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The Comparison of Er α Expression Between Endometriosis with No Endometriosis

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Abstract. Background: Estrogen receptors (ER) play an important role in mediating action. The ER α has a higher affinity for estrogen and the dominant form of the normal endometrium. A cross-sectional study from an ectopic tissue of endo-metriosis and normal was examined for immunohistochemistry. This research was conducted from November 2015 until the sample complete. The analysis was performed using Fisher Exact test, p <0.05 was considered to any difference of estrogen alpha receptor expression between endometriosis patients with no endometriosis. REα is more dominant in normal endometrium, whereas in the case of endometriosis in the presence of many negative expression of REα then the assumption that REβ is a receptor that many encountered. There is a dif-ference in the expression of REα between endometriosis with no endometriosis.

Keyword: Estrogen A Receptor, Endometriosis, Normal Endometrium.

Abstrak. *Reseptor estrogen (ER) memainkan peran penting dalam mediasi tindakan. ER α memiliki afinitas yang lebih tinggi untuk estrogen dan bentuk dominan dari endometrium normal. Sebuah studi cross-sectional dari jaringan ektopik endo-metriosis dan normal diperiksa untuk imunohistokimia. Penelitian ini dilakukan dari November 2015 hingga sampel selesai. Analisis dilakukan dengan menggunakan uji Fisher Exact, p <0,05 dianggap sebagai perbedaan ekspresi reseptor alpha estrogen antara pasien endometriosis tanpa endometriosis. REα lebih dominan pada endometrium normal, sedangkan pada kasus endometriosis di hadapan banyak ekspresi negatif REα maka anggapan bahwa REβ adalah reseptor yang banyak ditemui. Ada perbedaan dalam ekspresi REα antara endometriosis tanpa endometriosis.*

Kata Kunci: *Reseptor Estrogen A, Endometriosis, Endometrium Normal.*

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1. Introduction

Endometriosis is defined as the appearance of endometrial tissue outside of the uterine cavity. Endometriosis is strongly influenced by estrogen measure. In the United States, this disease affects 5 - 19% of women at the reproductive age. The main descriptions are chronic pelvic pain

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during coital and infertility [1]. Pelvic pain and complaints from endometriosis can be reduced by giving the anti-inflammatory drugs, so it supports that in endometriosis, the process of inflammatory gives the contribution as one of the pathogenesis of the disease [2].

The Proliferation of endometrial cells and endometriosis is induced by estrogen. In contrast, the progesterone stimulates cellular differentiation and suppresses the cellular proliferation. In the endometriosis, the increasing estrogen effects and abnormal progesterone work, leading to the increasing cell proliferation. Simultaneously, apoptotic disorders in the endometrial and endometrial cells from women with endometriosis can contribute to the pathogenesis of the disease [3].

The Estrogen receptor has an important role in mediating estrogen action in tissues. There are two forms of estrogen receptors, they are ERα and Erβ, which are encoded by different genes. The estrogen α receptor has a higher affinity for estrogen, and it is the dominant form of the normal endometrium. Recent studies have shown that ERα and ERβ express the human tissue endometriosis, but the distribution of iso form is different between eutopic endometrium and ovarian, endometrial tissue [4], [5].

From the description that has been described above, the researchers are very interested to know whether there is difference expression of REα on ectopic endometrial tissue endometriosis patients and normal endometrial tissue to further know about endometriosis disease.

2. Methodology

This was an analytic study with cross-sectional design in which it has been done the examination of immune histo hemical toward the ectopic endometrial endophilic tissue blocks of endometriosis and normal endometrial tissue. The study was conducted at Department of Obstetrics and Gynecology FK USU / RSUP H Adam Malik Medan, while immune histochemical examination was done at Department of Anatomical Pathology USU Medan. This research was conducted from November 2015 until the sample was met. This research had been approved by the Committee of Ethics of the Faculty of Medicine, University of Sumatera Utara. The preparations cannot be analyzed by the cause of poor paraffin preparation removed from the study. The immune histochemical assessment for the expression of the RE antibody uses Allred's score by summing up the percentage of the colored cell / Proportion Score (PS) and the intensity score of the staining / Intensity Score (IS). It is said negative expression if the score shows 0-2, while positive if the score shows ≥ 3.

2.1 Statistical analysis

The analysis of the research was conducted by using Fisher Exact test, p <0.05 was considered the different of the expression of REα between endometriosis patients with no endometriosis.

3. Results

This study has been done by using the subjects of cases of endometriosis as many as 23 people and control of non-Endometriosis (normal endometrium) as many as 23 people. The following are the characteristics of the research subjects we obtained (**Table 1**).

