

# The Correlation Between the Degree of Pain with Estradiol Hormone Levels, Interleukin 1 $\beta$ (il-1 $\beta$ ) Levels and Nitrite Oxide in Blood Serum of Endometriosis Patients

LIDYA METRI\*, AFRIWARDI AFRIWARDI

Biomedical Doctoral Study Program, Faculty of Medicine, Andalas University, Limau Manis Str - Pauh, 25163, Padang City, Indonesia

**Abstract:** Endometriosis is the chronic disease, in which the glandular and stromal-like endometrium grows outside the uterine cavity, Endometriosis is inflammatory and estrogen-dependent that affects 6-10% of women during their reproductive years and up to 50% of women receiving fertility treatment. The purpose of this study was to determine the correlation between the degree of pain with estradiol hormone levels, interleukin-1 $\beta$  (IL-1 $\beta$ ) levels and Nitrite Oxide (NO) in the blood serum of patients with endometriosis. This type of research is an observational analytic with a cross sectional comparative study design in which the dependent and independent variables are obtained simultaneously. The research was conducted in type B and C hospitals. To take blood serum samples for endometriosis patients and the Biomedical Laboratory of FK Unand to check levels of estradiol hormone, levels of Interleukin-1 $\beta$  (IL-1 $\beta$ ) and NO. The study was conducted in January - November 2020. The population was all patients who doing examination at the obstetrics gynecology department of the hospital. Samples were taken consecutively that met the inclusion and exclusion criteria with a total sample of 40 people. Data analysis using analyzed by univariate, bivariate and multivariate with chi-square test. The research results were obtained The mean age of endometriosis patients was 38.85 years, the mean pain degree of patients and the distribution of levels of estradiol, interleukin, 1 $\beta$  (IL-1 $\beta$ ) and Nitric oxide. The results of the bivariate analysis showed that there were differences degree of pain with each Estradiol level, interleukin, 1 $\beta$  (IL-1 $\beta$ ) as well as nitric oxide. The results of the multivariate analysis showed that there was a difference in the degree of pain with the three Estradiol levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ) and nitric oxide in the blood serum of people with endometriosis ( $P = 0,000$  then  $p < \alpha (0.05)$ ). From the research results it can be concluded that there are the relationship between degree of pain and level Estradiol, interleukin, 1 $\beta$  (IL-1 $\beta$ ) and nitric oxide in the blood serum of people with endometriosis.

**Keywords:** Pain degree, endometriosis, Estradiol levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ), Nitrite oxide

## 1. Introduction

Endometriosis is a chronic and painful disease which the endometrium such as glandular cells and stroma grows outside the uterine cavity [1,2]. Endometriosis is an inflammation and estrogen-dependent disease that affects 6-10% of women during their reproductive years and up to 50% of women receiving fertility treatment. When the endometrial tissue is present in the myometrium, it is called adenomyosis. The site of endometriosis is often found in the pelvic peritoneum but it can be found in other places such as the ovaries and utero-sacral ligaments [3,4]. Endometriosis represents a very significant problem in gynecology, affecting 10% -20% of women who are still menstruating. Found in 30% -45% of infertile women. In the world, 10% of women are estimated to have endometriosis. Endometriosis cases cause 20% of all gynecological operations and is the only cause of non-obstetric hospitalization (> 5%) in women aged 15-44 years [5-7]. For this reason, it is necessary to investigate the correlation between the degree of pain and Estradiol hormones levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ) levels and nitric oxide in the blood serum of people with endometriosis. This study aims to analyze the correlation between the degree of pain and Estradiol hormones levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ) levels and nitric oxide in the blood serum of people with endometriosis.

\*email:metrilidya1@gmail.com

## 2. Materials and methods

This study was an observational analytic study with a cross sectional comparative study design which the dependent and independent variables were obtained at the same time. The sample in this study was 40 patients with endometriosis diagnosed by a specialist in Gynecological Obstetrics in accordance with the ASRM criteria and transvaginal ultrasound examination in Hospital. This study was started from January to November 2020 in the City of Padang. Retrieving data by measuring the degree of pain in patients with endometriosis using a Visual analog scale / VAS (mm) and Estradiol levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ) and nitric oxide in blood serum in Andalas University Laboratory.

