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Original Article

The relationship of pelvic pain symptoms with CA-125 levels in endometriosis cases

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Abstract

Aim: This study aims to investigate the relationship between CA-125 levels and pelvic pain symptoms in patients with endometriosis.

Material and Methods: This study consisted of retrospective data of 31 patients who were admitted to the outpatient clinic of Faculty of Medicine, Amasya University between 01 January 2013 and 01 January 2018 for complaints of pelvic pain, dysmenorrhea or infertility, who had a preliminary diagnosis of endometriosis by clinical and ultrasonography examination and diagnosed with endometriosis by laparoscopy or laparotomy as well as 35 patients who received diagnostic laparoscopy for any reason or laparotomy or laparoscopy for benign or tubal ligation. The study included patients aged 18 to 45 years old. Patient data were recorded via an information form which included age, presence of infertility, duration of infertility, preoperative CA-125 values, presence of dysmenorrhea and dyspareunia symptoms, previous operation for endometriosis, presence of additional gynecological pathology, disease stage, operation notes, primary complaints, preoperative TVS information, gravida, parity, abortion and living children, used medication, if any, chronical diseases, if any.

Results: The blood CA-125 levels were statistically significant in the patients considering the presence of chronic pelvic pain, dysmenorrhea and infertility ($p < 0.05$). Mean CA-125 levels were 51.43 U/ml in patients with chronic pelvic pain symptoms. Mean CA-125 levels were 45.45 (U/ml) in patients with dysmenorrhea. Mean CA-125 was 45.67 (U/ml) in infertile patients and 45.58 (U/ml) in patients with endometriosis. Mean CA-125 levels in patients with additional gynecological diseases were 38.29 (U/ml), which was not statistically significant.

Conclusion: This study demonstrated that CA-125 levels were significantly associated with pelvic pain symptoms, infertility and endometriosis. In light of the results, preoperative serum CA-125 levels are a predictor and should be considered for patients with chronic pelvic pain.

Keywords: Endometriosis; CA-125; pelvic pain.

INTRODUCTION

Endometriosis is an estrogen-dependent disease that affects fertility, women's somatic health and quality of life throughout life. Endometriosis is seen in approximately 10-15% of adult women aged 25-35 years old (1). Endometriosis is seen in 80% of women with pelvic pain or infertility (2). It is the second most common gynecological condition after uterine myoma. The prevalence of endometriosis in the general population is unknown. The pathophysiology of endometriosis has begun to be investigated further in order to provide treatment for this condition that has been encountered commonly the last few decades and causes serious problems. Endometriosis is a condition characterized by endometrial gland and stroma outside the uterine cavity and muscle layer. Its prevalence is difficult to determine since some patients are asymptomatic and the presenting symptoms are non-specific and diverse. Endometriosis is seen in 12-32% of patients who received laparoscopy for pelvic pain, in 9-50% of patients who received laparoscopy for infertility, or in 50% of patients who received laparoscopy for chronic pelvic pain or dysmenorrhea (3,4). The possibility of familial tendency for endometriosis has been recognized for many years. The most common symptom of endometriosis is pain. Approximately 75% of symptomatic patients suffer from pelvic pain and/or dysmenorrhea (5). Other symptoms include chronic pelvic pain, dysmenorrhea, dyspareunia, subfertility, abnormal menstrual bleeding,

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low back pain (5,6). The pathology of endometriosis is not clearly defined. Although the pathogenesis is not yet known, there are many theories based on various evidences. These include retrograde menstruation-transplantation, coelomic metaplasia - induction, vascular dissemination, immune system theories. The fact that it is seen more frequently in women of reproductive age, regression of its symptoms with menopause, reoccurrence of symptoms in some postmenopausal women who received estrogen replacement therapy suggest that endometriosis is an estrogen-dependent disease. The immune system hypothesis explains the translocation of endometrial implant and inflammatory cells to peritoneal cavity, inducing the proliferation of implants along with cytokine secretion that leads to capillary support and to leukocyte chemotaxis of peritoneal inflammation in this area (7). Oxidative stress may be another component of the inflammatory component (8). The immune system may play a role in determining the clinical signs and extent of endometriosis (9,10). The stage of endometriosis is not correlated with the presence and severity of symptoms. The gold standard for the diagnosis of endometriosis is the laparoscopic visualization of the lesion (6). Endometriosis is a chronic disease that requires optimal treatment for a lifetime and avoidance of repeated operations. Despite intensive research, the optimal treatment for endometriosis is unclear.

