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Expression of CA-125 Level and Neutrophil to Lymphocyte Ratio in Infected and Non-infected Endometrioma

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Abstract

Introduction. Implantation and growth of endometriosis was determined by immune cell. There were several immunologic cells that promoting implantation and cell proliferation such as macrophages, Natural killer, lymphocyte and monocyte. Infected endometrioma was associated in women with revised American Society for Reproductive Medicine (ASRM) stage III-IV. Neutrophil lymphocyte ratio (NLR) was a simple systemic inflammation response markers. The sensitivity and specificity CA-125 in predicting endometrioma was very low but it had been used to monitor the progress of endometriosis. Therefore, measuring mean in leucocyte, NLR, PLR and CA-125 level in infected endometrioma was necessary. **Material & Method.** A retrospective study from medical record between January 2014-December 2014 that was diagnosed as endometriosis cyst and undergone either laparotomy and laparoscopy. **Result.** The mean of age 39.42±7.35, leukocyte 9,209,77±3,310,14, The mean and SD of each variables were in group infected WBC 16,433.33±7,277.13, NLR 11.04±9.63, PLR 342.13±156.23, CA-125 342.13±156.23 CA-125 adjunct to the NLR 2332.74±1,872.31. . The mean and SD of each variables were in group non infected WBC 8,475.27±2485.59, NLR 4.04±4.49, and CA-125 adjunct to the 981,99±1,229.55. This was correlate to the infection process. **Conclusion.** Increasing level of WBC, neutrophil, NLR and NLR adjunct CA-125 are different in infected endometrioma and non-infected endometrioma. The increasing level of those was due to response of the bacteria. However, endometriosis did not show cell immune to eliminate instead providing its cell to growth.

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1. Introduction

Endometriosis was the presence of endometrial gland and stroma outside the uterus cavity. It's affect 10% of women reproductive age. Implantation and growth of endometriosis was also determine by immune cell. There were several immunologic cells that promoting implantation and cell proliferation such as macrophages, Natural killer, lymphocyte and monocyte. Macrophage and monocyte secreted Vascular Endothelial Growth (VEGF) thus, promoting angiogenesis and cell growth. Natural Killer (NK) cells had activated killer-inhibiting receptor that decreasing cytotoxic activity in endometriosis. Lymphocyte subgroup B and T were increased in peritoneal fluid.

Both lymphocyte secrete interleukin-1 (IL-1) that stimulating angiogenic factors and helping endometrial cell that enter peritoneal cavity to disguise immunosurveilance by inducing the release of soluble form of intercellular adhesion molecule-1 (ICAM-1) from endometriotic cells that competes for immune recognition sites in NK and other immune cells [1-4].

Infected endometrioma was associated in women with revised American Society for Reproductive Medicine (ASRM) stage III-IV. One study report that there was only 18 patient who had infected endometrioma, The risk factor for the this condition was due to sexual behaciour, increased age, diabetes and immunocompromised status. Some case reports describe the development of infected endometrioma in advanced stage endometriosis following endometriosis aspiration and oocyte retrieval. he pathogenesis of the disease was due to the translocation of the bacteria from colon to the endometrioma. Thus, increased morbidity due to sepsis and increasing infertility due to salphyngooophorectomy [5-7].

Neutrophil lymphocyte ratio (NLR) was a simple systemic inflammation response markers. NLR possesses diagnostic value in certain pathologies characterized systemic or local inflammatory response such diabetes mellitus, coronary artery disease, ulcerative colitis and inflammatory arthritis. These two cells provided detecting inflammation. In one study NLR as an adjunct CA-125 could predict endometrioma [8,9].

Thrombosis and inflammation were closely linked pathophysiology process. Platelet interaction with granulocytes and monocyte had been studied extensively. Interaction between platelet and lymphocyte as such mechanism: influencing platelet on lymphocyte adhesion and homing, activation T cell, proliferation and antibody production B cell and others. Platelet lymphocyte ratio (PLR) could be used in describing inflammation process. PLR had been studied in prognostic factor for malignancy such breast, ovarian and colorectal cancer [10,11].