This study explores the differences in the degree of pain in endometriosis sufferers with Estradiol levels, interleukin, 1 $\beta$  (IL-1 $\beta$ ) and nitric oxide in blood serum. Then analyze the relationship between the dependent and independent variables. The dependent variables of this study were levels of the hormone estradiol; IL-1 $\beta$  levels; and NO, while the independent variable is the degree of endometriosis pain.

## 3. Results and discussions

Based on the results of research conducted on the Relationship between Pain Degree and Estradiol Hormone Levels, Interleukin-1 $\beta$  (IL-1 $\beta$ ) Levels and Nitrite Oxide in Blood Serum for Endometriosis Patients in 2020. with a sample size of 40 endometriosis sufferers. the following research results were obtained:

**Table 1.** Distribution of clinical frequency of Menstrual pain in patients with endometriosis

Variable	Percentage	<i>n</i>
Low	12.5	5
Moderate	35.0	14
Weight	52.5	21

Based on Table 1, it shows that of the 40 respondents, 21 people with endometriosis experienced severe pain (52.5%), while for moderate pain there were 14 people (35%) and 5 people with low pain degrees (12.5). Most endometriosis sufferers experienced severe pain degrees of 52.5%.

The results of the research that has been done, it is known that from 40 respondents It was found that the mean degree of pain in endometriosis patients was 5.98 with a standard deviation of 1.942. The lowest pain degree score was 2 and the highest was 9 in 2020. From the results of the research obtained after measuring the degree of pain using the Vas scale in endometriosis sufferers, it was found that 52.5% of respondents had a high pain scale above the average.

This is consistent with the research that endometriosis patients show a higher VAS value compared to normal women on the same pain stimulus. This suggests the possibility of sensitization in endometriosis patients [8-10].

**Table 2.** The Correlation between the variable degree of pain and Estradiol levels in blood serum of endometriosis patients

Estradiol	Pain scale			Total	P value
	Low	Moderate	weight		
normal	0	2	2	4	0.024
	, 0%	50.0%	50.0%	100.0%	
abnormal	5	12	19	36	
	13.9%	33.3%	52.8%	100.0%	
Total	5	14	21	40	
	12.5%	35.0%	52.5%	100.0%	

Based on Table 2. It shows 4 people with endometriosis with normal estradiol levels with 2 people with moderate pain degrees (50%) and 2 people with severe pain degrees (50%). While there were 36 patients with endometriosis with abnormal estradiol levels with 5 people (13.9%) with low pain degrees, 12 people with moderate pain degrees (33.3%) and 19 severe pain degrees (52.8%). Most endometriosis sufferers experience severe pain with abnormal estradiol levels.

The statistical test results obtained by the value of  $P = 0.024$ , then  $p < \alpha (0.05)$ , it can be concluded that there is a correlation between the degree of pain and the level of the hormone estradiol in the blood serum of patients with endometriosis.

**Table 3.** The correlation between the variable degree of pain and levels of IL1 $\beta$  in blood serum of endometriosis patients

IL1 $\beta$	Pain scale			Total	P value
	Low	Moderate	Weight		
normal	0	1	0	1	0,000
	, 0%	100.0%	, 0%	100.0%	
abnormal	5	13	21	39	
	12.8%	33.3%	53.8%	100.0%	
Total	5	14	21	40	
	12.5%	35.0%	52.5%	100.0%	

Based on Table 3, it shows that 1 person with endometriosis with normal blood serum IL1 $\beta$  levels with moderate pain degrees. Meanwhile, there were 39 patients with endometriosis with abnormal estradiol levels with 5 people (12.8%) with low pain degrees, 13 people with moderate pain degrees (33.3%) and 21 people with severe pain degrees (53.8%). Endometriosis sufferers experience the most severity of pain with abnormal IL1 $\beta$  levels. The statistical test results showed that the value of  $P = 0.000$ , then  $p < \alpha (0.05)$ , it can be concluded that there is a correlation between the degree of pain and the IL1 $\beta$  level in the blood serum of patients with endometriosis [11-16].

