

Pro-inflammatory Cytokines (IL6, IL8 and TNF- α) in the Evaluation of Ovarian Endometriosis Cyst

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Endometriosis is the abnormal growth of cells (endometrial cells) similar to those that form the inside of the uterus, but in a location outside of the uterus. Endometriosis is most commonly found on other organs of the pelvis. These lesions are most commonly found on the ovaries, the Fallopian tubes, the surface of the uterus, the bowel, and on the membrane lining of the pelvic cavity (i.e. the peritoneum). We corroborate TNF- α , IL-6 and IL-8 markers with intraoperative laparoscopic on 39 patients diagnosed with endometriosis in January 2016 - December 2017, aged 20-45 years. There has been a preoperative evaluation in the patients from this that included the anamnesis, clinical examination and laboratory tests. Anamnesis recorded demographic details, patient's personal, physiological and pathological medical history. Evaluation of preoperative investigations consisted of general and local systems examination, a gynecological examination in order to identify the specific signs of endometriosis. Making matters worse is that endometriosis exhibits significant immunological dysfunction, including the over-expression of pro-inflammatory cytokines like interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF), all of which contribute to a chronic up-regulation of painful, tissue-damaging inflammatory processes. Because the cause of endometriosis is poorly understood, there are no known ways to prevent its development.

Key words: ovarian endometriosis cyst, pro-inflammatory cytokines, IL6, IL8, TNF- α

Endometriosis is defined as the presence of endometrial tissue outside of the uterus. Unfortunately, this pathology is more common in fertile people aged 16-50 years, characterized by increasingly worsened pain and subfertility [1-2]. Women with endometriosis have symptoms that include chronic pelvic pain, dysmenorrhea and dyspareunia, that significantly reduce the quality of their life.

In the pathogenesis of endometriosis inflammation plays an important role. Infiltration of local pro-inflammatory mediators in the peritoneal environment affects ovarian function and anatomy of the pelvis. All these outlines, later, the picture of symptomatic endometriosis. Pathophysiological, there is an acute inflammation followed by macrophage infiltration, tissue remodelling and neovascularization [3].

The responses to the inflammatory process are directly correlated with the growth of activated macrophages and cytokines secreted into the peritoneal fluid, thereby producing maintenance of endometriosis by endometrial adhesion, invasion, angiogenesis and endometrial cell proliferation within endometrial deposits [4-6].

Although the pathogenesis of endometriosis is still controversial, a widely accepted explanation is that of Sampson's theory according to which the flow of menstrual blood determines the displacement and storage of endometrial cells at unusual locations (Sampson's theory of retrograde menstruation).

There are numerous studies that report that a series of biomarkers (IL-6, IL-8, TNF- α , high sensitivity C-reactive protein and antigens CA125 and CA19-9) show with high sensitivity and correlated with clinical symptoms the clinical forms of endometriosis.

Experimental part

Material and methods

In our study group of 39 patients diagnosed with ovarian endometriosis cyst, the dosage of immunological markers and cytokine IL-6, IL-8 and TNF- α levels in serum was performed preoperatively and 6 months after surgery. We compared marker values for patients diagnosed with endometriosis with those of a control group (26 cases) to whom this diagnosis was not confirmed. The data was processed using SPSS v17 statistical package software.

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Table 1
VALUES OF CENTRAL AND DISPERSION TREND INDICATORS FOR THE IL-6
VARIABLE

Indicators	IL-6 Control	IL-6 Study
Mean	3.628	6.36
95% Interval Confidence Lower Bound	2.401	5.244
95% Interval Confidence Upper Bound	4.8556	7.476
Median	2.195	6.01
Variance	9.236	11.852
Std. Deviation	3.039	3.443
Std. Error	0.596	0.551
Minimum	0.36	1.37
Maximum	14.30	13.32
Range	13.94	11.95
Skewness	1.901	0.120
Kurtosis	4.888	-1.207

