-20</sup>

## II. Method

This research was an observational analytic research with cross sectional design to determine the correlation between body mass index and leptin level in hormonal contraceptive users of Depo Medroxy Progesterone Acetate (DMPA). The research was conducted at Department of Obstetrics and Gynecology, Faculty of Medicine, University of Sumatera-Utara Haji Adam Malik, while the data was taken from Public Health Center of Helvetia in August 2017. Samples in this research were ninety-five hormonal contraceptive acceptors of Depo Medroxy Progesterone Acetate (DMPA) that met the research inclusion criteria and were selected by non-random selection method with consecutive sampling technique.

## III. Results

Frequency distribution of DMPA users according to age can be seen in the following table.

**Table 1.** Frequency distribution of DMPA Users according to Age Group

A g e G r o u p	D M P A U s e r s	
	N	%
2 0 - 2 9 y e a r	2	9 3 0 . 5
30-39 year	4	2 4 4 . 2
≥ 4 0 y e a r	2	4 2 5 . 3
T o t a l	9	5 1 0 0 . 0

From the 95 subjects using DMPA, age characteristics were divided into 3 age groups. The largest frequency of DMPA users in the age group of 30-39 years (44,2%), age group of 29-30 years (30,5%), and age group ≥ 40 years (25,3%). Frequency distribution of leptin content based on age characteristics can be seen in the table below.

**Table 2.** Frequency Distribution Of Leptin Content Based On Age Group

V a r i a b l e	A g e G r o u p		
	2 0 - 2 9 y e a r s	3 0 - 3 9 y e a r s	≥ 4 0 y e a r s
Meanof Leptin Levels	1 0 . 0 3	1 1 . 9 2	1 3 . 3 5

The average leptin level in women in the age group of 20-29 years was 10,03, the age group 30-39 years was 11.92, and the age group ≥40 years was 13.35.

**Table 3.** Distribution of Body Mass Index Based on Duration of DMPA Use

B o d y M a s s I n d e x	D u r a t i o n o f D M P A u s e					
	0 m o n t h s		1 2 m o n t h s		2 4 m o n t h s	
	N	%	n	%	n	%
U n d e r w e i g h t	0	0	0	0	0	0
N o r m a l w e i g h t	39	4 1 . 1	3	1 3 2 . 6	1	7 1 7 . 9
O v e r w e i g h t	42	4 4 . 2	3	3 3 4 . 7	3	2 3 3 . 7
C l a s s I O b e s i t y	14	1 4 . 7	3	1 3 2 . 6	4	6 4 8 . 4

Class II Obesity	0	0	0	0	0	0
T o t a l	195	100.0	95	100.0	95	100.0

At the age of 0 months (before DMPA), body mass index of the research subjects showed categories of less weight and obesity II were not found, normal category was 39 people (41,1%), obesity risk was 42 people (44,2%), and obesity was 14 people (14,7%). At 12 months after DMPA, body mass index of obese research subjects increased to 31 people (32,6%). At 12 months after DMPA, body mass index of obese research subjects increased to 31 people (32,6%). While they who have normal BMI as many as 31 people (32,6%) and obesity risk of 33 people (34,7%). At 24 months after DMPA, the number of obese subjects increased again to 46 (48,4%), while the category of normal BMI was 17 (17,9%) and obesity risk was 32 (33,7%).

Table 4. Frequency distribution of DMPA Users Based on the Leptin Level

Leptin Level	N	%
≤ 5 (normal)	16	16.8
> 5 (increasing)	79	83.2
T o t a l	95	100.0

Table 4 shows that the subjects frequency with leptin > 5 (increasing) is 79 people (83,2%), while the subjects frequency with leptin ≤ 5 (normal) is 16 (16,8%).

Table 5. The relationship of Body Mass Index with Leptin Levels

BMI	Leptin Levels		p value
	≤ 5	> 5	
Normal weight	15 (88.2%)	2 (11.8%)	0,0001
Overweight	1 (3.1%)	31 (95.9%)	
Obesity grade I	0 (0%)	46 (100%)	
T o t a l	16 (16.8%)	79 (83.2%)	

Table 5 shows that DMPA acceptors with normal BMI have at most leptin ≤ 5 of 15 people (88.2%), whereas with leptin > 5 levels of 2 people (11.8%). DMPA acceptors with the highest risk of obesity have leptin > 5 levels of 31 people (95.9%), whereas with ≤ 5 the number of 1 person (3.1%). All DMPA acceptors with obesity I of BMI have leptin > 5 levels of 46 (100%). From this research was found a significant relationship with p value = 0,0001 whose value is smaller than 0.05. Thus it can be concluded that there is a significant relationship between body mass index and leptin levels.

