

**PERBEDAAN KADAR KORTISOL ANTARA PASIEN DISMENOREA  
PRIMER KRONIS DENGAN  
NON-DISMENOREA**

**TESIS**



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# Differences in Cortisol Levels between Chronic Primary Dysmenorrhoea Patients and Non-Dysmenorrhoea

*Perbedaan Kadar Kortisol antara Pasien Dismenorea Primer Kronis dengan Non-Dismenorea*

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## Abstract

**Objective:** To investigate whether chronic primary dysmenorrhoea will significantly increase cortisol levels in the body. This study can provide an overview of the importance of handling primary dysmenorrhoea so that it does not continue to become menstrual disorders.

**Method:** This study used a cross sectional comparative study method with a total sample of 26 subjects with 13 subjects included in the dysmenorrhea group and 13 other subjects belonging to the non-dysmenorrhea group. The study was conducted at Department of Obstetric and Gynecology Faculty of Medicine Universitas Andalas network primary healthcare and Dr. M. Djamil Padang Central General Hospital. Data were analyzed using computational calculation of SPSS program with bivariate test using  $X^2$  test or chi-square test with a significance degree of 0.05.

**Results:** Twenty six subjects (13 each group) have been sampled in this study, the mean age of the dysmenorrhea group was  $26.23 \pm 3.92$  while the mean age of the non-dysmenorrhea group was  $28.62 \pm 7.10$ . The age difference between groups was not statistically significant with a value of  $p = 0.30$  ( $p > 0.05$ ). In the comparison of cortisol levels between the two groups, it was found that the dysmenorrhea group had a higher cortisol level of  $72.3077$  ( $7.2 \mu\text{g} / \text{dL}$ ) compared to the non-dysmenorrhoea group of  $60.3846$  ( $6 \mu\text{g} / \text{dL}$ ). Based on the results of the bivariate analysis using the chi-square test, the value of  $p = 0.148$  ( $P > 0.05$ ) showed that there was no significant difference between the cortisol levels of the group with chronic primary dysmenorrhea compared with the non-dysmenorrhea group.

**Conclusion:** Chronic primary dysmenorrhea can not significantly increase cortisol levels in the body.

**Keywords:** comparative study, Chronic primary dysmenorrhea, non-dysmenorrhea, cortisol levels, menstrual disorders

## Abstrak

**Tujuan :** Mengetahui apakah dismenorea primer kronis akan meningkatkan kadar kortisol dalam tubuh secara signifikan. Penelitian ini dapat memberikan gambaran pentingnya penanganan dismenorea primer agar tidak berlanjut menjadi gangguan menstruasi.

**Metode :** Penelitian ini merupakan penelitian dengan desain potong lintang comparative study dengan jumlah total sampel sebanyak 26 subjek dengan rincian 13 subjek termasuk ke dalam kelompok dismenore dan 13 subjek lainnya termasuk ke dalam kelompok non-dismenore. Penelitian dilakukan di Puskesmas jejaring PPDS Obgyn FK Unand dan RSUP Dr. M. Djamil Padang. Data dianalisis menggunakan perhitungan komputasi program SPSS dengan uji bivariat menggunakan uji  $X^2$  atau uji chi-square dengan derajat kemaknaan 0,05.

**Hasil :** Dari 26 subjek (masing-masing 13 subjek) yang dijadikan sampel dalam penelitian ini, didapatkan usia rerata kelompok dismenore ialah  $26,23 \pm 3,92$  sedangkan usia rerata kelompok non-dismenore ialah  $28,62 \pm 7,10$ . Perbedaan rerata usia antar kelompok ini tidak signifikan secara statistic dengan nilai  $p = 0,30$  ( $p > 0,05$ ). Pada perbandingan kadar kortisol antar kedua kelompok, didapatkan kelompok dismenore memiliki kadar kortisol yang lebih tinggi yaitu  $72,3077$  ( $7,2 \mu\text{g}/\text{dL}$ ) dibandingkan dengan kelompok non-dismenorea yaitu  $60,3846$  ( $6 \mu\text{g}/\text{dL}$ ). Berdasarkan hasil analisis bivariat menggunakan uji chi-square, didapatkan nilai  $p = 0,148$  ( $P > 0,05$ ) yang menunjukkan tidak adanya perbedaan yang signifikan antara kadar kortisol kelompok dengan dismenore primer kronis dibandingkan dengan kelompok non-dismenore.