Serum CA-125 is a glycoprotein and can be elevated in many benign and malignant gynecological diseases including endometriosis (11). This study aims to determine the relationship of CA-125 levels with pelvic pain and dysmenorrhea symptoms in patients with endometriosis.

MATERIAL and METHODS

This study consisted of retrospective data of 31 patients who were operated in the clinic of Obstetrics and Gynecology, Faculty of Medicine, Amasya University between 01 January 2013 and 01 January 2018 for complaints of pelvic pain, dysmenorrhea or infertility, who had a preliminary diagnosis of endometriosis by clinical and ultrasonography examination and diagnosed with endometriosis by laparoscopy or laparotomy as well as 35 patients who received diagnostic laparoscopy for any reason or laparotomy or laparoscopy for benign or tubal ligation. Patients who were included into the study group with the diagnosis of endometriosis by laparoscopy or laparotomy were classified according to the endometriosis classification of American Society for Reproductive Medicine (ASRM). The study included patients aged 18 to 45 years old. Age, presence of infertility, duration of infertility, preoperative CA-125 values, presence of dysmenorrhea and dyspareunia symptoms, previous operation for endometriosis, presence of additional gynecological pathology, disease stage, operation notes, primary complaints, preoperative TVS information, gravida, parity, abortion and living children, used medication, if any, chronical diseases, if any were recorded in the information form.

Statistical analysis

Descriptive statistics were performed on all data. The statistical significance of the parameters with blood CA-125 levels was examined by chi-square test and the correlation between the parameters was examined by chi-square test. GraphPad Prism v6 software was used for statistical analysis. The confidence interval was considered at 95% and the statistically significance was accepted at $p < 0.05$.

RESULTS

Descriptive statistics for the data of 65 patients are presented in Tables 1 and 2. The blood CA-125 levels were statistically significant in the patients considering the presence of chronic pelvic pain, dysmenorrhea and infertility ($p < 0.05$). Mean CA-125 levels were 51.43 U/ml in patients with chronic pelvic pain symptoms. Mean CA-125 levels were 45.45 (U/ml) in patients with dysmenorrhea. Mean CA-125 was 45.67 (U/ml) in infertile patients and 45.58 (U/ml) in patients with endometriosis. Mean CA-125 levels in patients with additional gynecological diseases were 38.29 (U/ml), which was not statistically significant (Table 3). A significant relationship was found between the presence of infertility and chronic pelvic pain ($p = 0.00012$), endometriosis ($p = 0.001$) and dysmenorrhea ($p = 0.02006$) symptoms. There was no correlation of past operation and past operation for endometriosis with infertility ($p > 0.05$) (Table 4).

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Table 1. Demographic Characteristics Table

Parameters	Mean	Standard deviation
Age	32.06	5.82
Number of Pregnancies	1.11	1.36
CA-125	34.28	22.33

Table 2. Proportional distribution of some parameters of patients to all patients

	Present	%	None	%
Infertility	30	46.15	35	53.85
Past operation	6	9.23	59	90.77
Past operation for endometriosis	4	6.15	61	93.85
Additional Gynecological Disease	14	21.54	51	78.46
Primary complaint	38 8 with pain (12.31%) 30 with infertility (46.15%)	58.46	27	41.54
Chronical disease	65	100	0	0
Endometriosis	33	50.77	32	49.23
Chronic pelvic pain	23	35.38	42	64.62
Dysmenorrhea	29	44.62	36	55.38