#### IV. Discussion

Age is one of the factors that influence a person's behavior including the use of contraception, parents less use contraception than young children. The statement is in accordance with the results of this research, which DMPA users are most commonly found in the age group of 30-39 years as much as 44.2% (Table 1). But age is not the main reason for the use of contraception, because the number of children is also one of considerations of devices to use contraceptives. It plays an intrinsic factor in relation to family planning. Age associated with organ structure of body, physiology function, biochemical composition including female hormonal system. The period of reproduction (fertility) is the basis of the pattern of rational contraceptive use is divided into 3, namely: the period of delaying pregnancy (fertility), the period of regulating fertility (increase), the end of fertility (not pregnant again)<sup>21</sup> based on the survey results of BKKBN (2013), younger women (15-19 years) and older (age 45-49 years) were less use of contraception than middle-aged women (20-44 years). In older women (age 30-44 years), in addition to FP injections, the use of the pill long-term methods of long-term contraception such as IUD, implant and sterilization of women is higher than in young women. This is similar to the results of this research conducted to DMPA users in the fertile age group. based on the results of research Pratiwi showed that the most accepted acceptor of DMPA injection is the acceptor with the age of 41-45 years, as many as 9 acceptors (22,5%). But this results is not much different from other age groups. Infertile couples

use contraceptives to adjust the number of children and birth interval desired.<sup>19</sup>he resarch results of Lange et al for the average age of DMPA users in adolescents were  $16,2 \pm 1,5$  years (fertile age) with an increase in BMI of  $23,7 \pm 5,3$  to  $25,3 \pm 5,7$  in 12 months.<sup>22</sup>he results of 95 DMPA subjects treated with DMPA had leptin  $> 5$  (increasing) of 79 persons (83,2%), whereas with leptin level  $\leq 5$  (normal) 16 persons (16,8%). Leptin is a hormone produced by adipocyte cells that hve the function of inhibiting feeding and increasing thermogenesis. The function of leptin is regulated by hypothalamus via a feedback mechanism through: sensory signal is regulated from the adipose tissue mass, hypothalamus as the sensory acceptance center and the integration of leptin signal through leptin receptor (LRB), the effector pathway includes a sympathetic system that regulates energy balance and energy expenditure. Leptin has functions such as fertility through the Hiphalamo-Pituitary-Gonadal-Axis system through the control of gonadotropin-releasing hormone (GnRH) and contributes to energy regulation and body mass index through neuroendocrine mechanism. The factor that regulates leptin production is adipocyte. Leptin level is higher in women than men because of estrogen effect known to encourage the synthesis of leptin and androgen. In DMPA users, MPA binds to glucocorticoid receptor and has properties such as glucocorticoid that affects the composition of body fat (including visceral fat), altering neurohormonal regulation of appetite. The effect of glucocorticoid on appetite and high energy intake can lead to an increase body mass index. Glucocorticoid primarily stimulates the intake of protein and carbohydrate in humans. Glucocorticoid is an important hormone that not only gives catabolic peripheral tissue but also plays a role in the synthesis and release of neuropeptide in hypothalamus, affecting food intake and central nervous system. Hormones that work on hypothalamic neuropeptides aim to regulate food intake and help peripheral metabolism through the efferent nerves in the autonomic nervous system. A slight increase in glucocorticoid production and excessive cortisol response in obese people due to hyper responsive responses of HPA axis or reduced HPA-Axis sensitivity to negative feedback. It can also be accompanied by peripheral tissues that become more sensitive to glucocorticoids.<sup>14,15</sup>In obesity high plasma leptin level is associated with an amount of adipose tissue but without an appropriate response (e.g. appetite suppression). There is a defect in the leptin receptors on appetite of central nervous system. In obese patients it leads to leptin resistance whereas when energy deficits leptin levels in plasma decreases which fat storage decreases. Based on the research of Chow and Phoon differences in the content of leptin in women normoweight and underweight was significant ( $p = 0,001$ ) with a value of  $r = 0,44$ . Similar to the research of Monti et al. on the levels of leptin and ghrelin and its relationship with BMI. Leptin level was significantly associated with BMI ( $r = 0,72$ ,  $p = 0,001$ ) and waist circumference ( $r = 0,71$ ,  $p = 0,0001$ ) while ghrelin had a protective factor to for increasing BMI and waist circumference.<sup>23-26</sup>

## V. Conclusion

1. Most of the research subjects were age group 30-39 years old.
2. The highest average leptin level was found in age group  $\geq 40$  year amounted to 13,35.
3. Most of research subjects had BMI obesity index at months 0 and 12, whereas at month 24, most subjects had a BMI index of obesity I.
4. Most of the research subjects had obesity I of BMI with leptin levels  $> 5$  levels.
5. There was a significant relationship with  $p = 0,0001$  between body mass index and leptin levels.

## VI. Suggestion

Given the diverse role of leptin in life, especially its relationship with reproduction, Further research expected will compare other variables in women with DMPA.

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