Original Article

Association of CA-125 Levels with the Severity of Endometriosis

Sobia Luqman[1], Fatima Qazi[2], Shumaila Naeem[3], Nasira Tasnim[4]

[1,3]Assistant Professor, [2]Postgraduate Trainee, [3]Professor
MCH Center, Pakistan Institute of Medical Sciences, Islamabad

Correspondence: *Dr Sobia Luqman*
Assistant Professor, Dept. of Obs & Gynae
MCH Center, Pakistan Institute of Medical Sciences, Islamabad
sobialuqman8@gmail.com

Abstract

Objective: The study was done to determine the association of serum CA-125 levels with the severity of endometriosis according to the Revised ASRM scoring system.

Methodology: It was cohort study of patients with diagnosed endometriosis undergoing laparoscopy, conducted at mother and child health center, PIMS hospital Islamabad between Jan 2017 to Jan 2018. A cohort of 100 patients was selected, using WHO sample size calculator for laparoscopy with diagnosed endometriosis. The technique used for sampling was convenience sampling considering the nature of the research. Serum CA-125 levels were determined preoperatively for all patients and levels were compared with the laparoscopically assigned stage of endometriosis according to the revised ASRM scoring system. All the selected patients had diagnosed endometriosis with ovarian involvement (endometrioma), while the preliminary diagnosis was made by a detailed gynaecological history, physical examination, transvaginal ultrasonography, MRI, and serum CA-125 levels. After doing the data collection procedure, for the data analysis, Pearson correlation was performed; MS Excel and SPSS 20.0 were used to analyze and interpret the results.

Results: The value of Pearson coefficient for the selected variables and the collected dataset indicated the large or high relationship between serum CA-125 levels and severity of endometriosis. Sig. (2-tailed) value i.e. 0.000 also indicated that the findings are highly significant.

Conclusion: Serum CA-125 is an indicator of the severity of endometriosis and it is important to consider it when surgical treatment is considered or necessary.

Keywords: CA-125 level, Endometriosis, Severity of endometriosis, Stages of endometriosis, Laparoscopy.

Cite this article as: Luqman S, Qazi F, Naeem S, Tasnim N. Association of CA-125 Levels with the Severity of Endometriosis.J Soc Obstet Gynaecol Pak.2020; Vol 10(4):228-232.

Introduction

Endometriosis is characterized by the presence and growth of endometrial tissue outside the uterus. Mostly these foci of endometriosis are present in the pelvic area (on the peritoneum, in the ovaries, the intestine, or the bladder), and rarely they can be found in other areas, such as the skin or lungs.[1]

Endometriosis is commonly found in women of reproductive age. The ectopic area of the endometrium bleeds every month, resulting in inflammation, scarring, and adhesions. Its prevalence is about 10 to 15 % of the general female population. 35 to 50 % of women present with severe dysmenorrhea, noncyclical chronic

Authorship Contribution: [1,3]Conception, Synthesis and planning of the research, [2]Active participation in active methodology, [4]Supervised the study all along, planned.

Funding Source: none
Conflict of Interest: none

Received: Oct 10, 2020
Accepted: Feb 12, 2021

pelvic pain, and infertility.[2]

Staging of endometriosis is dependent on the number, size, and location of implants, the degree of adhesions and whether other pelvic organs are affected. The amount of pain one feels may not be indicative of the severity of the illness. Even though endometriosis is mild, it can cause a lot of pain. Following are the stages:

Stage I (Minimum): Surface implants, mainly in the ovary; thin adhesions.

Stage II (Light): Surface implants in the pelvic lining and ovary.

Stage III (Moderate): Deep implants in the pelvic lining and ovary; dense and firm adhesions.

Stage IV (Severe): Deep implants in the ovaries and pelvic lining; dense adhesions on the ovaries, fallopian tubes, and intestines[3]

The disease is very common yet remains underdiagnosed because of having nonspecific symptoms and is usually diagnosed in a very advanced stage of the disease. The definite diagnosis is made only by laparoscopy (gold standard). Several researches have been done for the diagnosis of endometriosis by non-invasive methods including transvaginal ultrasonography, magnetic resonance imaging, and a biologic marker called CA-125.[4,5]

Different studies have proved the fact that there is an association between CA-125 levels and degree of severity of endometriosis. It should be noted that CA-125, is a glycoprotein that is expressed on the cell surface of embryonic ceolomic epithelium and is raised in about 80% of epithelial ovarian tumours. Multiple studies have proved that CA-125 is possessed by many tissues present in the pelvis therefore moderate rise is associated with endometriosis.[6] Several studies have also confirmed the rise of CA-125 levels in endometriosis in both mild and severe stages.[7,8] In this regard, the present study intends to determine whether there is any relationship between the rise of CA-125 and the severity of endometriosis as laparoscopy is an invasive procedure and is associated with many risks. The goal is to have an idea of the extent of the disease before undergoing surgery so that informed consent, detailed counselling and risks of conversion to laparotomy and major organ injury are explained to the patients before undergoing surgery and to ensure the availability of the expert surgeon.