**Kesimpulan :** Dismenore primer kronis dapat meningkatkan kadar kortisol dalam tubuh secara signifikan.

**Kata kunci:** Studi perbandingan, dismenore primer kronis, tidak dismenore, kadar kortisol, gangguan menstruasi

## INTRODUCTION

Dysmenorrhea is spasmodic pain in the hypogastric and lumbar regions between, before and during menstruation. Dysmenorrhea is generally classified as primary or secondary. Primary dysmenorrhoea is associated with the ovulation cycle and resulted from myometrial contraction, in the absence of proven disease. Secondary dysmenorrhea refers to pain during menstruation that is associated with pelvic pathology, such as endometriosis, adenomyosis, or uterine myoma.<sup>1-3</sup>

Dysmenorrhea is one of the most common gynecological problems in women of reproductive age. Primary dysmenorrhea usually begins during adolescence, but only after ovulation occurs; 20–45% of adolescent girls ovulate 2 years after menarche, and 80% at 4-5 years. 20-90% of young women experience dysmenorrhea, 15% experience severe dysmenorrhoea. Overall prevalence of primary dysmenorrhoea in adolescent girls is between 60% and 90% and decreases with age. However, only about 15% of teenage girls seek medical treatment for painful menstrual complaints.<sup>1</sup>

Cortisol is synthesized from cholesterol in the adrenal gland (suprarenal). It is controlled through the Hypothalamus-Pituitary-Adrenal (HPA) axis, while secretions will increase if exposed to Stress.<sup>4-6</sup> The levels of cortisol in the blood varies, the highest levels are found in the morning (08.00 WIB) 20 g / dL and decrease at night 5 g / dL.<sup>7,8</sup> High cortisol level will enter the circulation suppressing growth of the body's immune cells and affect the release of adrenaline neurotransmitters which results in blockage of Gn-RH secretion resulting in impaired FSH and LH production which results in menstrual disorders. Until now, the "gold standard" biomarkers and values for chronic stress examination were debated because of the complex etiology and diverse manifestations in each individual.<sup>7</sup>

## OBJECTIVES

In this study, we hypothesize that primary dysmenorrhoea that lasts a long time (at least 6 months) has the potential to cause a significant increase in cortisol levels due to chronic stress it caused. These increased levels of cortisol are feared to increase the disturbance of menstruation in women.

## METHODS

This study used a cross sectional comparative study design. Samples were taken from women diagnosed with chronic primary dysmenorrhea with VAS > 7 in the Network puskesmas and RSUP Dr. M. Djamil Padang. Informed consent was carried out by providing a detailed explanation of the purpose, objectives, procedures and benefits of the study and the signing of a statement form willing to join the study without any coercion from any party. Subjects that met the inclusion and exclusion criteria were continued for clinical and supportive examinations (USG). Blood samples for examination of serum cortisol levels are taken on the first or second day of menstruation at 8:00 am by qualified health workers. All collected data is then processed statistically. This Study has been qualified and approved by the Research Ethics Committee of the Medical Faculty of Universitas Andalas, Padang.



## RESULTS

The twenty six groups have been sampled in this study, the mean age of dysmenorrhea group was  $26.23 \pm 3.92$  while the mean age of non-dysmenorrhea group was  $28.62 \pm 7.10$  (Table 1). The difference between groups is not statistically significant with a value of  $p = 0.30$  ( $p > 0.05$ ).

**Table 1.** Characteristics of Respondents by Age

Group	Age (year) Mean $\pm$ SD	p-value
Non -dysmenorrhea	$28.62 \pm 7.10$	0.30
Dysmenorrhea	$26.23 \pm 3.92$	

Before the bivariate analysis test is carried out, the data normality test is conducted first. The normality test of the data using the Saphiro-Wilk test (Table 2) showed a value of  $P > 0.05$  (the P value of the dysmenorrhoea group = 0.774 and the P value of the non-dysmenorrhoea group = 0.987), indicating that the subject data from this study were normal.

In the comparison between the two groups (Table 3), it was found that the dysmenorrhea group had a higher cortisol level of 72.3077 ( $7.2 \mu\text{g} / \text{dL}$ ) compared to the non-dysmenorrhoea group of 60.3846 ( $6 \mu\text{g} / \text{dL}$ ). However, there are still in the normal reference range of  $2.9 - 17.3 \mu\text{g} / \text{dL}$ . The test of the value of  $p = 0.148$  ( $P > 0.05$ ) showed that there was no significant difference in the cortisol levels of the group with chronic primary dysmenorrhea compared with the non-dysmenorrhea group.

**Table2.** Test of Normality

Diagnosis		Kolmogorov-Smirnov			Shapiro-Wilk		
		Statistic	df	Sig	Statistic	df	Sif
Cortisol level	Dysmenorrhea	0.138	13	0.200*	0.961	13	0.774
	Non Dysmenorrhea	0.098	13	0.200*	0.982	13	0.987

\* this is a lower bound of the true significance, a.Lilie fors significance correction.

**Table 3.** Differences in Cortisol Levels between Non-Dysmenorrhea and Dysmenorrhea

Group	Mean Cortisol Levels $\pm$ SD	p- value
Non-Dysmenorrhea	60.3846	0.148
Dysmenorrhea	72.3077	

## DISCUSSION

Increased cortisol levels in the group with a history of dysmenorrhoea was believed to be the result of the mechanism of anxiety inherent in individuals experiencing chronic pain. Psychological factors play an important role in the occurrence of primary dysmenorrhea. Factors such as social support, anxiety, depression, stress, neurosis, comfortness, and personality have an influence on the onset of menstrual pain.<sup>9,10</sup> This dysmenorrhea itself will also cause anxiety to the subject and can change the perception of pain. A person who experiences dysmenorrhea every month feels a negative impact on her life. A study showed a positive relationship between psychological stress and dysmenorrhea ( $p = 0.001$ ).<sup>11</sup>