Table 2
VALUES OF CENTRAL AND DISPERSION TREND INDICATORS FOR THE
TNF VARIABLE

Indicators	TNF Control	TNF Study
Mean	57.731	54.525
95% Interval Confidence Lower Bound	54.894	52.308
95% Interval Confidence Upper Bound	60.578	56.743
Median	58.38	54.61
Variance	49.331	46.782
Std. Deviation	7.024	6.839
Std. Error	1.377	1.095
Minimum	40.03	37.24
Maximum	67.92	68.06
Range	27.89	30.82
Skewness	-0.520	-0.197
Kurtosis	-0.141	-0.302

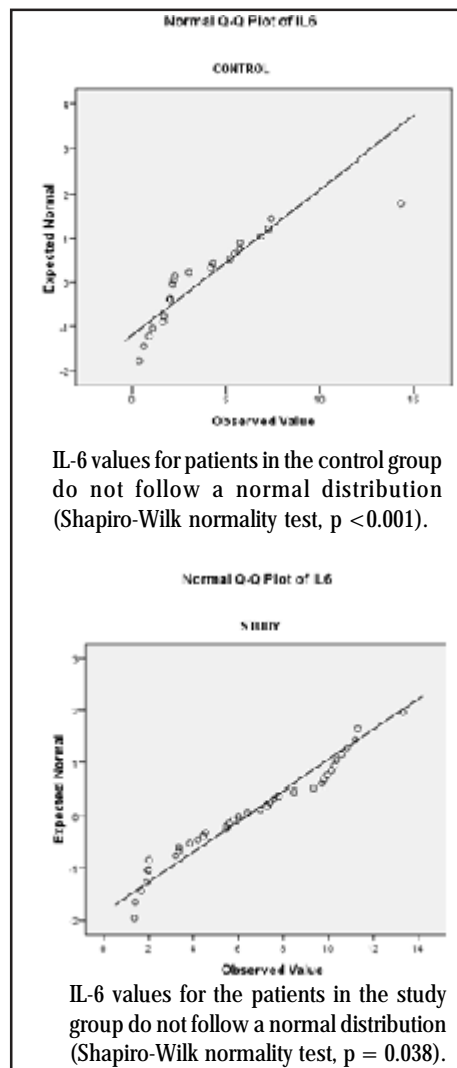


Fig. 1. The normal Q-Q plots for the IL - 6 values

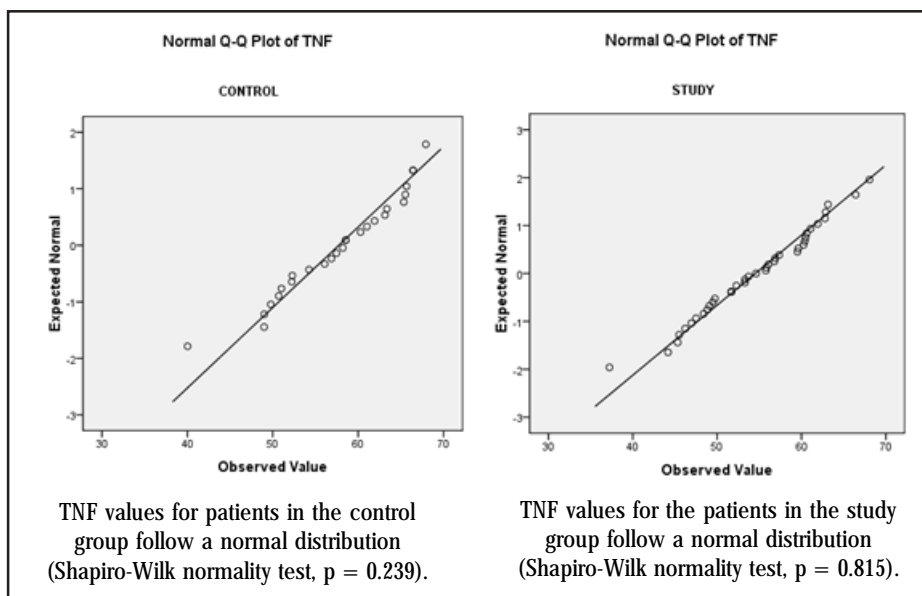


Fig. 2. The normal Q-Q plots for the TNF values

The numerical variables were compared with the nonparametric Mann-Whitney U test (in the case of two independent groups). For $p < 0.05$ were considered statistical significance [7-8].