CA-125 was an antigen cell surface that present in epithel coelemik and Müller, including endometrium, endocervix, peritoneum pleura and pericardium. The increasing CaA-125 level was due to malignant and benign ovary lesion, leiomyoma, endometrial cancer, cervical cancer, pregnancy, infection and endometriosis. The sensitivity and specificity CA-125 in predicting endometrioma was very low but it had been used to monitor the progress of endometriosis. However, there were no study measuring CA-125 in infected endometrioma. Therefore, measuring mean in leucocyte, NLR, PLR and CA-125 level in infected endometrioma was necessary [12-15].

2. Methods

A case control study was conducted in the Cipto Mangunkusumo Hospital between 2014-2015 from medical records. The study was included 114 patient with endometrioma and confirmed by ultrasound and undergone whether laparoscopy or laparotomy. Preoperatively patient was collected for the complete blood count including differential

Variables	Mean
Age	39.47±7.42
White Blood Count (WBC)	9216.81±3449.24
Basophil	0.32±27
Eosinophil	1.68±1.39
Neutrophil	69.9±11.35
Lymphocyte	23.18±13.13
Monocyte	5.80±2.11
Erythrocyte Sediment Rate (ESR)	44.02±31.23
Platelet	342,545.45+101,040.27
Neutrophil to Lymphocyte Ratio (NLR)	6.98±5.62
Platelet to Lymphocyte Ratio (PLR)	243.80±248.76
CA-125	205,13±7.56
Ca-125xNLR	1,014.66±7.57

Table 1: Mean of Age, White Blood Count, CA-125, NLR, and PLR.

count and CA 125 level in Cipto Mangunkusumo laboratory. After that patient was planned whether laparotomy or laparoscopy. The diagnosis infected endometrioma was established finding pus intraoperatively and confirmed by histopathology. The exclusion criteria were data that was not complete such, no measuring differential count and CA-125 level. After the exclusion criteria there was only 52 with 12 patients with infected endometrioma and 40 patient non-infected endometrioma.

The data were evaluated by SPSS version 11.5 statistic software. The data were expressed as mean+standard deviation. Pearson Correlation test was used to evaluate the correlation between two groups. Correlation analysis dor nonparametric variables were conducted using Spearman Rho test. The two groups were compared with each other using One-way and ANOVA test. Statistical evaluation between two groups were conducted using independent t test. The level statistical significance was set at $p<0.05$.

3. Result

The mean of age 39.42±7.35, leukocyte 9,209,77±3,310,14, basophil 0.31±0.26, eosinophil 1.68±1.38, neutrophil 69.89±11.22, lymphocyte 23.23±12.98, monocyte 5.73±2.13, ESR 43.32±30.84, NLR 6.99±5.57 Ca-125 205.13±7.56, thrombocyte neutrophil ratio, Ca-125xNLR 1,014.66+7.75 were presented in Table 1.

The mean WBC ($p<0.05$), NLR and CA-125 as adjunct NLR showed statistical significance. Basophil, eosinophil, neutrophil, lymphocyte, monocyte, ESR, platelet, PLR, and CA-125 level did not showed statistical significance. The mean and SD of each variables were in group infected WBC 16,433.33±7,277.13, basophil 0.35±0.26, eosinophil 0.8±0.87, neutrophil 77.05±15.15, Lymphocyte 17.35±12.81, monocyte 4.45±2.40, ESR