Stressors such as chronic pain can trigger the hypothalamus to secrete corticotropin-releasing hormones (CRH aka CRF, Corticotropin Releasing Factor) and Arginine Vasopressin

(AVP), thus triggering the production of Adrenocorticotropin hormone (ACTH) from the posterior pituitary and its activation.<sup>12</sup> ACTH pushes the adrenal cortex to produce cortisol, which results in an increase in cortisol levels. The glucocorticoid (cortisol) and their receptors bonds in the limbic system will activate the pathway of the hypothalamus pituitary adrenal axis so that the cycle will repeat itself. The limbic system will also affect the sympathetic nerves which will increase heart rate (palpitations), sweating, and increased intestinal peristalsis. High levels of cortisol will enter the body's circulation to suppress the growth of the body's immune cells. This hormone will also affect the release of adrenaline neurotransmitters which will result in inhibition of Gn-RH secretion resulting in impaired FSH and LH production and result in menstrual disorders.<sup>9,12,13</sup>

Stress can directly change the regulation of the pituitary-hypothalamus from a person's reaction. Stress activates the hypothalamic pituitary axis that affects menstrual function, causing menstrual disorders such as dysmenorrhoea and irregular menstrual patterns.<sup>13</sup> Prove that in groups with inherent anxiety, cortisol production increases and CD3 + T cells, CD45 + T cells, CD3 + CD4 + helper T cells, and CD3 + CD8 + cytotoxic T cells are fewer, so this can affect someone's immunity and health. This is in accordance with the results of this study, which shows higher cortisol levels in the group of subjects with chronic primary dysmenorrhea than in the group without a history of dysmenorrhoea.<sup>14</sup>

The results of this study indicates that chronic primary dysmenorrhoea has an influence on increasing blood cortisol levels. Cortisol levels in the group of women with chronic primary dysmenorrhoea showed slightly higher levels when compared to the group of subjects who did not experience primary dysmenorrhoea. It was found from the results obtained that there were indeed differences in mean cortisol levels in the two groups of subjects, namely the dysmenorrhoea group and the non-dysmenorrhoea group. In the dysmenorrhoea group, the mean cortisol level was indeed higher at 72.3077 (7.2 µg / dL), compared to the non-dysmenorrhoea group of 60.3846 (6 µg / dL). The incidence of chronic primary dysmenorrhoea can increase blood cortisol levels. But further need to be underlined that in the statistical calculation using bivariate analysis, the ratio of cortisol levels between the two groups had a P value of 0.148 ( $P > 0.05$ ), which meant that the difference in cortisol levels in the dysmenorrhoea group and those without statistics. This statistical meaninglessness can be caused by differences in stress coping between subjects with one another.

In the data of the study conducted by the author, there is an interesting thing to note, that the oldest subject age was 47 years in the non-dysmenorrhoea group, the cortisol level was the least among the other subjects, which was 2.7 µg / dL. This needs to be further analyzed by regression analysis whether the older the age, the less the cortisol hormone level, of course with data or a larger number of subjects.

Higher levels of cortisol in the group with dysmenorrhea in this study were still in the range of normal reference values (2.9 - 17.3 µg / dL) with the highest levels of 11 µg / dL in subjects aged 22 years. It should be noted that different sampling times can affect the results of cortisol levels. Cortisol production is usually higher in the morning and in the day or afternoon, the production is getting lower. The time for taking samples in this study is uniformly carried out on the morning of 08.00 on the first or second day of menstruation, so that minor biases that can occur due to differences in sampling time can be avoided. The best and most informative sample collection is the morning when cortisol is at one's optimal level.<sup>12,15</sup>

The strength of this study is the focus in objective data collection, blood cortisol levels. Taking blood samples from each subject conducted by qualified health workers can minimize the study bias that can occur. Determination of diagnosis Chronic primary dysmenorrhoea is also carried out by clinicians (doctors) so that the determination of the subject group is more

adequate based on the objective clinical judgment conducted by experts. Measurement of body weight or body mass index and physical activity were not included in this study because it was not the main focus of the study, both of these factors were believed to have no effect on the onset of menstrual pain.<sup>16,17</sup>

The weakness of this study is that it has not excluded non-organic risk factors from dysmenorrhea such as early menarche, BMI < 20 kg/m<sup>2</sup>, smokers, heavy menstrual bleeding, nulliparity, strict diets, anti-social life, anxiety and depression. These factors were not included in the exclusion criteria because there were too many and if included, it would be difficult to find the subject of the study and reduce the sample.<sup>1,16</sup>

## CONCLUSION

In this study, the average cortisol level in the group with chronic primary dysmenorrhoea was higher, namely 72,3077 (7.2 g / dL) compared to the non-dysmenorrhoea group with 60,3846 (6 g / dL) but the values of both were still within normal limits . From the results of bivariate analysis, the value of  $p = 0.148$  ( $p > 0.05$ ). So we can conclude that there is no statistically significant difference between serum cortisol levels of patients with chronic primary dysmenorrhoea and non-dysmenorrhoea.

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