Methodology

The research aimed to determine the relationship of serum CA-125 levels with the severity of endometriosis according to the Revised ASRM scoring system, a cohort of 100 patients was selected from the outpatient department of mother and child health center of PIMS hospital, Islamabad; duration of the study was 1 year between Jan 2017 to Jan 2018. The technique used for sampling was convenience sampling considering the nature of the research.[9] Women with any medical history like diabetes and blood pressure were excluded from the sample population. All the selected patients had diagnosed endometriosis with ovarian involvement (endometrioma), while the preliminary diagnosis was made by a detailed gynecological history, physical examination, transvaginal ultrasonography and serum CA-125 levels. Women were of ages (16-45 years) with complaints of chronic pelvic pain, severe dysmenorrhea and/or infertility and confirmed evidence of endometrioma by ultrasonography and/or MRI. On the other hand, it should also be noted that their education level and age of marriage was primary to intermediate and 16-32 years respectively. Considering this fact, ethical approval was received from the hospital ethical committee. The eligible patients agreed to participate in the study by giving informed consent. All patients underwent laparoscopic surgery in the physical presence of expert laparoscopic surgeons after having all the baseline investigation, anesthesia fitness, pre-op preparation and informed consent done. During surgery, stage of endometriosis was assigned according to revised scoring system of ASRM.[5]

As rASRM is the most used scoring system, so it was used in this research to determine the stage of endometriosis. This scoring system is based on the location (if the ovary or peritoneum is found) and extension of the implants of endometriosis, as well as on existence, quality (fine or dense) and location of adhesions. For each of these parameters points were added according to the table below, leaving a classification as follows:

- Stage I, minimal endometriosis: 1-5 points
- Stage II, mild endometriosis: 6-15 points
- Stage III, moderate endometriosis: 16-40 points
- Stage IV, severe endometriosis: > 40 points[10]

To analyze the results, MS Excel and SPSS 20.0 were also used; Pearson correlation was performed to

determine the relationship of CA-125 levels with severity of endometriosis.

Results

In this study, the sample population was already diagnosed with endometriosis, the main purpose was to compare the severity of the disease with the CA-125 level; this can be the reason only 2 patients out of 100 (2%) have normal CA-125 level i.e. <35. 15% of the participants have 36-59 CA-125 level, 39% of the participants have 60-89 CA-125 level while 44% of the participants have >90 CA-125 level. (Figure 1) It should be noted that these are the pre-operative readings of CA-125 levels.

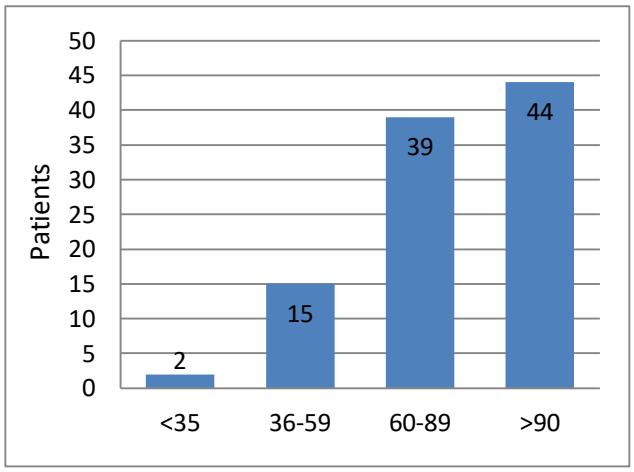

Figure 1 CA-125 levels.

Diagnosing the type of endometriosis, it was found that 51 patients had unilateral while 49 were suffering from bilateral endometriosis. In the meanwhile, the size of endometriosis determined were <=3, 4-5, 6-7 and 8-10 of 0, 24, 49 and 27 patients respectively.

Moving towards the main point of concern, the stage of endometriosis was analyzed and then they were compared to the pre-operative measurement of CA-125 levels. Following the Revised ASRM scoring system, it was determined that no patient was suffering from stage 1 endometriosis while 17 patients, 45 patients and 38 patients were suffering from stage 2, stage 3, and stage 4 endometriosis.

Comparing the CA-125 level following the severity of endometriosis, it came to know that CA-125 level and severity of endometriosis have a connection; however, it may vary from mild to strong but the association exists as shown in the graph given below. (Figure 2) According to the findings, the patients with stage 4 and stage 3 endometriosis had the CA-125 levels 60-89 and >90, which are abnormal levels as mentioned earlier. On the other hand, the patients with stage 2 endometriosis had the CA-125 levels lesser than those of stage 3 and stage 4 patients. 2% of the patients had <35 CA-125 level (normal) that are suffering from stage 2 endometriosis, in the meanwhile, 15% of the patients had also stage 2 endometriosis but with increased CA-125 level i.e. 36-59. On the other hand, with the increase in severity of endometriosis, the CA-125 level has also changed. It should also be noted that however the severity increases and so is the CA-125 level but two stages might have same CA-125 level but overall, severity and CA-125 level has direct relation with each other. For instance, 4% of the patients had 60-89 CA-125 level with stage 4 endometriosis 34% had also stage 4 endometriosis with >90 CA-125 level; in the meanwhile, the level increases with the severity of endometriosis, on the whole, as demonstrated in the graph given below.