	Infected n=12	Non-Infected n=40	P value
WBC	16,433.33±7277.13	8,475.27±2485.59	p<0.05
Basophil	0.35±0.26	0.31±0.25	p>0.05
Eosinophil	0.8±0.87	1.80±1.37	p>0.05
Neutrophil	77.05±15.15	67.75±9.37	p>0.05
Lymphocyte	17.35±12.81	25.18±12.63	p>0.05
Monocyte	4.45±2.40	6.03±2.05	p>0.05
ESR	61.50±41.62	42.93±28.60	p>0.05
Platelet	486,000.00+24,758,83	343,724.13+88,406.89	p>0.05
NLR	11.04±9.63	4.04±4.49	p<0.05
PLR	283,68±177.67	250.69±294.22	p>0.05
CA-125	342.13±156.23	224.15±202.66	p>0.05
CA-125xNLR	2,332.74±1,872.31	981,99±1,229.55	p<0.05

Table 2: Comparison White Blood Count, Platelet, NLR, PLR, and CA-125 in Infected and Non-Infected Endometrioma.

61.50±41.62, platelet 486,000.00±24,758.83, NLR 11.04±9.63, PLR 342.13±156.23, CA-125 342.13±156.23 CA-125 adjunct to the NLR 2332.74±1,872.31. The mean and SD of each variables were in group non infected WBC 8,475.27±2485.59, basophil 0.31±0.25, eosinophil 1.80±1.37, neutrophil 67.75±9.37, Lymphocyte 25.18±12.63, monocyte 6.03±2.05, ESR 6.03±2.05.62, platelet 4.04±4.49, NLR 4.04±4.49, PLR 250.69±294.22, CA-125 224.15±202.66 CA-125 adjunct to the 981,99±1,229.55.

4. Discussion

WBC in infected endometrioma was increasing until 16,433.33±7277.13 compared non-infected 8,475.27±2485.59. This was correspond due to infection process. The infection process elevated WBC due to self defense immune response to the infection. However, response to the implantation of endometriosis was not elevated WBC. This condition as similar to the study Yavuzcan et all finding WBC level in endometriosis were 7081.5+2170.6. This showed that inflammation process in the endometriosis did not correlated to the foreign body. However, inflammation process in endometriosis had aimed proliferation and growth of the endometriosis. Even though endometriosis was an immunological abberant disease, a locally impaired immunity in the pelvic cavity of women with endometriosis makes them vulnerable to infection. Role of basophil and eosinophil still contradiction. In this study showed response of the basophil and eosinophil was not different in infected endometrioma and endometrioma [10,15,16,20,21].

Increasing neutrophil in infected endometrioma compared to the endometriosis showed self defense system to the infected. In endometriosis role of the neutrophil was also promoting angiogenesis and provide proliferation cell. Role neutrophil in infected endometrioma was not only eliminate bacteria but also proving endometriosis

cell to grow. In this study neutrophil level was increasing 77.05+15.15 compared in endometriosis only 67.75+9.37.One study reveled level of the neutrophil in endometriosis was 4.14+1.73 103/uL) and this correspond to this study [12,13,14,16].

NLR in both groups were statisticaly significance. Bacteremia increasing the NLR with cutoff 6.2. This was correlate to the infection process. In one study endometriosis NLR alone cannot predict endometriosis and the mean NLR was 4.04+4.49. But in this study NLR in infected endometrioma 11.04+9.63 showed correspond to the previous study. This is because the neutrophil act as innate immunity and suppressed the lymphocyte as a response to the bacteria [8,9,10].

CA-125 in adjunct NLR was statistic significance in infected endometrioma. This was similar to the study of Cho et all in diagnosis of endometriosis. In that study the combination with cutoff 62 could predict endometriosis. CA-125 level alone couldnot predict endometriosis but it could predict the severity of disease. Because CA-125 level also elevated in ovarian malignancy and other [9].

5. Conclusion

Increasing level of WBC, neutrophil, NLR and NLR adjunct CA-125 are different in infected endometrioma and non-infected endometrioma. The increasing level of those was due to response of the bacteria. However, endometriosis did not show cell immune to eliminate instead providing its cell to growth.

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