Results and discussions

Endometriosis is a polygenic disease with a complex, multifactorial ethology that affects approximately 10% of reproductive-age women. Women with endometriosis

have symptoms that include chronic pelvic pain, dysmenorrhea and dyspareunia, that significantly reduce the quality of their life [9-10]. Endometriosis is also the main cause of infertility in women, the prevalence rate ranging from 20 to 50% [11-12].

In order to describe the IL - 6, IL - 8 and TNF values we calculated the central tendency and dispersion parameters and we plotted the recommended figures (tables 1-3, figures 1- 4).

Indicators	IL-8 Control	IL-8 Study
Mean	31.995	76.613
95% Interval Confidence Lower Bound	28.238	59.340
95% Interval Confidence Upper Bound	35.752	93.886
Median	34.900	44.300
Variance	215.214	2839.394
Std. Deviation	14.670	53.286
Std. Error	1.878	8.533
Minimum	4.700	40.100
Maximum	110.800	228.000
Range	106.100	187.900
Skewness	2.080	1.560
Kurtosis	13.348	1.668

Table 3
VALUES OF CENTRAL AND DISPERSION TREND
INDICATORS FOR THE IL-8 VARIABLE

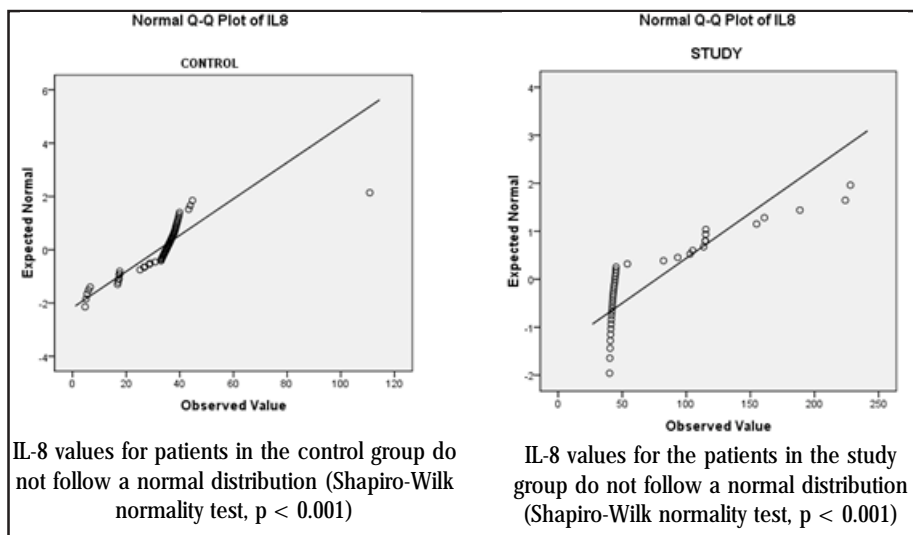


Fig. 3. The normal Q-Q plots for the IL - 8 values

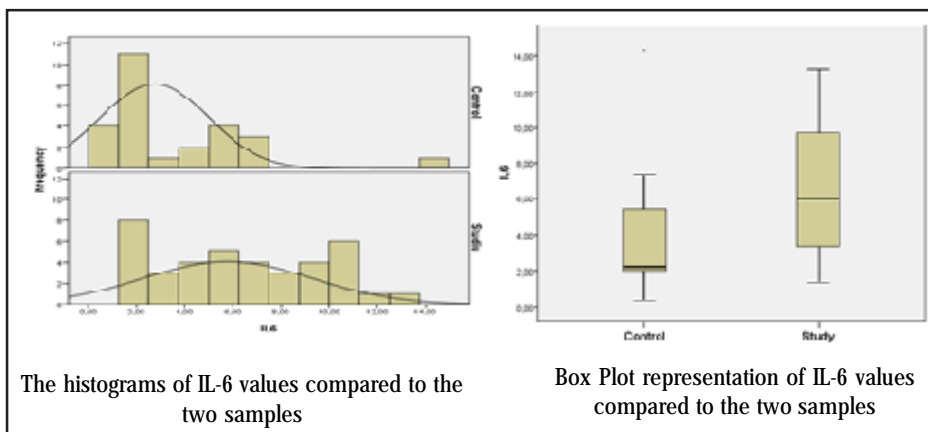