Table 3. The Relationship of Parameters with Blood CA-125 Levels

		N	Mean	Std. Deviation	Std. Error	p
	Chronic pelvic pain					
CA-125(U/ml)	Present	23	51.43	25.88	5.40	0.0001*
	None	42	24.88	12.77	1.97	
CA-125 (U/ml)	Dysmenorrhea					
	Present	29	45.45	26.19	4.86	0.0001*
	None	36	25.28	13.27	2.21	
	Infertility					
CA-125(U/ml)	Present	30	45.67	23.90	4.36	0.0001*
	None	35	24.51	15.45	2.61	
	Endometriosis					
	Present	30	45.58	23.42	4.07	0.0001*
	None	35	22.63	13.67	2.41	
	Additional Gynecological Disease					
CA-125(U/ml)	Present	14	38.29	21.68	5.80	0.453
	None	51	33.18	22.58	3.16	

Table 4. The relationship of the presence of infertility with other parameters

		Infertility is present	No infertility	χ^2	p
		n	n		
Past operation	Present	3	3	0.0393	0.8427
	None	27	32		
Past operation for endometriosis	Present	4	3	0.3812	0.5369
	None	26	32		
Endometriosis	Present	29	2	54.5757	0.001*
	None	1	33		
Chronic pelvic pain	Present	18	5	14.7649	0.00012*
	None	12	30		
Dysmenorrhea	Present	19	10	5.406	0.02006*
	None	11	20		

DISCUSSION

In women with endometriosis, endometrial cells/fragments escape from the immune system/inflammatory response, are attached to the peritoneal mesothelial cells, invade sub-mesothelial extracellular matrix, resulting in macroscopic disease. However, when endometriosis develops this way, factors such as the invasive potentials of endometriotic cells and immunological, hormonal, genetic, environmental factors of the peritoneal fluid and its content are predictive factors (12). In the development of endometriosis, factors such as the invasive potentials of endometriotic cells and immunological, hormonal, genetic, environmental factors of the peritoneal fluid and its content are predictive factors (13).

Diagnostic Verification should still be the first step in laparoscopy (14). The etiology of chronic pelvic pain is complex and often multifactorial. The most common gynecological causes are endometriosis and chronic pelvic inflammatory disease. Non-gynecological causes include musculoskeletal, urinary and gastrointestinal disorders (15). Amara et al. found higher CA-125 serum levels during the menstrual cycle in patients with endometriosis compared to the control group (16). Karimi-Zarchi showed that serum CA-125 level in patients with pelvic pain, infertility, and infertility with pain has been increased (17). Ramos et al. found elevated serum CA-125 serum levels in infertile women with endometriosis compared to fertile women (18). In our study, we found a significant relationship between CA-125 levels and endometriosis, infertility and chronic pain symptoms. CA-125 levels were higher in the ectopic focus than uterine cavitary endometrium (19). In addition, high CA-125 may also be caused by the inflammatory reactions that alter the endothelial permeability leading to the liberation of the marker into circulation (20). Serum CA-125 levels were found to be significantly higher with endometrioma that was ruptured or more adherent to Peritone CA,

fallopian tube, ovary, omentum, colon and cul-de-sac. Preoperatively, women with endometriosis greater than 65 IU/mL with CA-125 were found to be at high risk for intense pelvic adhesions (21). Garzetti et al. found that the serum CA-125 concentration was directly correlated with the adhesion score and peritoneum. It has also been reported that CA-125 increases the invasiveness of the benign endometriosis cell line and affects in vitro cell adhesion (22).

A study by Vercellini et al. evaluated the relationship between the severity and extent of the pain symptoms and the stage and localization of endometriosis. They reported that the frequency and severity of dysmenorrhea and dyspareunia were lower in patients who had lesions only in the ovary than in those with endometriotic lesions in other areas. In addition, they argued that the endometriosis stage was not correlated with the frequency and severity of dysmenorrhea and non-cyclic pelvic pain, and that there was no relationship between the frequency of dysmenorrhea and non-cyclic pelvic pain and endometriosis stage (23).

In our study, we found higher CA-125 levels in symptomatic patients. Although this suggests the relationship between pelvic pain and CA-125 levels, it does not give information about the importance of determining the severity of the disease. The limitations of our study were its retrospective nature and the fact that it could not elucidate the relationship between endometriosis stage and CA-125 levels.

CONCLUSION

CA-125 levels were significantly correlated with pelvic pain symptoms, infertility and endometriosis. In light of the results, serum CA-125 levels could be a safe predictor for chronic pelvic pain and should be considered in patients suffering from it.

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