**Table 4.** The Correlation between the variable degree of pain and levels of Nitric Oxide (NO) in blood serum of endometriosis patients

NO	Pain scale			Total	P value
	low	moderate	Weight		
abnormal	5	14	21	40	0,000
	12.5%	35.0%	52.5%	100.0%	
Total	5	14	21	40	
	12.5%	35.0%	52.5%	100.0%	

Based on Table 4, it was found that all (100%) endometriosis sufferers had abnormal blood serum NO levels. Endometriosis sufferers experience the most severe degrees of pain having abnormal NO levels. The statistical test results showed that the value of  $P = 0.000$ , then  $p < \alpha (0.05)$ , it can be concluded that there is a correlation between the degree of pain and the NO level in the blood serum of endometriosis sufferers. This is in accordance with the increase in the number and activity of macrophages in endometriosis patients is accompanied by excessive release of cytokines and immune mediators such as NO (a type of ROS). Previous studies have also shown that increased NO and NOS are found in endometriosis patients [17-24].

**Table 5.** Results of Multivariate Analysis of a sample of patients with endometriosis

No.	Independent Variable	P value	R Square
1	Estradiol	0.03	0.19
2	IL-1 $\beta$	0.02	
3	NO	0.01	



Based on Table 5 is the final result of the multivariate analysis of multiple logistic regression tests. Because the levels of estradiol, IL-1 $\beta$  and NO have  $p < 0.05$ , these variables were not excluded from the model and all three are factors that influence the degree of pain in endometriosis sufferers. In addition, the R square value is 0.19, this means that the variable levels of estradiol, IL-1 $\beta$  and NO have a contribution of 19% to the degree of pain in endometriosis patients.

#### 4. Conclusions

Based on the results of the research conducted the results showed that the levels were increased from normal, so there was a close correlation between the degree of pain and blood serum levels of estradiol, IL-1 $\beta$  and NO and the threshold of menstrual pain. The higher the blood serum levels of estradiol, IL-1 $\beta$  and NO accompanied by the heavier a person's menstrual pain, it helps prove the existence of an endometriosis. the year 2020.

**Acknowledgments:** Thanks to all the people who took part in guiding and helping this research so that it can be completed properly.