Fig. 4. The histogram and the Box plot for the I - 6, TNF and IL - 8

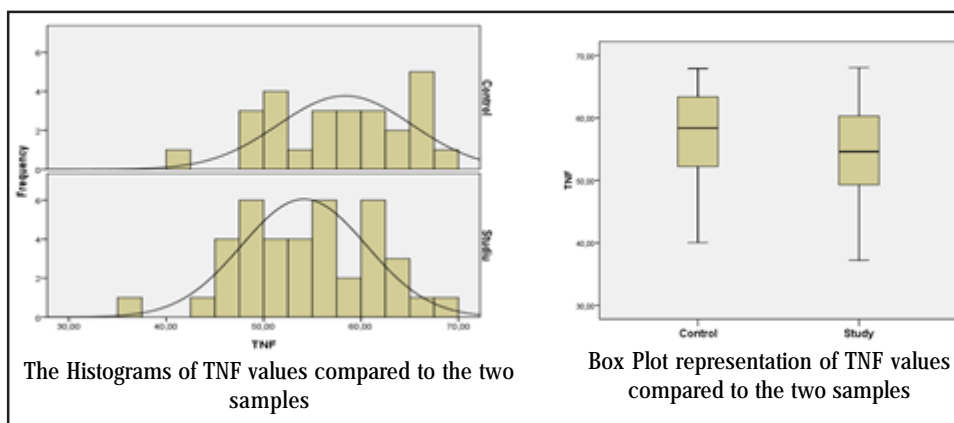


Fig.5

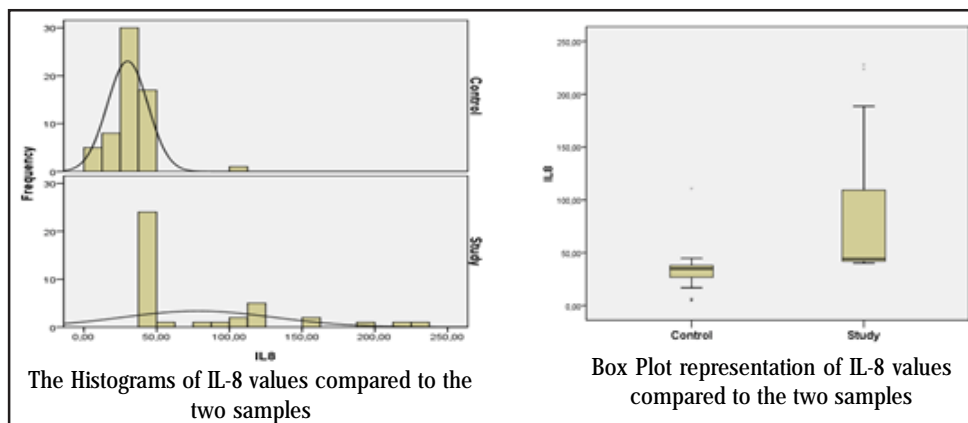


Fig.6

IL-6 values are significantly increased for the study group compared to control (Mann-Whitney U Test, $p = 0.001$).

TNF values for the endometriosis group are insignificantly low (Unpaired t Test, $p=0.072$) (fig.5).

IL-8 values are significantly increased for the study group compared to control (Mann-Whitney U Test, $p < 0.001$) (fig. 6).

Conclusions

Pro-inflammatory cytokines appear to play an important role in the development of endometriosis, initially acting locally and then manifesting systemically, thus rendering the clinical picture of endometriosis. The high prevalence and severe consequences of this disease caused a major public health issue in modern society. And yet, the mechanism responsible for the initiation and development of this disease still remains an enigma.

Identifying a non-invasive diagnostic marker for endometriosis could facilitate the early diagnosis of this pathology and early medical management with an appropriate treatment for each case.

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