Table 1 Frequency Distribution Based on the Characteristics of research subjects based on Age and Parity

Characteristic	Research Group			
	Endometriosis		Normal	
	n	%	n	%
Age				
< 30	11	47.9	11	47.9
30 – 40	8	34.8	12	52.1
> 40	4	17.3	0	0
Total	23	100.0	23	100.0
Parity				
Nullipara	23	100.0	7	30.4
Primipara	0	0	7	30.4
Multipara	0	0	9	39.2
Total	23	100.0	23	100.0

From the results of research, we also found the distribution of research subjects based on the end ometriosis stage as seen in **Table 2** below.

Table 2 Frequency Distribution of Respondents Based on Endometriosis Stage

Stage	Endometriosis	
	n	%
Stage I (minimum)	0	0
Stage II (light)	2	8.7
Stage III (medium)	10	43.5
Stage IV (weight)	11	47.8
Total	23	100

In this study, it's found that there was a signif icant difference in the expression of alpha estrogen receptor on endometriosis group stroma with non-endometriosis, and the expression value of alpha estrogen receptor in the epithelial group of endometriosis with non-endometriosis as seen in **Table 3** and four below.

Table 3 Differentiation of Alfa Estrogen Receptor Expression on Stroma Group Endometriosis and Non-Endometriosis

Expression of Estrogen Receptor α (Stroma)	Research Group		*p*
	Endometriosis	Normal	
Negative (Score 0-2)	21 (91.3%)	9(39.2%)	.000*
Positive (Score ≥ 3)	2 (8.7%)	14(60.8%)	

*Test *Fisher exact*

Table 4 Differences Expression of Alfa Estrogen Receptor on Epithelial Endometriosis and Non-Endometriosis

Expression of Estrogen Receptor α (Epitel)	Research Group		*p*
	Endometriosis	Normal	
Negative (Score 0 - 2)	23 (100%)	11 (47.8%)	.000*
Positive (Score ≥ 3)	0 (0%)	12 (52.2%)	

*Test *Fisher exact*

The Endometriosis occurrences are rarely found in the teenage girl of primers, but it can be identified in more than 50% of women younger than 20 years with chronic pelvic pain or dyspareunia. The ave rage age in which a patient is diagnosed with endometriosis is between the ages of 25-30 years [4]–[6]. In this study, the largest group of endometriosis in under 30 years was 11 people (47.9%), while the whole patient was nullipara (100%).

Endometriosis is an inflammatory disease that depends on estrogen levels, due to P450 aromatase and deficiency of 17 Beta-hydroxysteroid de-hydrogenase. 17 Beta-hydroxysteroid dehydrogenase converts estradiol into a less active estrogen, which is not found in the luteal phase of endometrial tissue. Therefore, endometriosis occurs in many women at the reproductive age [2], [7].

The exact incidence of endometriosis in Indonesia currently has not known yet for sure. At least 20-40% of women with infertility have endometriosis. Meiling H stated that high parity would reduce the risk of endometriosis [4], [8], [9].

Endometriosis tissue has a high rate of proliferation. Proliferation is associated with the progression of disease that characterized by the ability to form large masses such as endometriosis cysts and invasion of adjacent tissues that characterized by degrees of disease or staging. In this study, we encountered cases of endometriosis mostly at an advanced stage. We also found a significant difference in the value of alpha estrogen receptor expression in the endometriosis group stroma with non-endometriosis, and the expression value of alpha estrogen receptors in epithelial endometriosis with non-Endometriosis.

States that alpha estrogen receptor expression in stromal endometriosis cells is lower when compared to the normal endometrial stroma. This is most likely due to the failed response of estradiol (E2) to induce expression of progesterone (PR), which ultimately leads to secondary progesterone deficiency and progesterone resistance in the study subjects. The alpha-estrogen receptor gene in humans itself is regulated by various types of promoters [8], [10]. Says that stromal cells can produce the paracrine growth factors necessary to induce the proliferation of epithelial cells by estrogen. RE-α and RE-β are proteins with high affinity for E2 and encoded by separate genes. Although RE-α and RE-β are present in the endometrium, RE-a is the major mediator of estrogenic action in endometrial tissue.

The human endometrium is a unique tissue that can cycle in proliferation, differentiation, implantation, and regeneration in response to ovarian steroid production. The effects of estrogen itself are media ted by two different estrogen receptors, REα and REβ, which are families of nuclear receptors and act as activating transcription factors. Biological action of estrogen in the target tissue is modulated by hormone levels and receptor distribution. In the normal endometrium both REα and REβ are encountered, but with different expressions during the menstrual cycle, where the REα is more expressed than REβ in the normal endometrium, therefore estrogen-mediated proliferation is largely due to activation of Reα [11].

Further research is needed on the ratio of estrogen and beta estrogen receptors to normal endometriosis and endometrium. Also, there is a need to take a deeper look at other biomolecules concerning the use of drugs that act as selective estrogens modulator to regulate estrogen levels that affect the occurrence of endometriosis.

4. Conclusions

In the normal endometrium, REα is more dominant, whereas in the case of endometriosis in the presence of many negative expression of REα then the assumption that REβ is a receptor that is mostly being encountered.

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