#### References

1. ADAMSON, G. D., KENNEDY, S., HUMMELSHOJ, L., Creating solutions in endometriosis : global collaboration through the World Endometriosis Research Foundation, (January), 2010
2. HIFERI, POGI, Konsensus tata laksana nyeri endometriosis, Revisi Pertama, 2017
3. \*\*\*ASRM. The Practice Committee of the American Society for Reproductive Medicine. *Fertil Steril*, 2014;10(4):927-35.
4. DUNSELMAN G., et. al., ESHRE guideline, management of women with endometriosis. *Hum Rep* 2014,29(3):400-12.
5. MEDEIROS L., et.al., Accuracy of magnetic resonance in deeply infiltrating endometriosis: a systematic review and meta - analysis. *arch gynecol obstet*, 2014.
6. ALLEGRA, A., et. al., The gene expression profile of cumulus cells reveals altered pathways in patients with endometriosis, 2014, 1277–1285. <https://doi.org/10.1007/s10815-014-0305-1>
7. ALPAY, Z., SAED, G. M., DIAMOND, M. P., Female Infertility and Free Radicals : Potential Role in Adhesions and Endometriosis, 2016 0. <https://doi.org/https://doi.org/10.1016/j.jsgi.2006.05.002>
8. FITRI, DKK, Perbedaan derajat nyeri haid pasien Endometriosis sebelum dan sesudah tindakan laparoscopi di RSUP dr. Mohammad Hoesin Palembang, FK Universitas Sriwijaya, 2015
9. MUSYARROFAH, DKK., Penurunan Skala Nyeri Penderita Endometriosis Sebelum dan Sesudah Laparoscopi, FK UNAIR, 2015
10. \*\*\*Perhimpunan dokter spesialis anestesiologi dan terapi intensif indonesia, Panduan Tatalaksana Nyeri Operatif. Jakarta: 2009, PP IDSAI.
11. ANWAR R., et.al., .Association between mRNA Expression of Aromatase, 17 $\beta$ -HSD2, Level of TGF- $\beta$ 1 and Stage of Endometriosis. *Open Journal of Obstetrics and Gynecology* 2016;6:411-8
12. BHANOORI, M., et. al., The endothelial nitric oxide synthase Glu298Asp polymorphism is not a risk factor for endometriosis in south Indian women. *Eur J Obstet Gynecol Reprod Biol*, 2010, 139(1): 53-58.
13. DUDA, D. G., FUKUMURA, D., JAIN, R. K., Role of eNOS in neovascularization: NO for endothelial progenitor cells. *Trends Mol Med*, 10(4): 143-5. Factor Expression in a Rat Hindlimb Ischemia Model. 2004, <https://doi.org/10.1161/01.CIR.0000093190.53478.78>
14. CAHYONO, polimorfisme gen endothelial nitric oxide synthase (nNOS) dan kadar interleukin 1 Beta (IL-1beta), Nitric oxide (NO) dan 8-Hydroxy -2 deoxyguanosine (8-OH-dG) cairan folikuler pada pasien endometriosis, 2015
15. FAN, X., et. al., Endometrial VEGF induces placental sFLT1 and leads to pregnancy complications Find the latest version: Endometrial VEGF induces placental sFLT1 and leads to pregnancy complications, *I24(11)*, 2014.4941–4952. <https://doi.org/10.1172/JCI76864.7>

- 16.HOFFMAN B., et. al., polimorfisme gen endothelial nitric oxide synthase (nNOS) dan kadar interleukin 1 Beta (1L-1beta), Nitric oxide (NO) dan 8-Hydroxy -2 deoxyguanosine (8-OH-dG) cairan folikuler pada pasien endometriosis, 2015,1-9.
- 17.MACMICKING, J., XIE, Q. W., NATHAN, C., Nitric oxide and macrophage function. *Annu Rev Immunol*, 1997.15323-50.
- 18.NAMBA, T., et. al., Angiogenesis Induced by Endothelial Nitric Oxide Synthase Gene Through Vascular Endothelial Growth Physiology, C. Effect of Mst1 on Endometriosis Apoptosis and Migration : Role of Drp1-Related Mitochondrial Fission and Parkin-Required Mitophagy, 2015, 1172–1190. <https://doi.org/10.1159/000487450>
- 19.OTA, H., IGARASHI, S., HATAZAWA, J., TANAKA, T., Endometriosis and free radicals. *Gynecol Obstet Invest*, 1999.48 Suppl 129-35.
- 20.WILLIAMS GYNECOLOGY (3RD ED), New York: McGraw Hill, 2016.
- 21.RUNESSON, E., et.al., Evidence for nitric oxide acting as a luteolytic factor in the human corpus luteum, 2017, 6(5), 397-403.
- 22.TAVANA, Z., et. al., Prevalence of common polymorphisms of AT-rich interaction domain 1A and endothelial nitric oxide synthase in patients with endometriosis compared to control group. 2018, <https://doi.org/10.1177/2284026518764352>
- 23.WINGROVE, J. A., FARRELL, P. H. O., FRANCISCO, S., Nitric Oxide Contributes to Behavioral, Cellular , and Developmental Responses to Low Oxygen in *Drosophila*, 2016. 98, 105-114.
- 24.YUDIYANTA, NOVITA, Assessment Nyeri. Patient Comfort Assessment Guide, 2015

---

Manuscript received: 22.02.2021