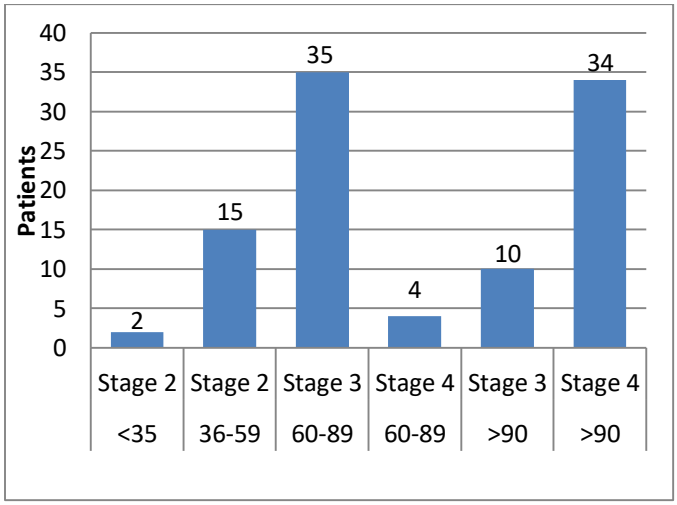

Figure 2 CA-125 level vs.Severity of Endometriosis.

To statistically analyze the results, SPSS 20.0 was used and the Correlation was performed. The data was analyzed using Pearson correlation test as shown in table I. CA125 and stage were the two variables entered into SPSS to examine their relationship with each other. The purpose of using Pearson correlation was to measure the strength of association between these two variables. The Pearson correlation coefficient varies from -1 to 1; -1 to 0 indicates the negative correlation between the two variables while 0 to 1 shows the positive association. Besides, strength of association is interpreted in terms of small, medium and large where 0.1 to 0.3 refers to small, 0.3 to 0.5 refers to medium and 0.5 to 1.0 refers to large association between the two variables.[12] In this context, the value of Pearson coefficient for the selected

variables and the collected dataset is 0.861 which indicates the large or high association between CA-125 levels and severity of endometriosis. In the meanwhile, it should also be noted that Sig. (2-tailed) value i.e. 0.000 also indicates that the findings are highly significant.

Table I: Correlations

		CA125	Severity/ stage
CA125	Pearson Correlation	1	.861
	Sig. (2-tailed)		.000
	N	100	100
Severity/ stage	Pearson Correlation	.861	1
	Sig. (2-tailed)	.000	
	N	100	100

Also, the graph is given below also presents the relationship between CA-125 levels and severity of endometriosis (Figure 3); it indicates that CA-125 level and the stages (severity) have direct relation with each other. Increase in CA-125 level leads to an increase in the severity of endometriosis. However, one stage might have different CA-125 levels but there would be an increase in both variables but not an inverse relationship as proved by the graphical representation of Pearson test; there might be no change in some cases but overall a direct relationship exists between the variables.

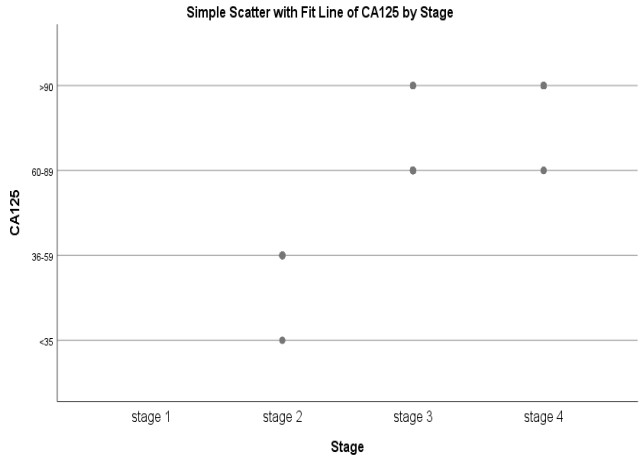

Figure 3 CA-125 levels vs. Severity of endometriosis.

Besides the stage of endometriosis, CA-125 level, size of endometriosis, the other variables included in this study were age, height, BMI, years of marriage, weight and duration in pelvic pain but they do not have any association with CA-125 serum level but it exists with the severity of endometriosis.

Discussion

Analyzing the findings of the present study, various other studies have also been reviewed to support the current findings. According to Bianchi et al. (2003), endometriosis affects at least 15% of infertile women.[13]

The visualization of endometriotic implants is done by either laparoscopy or laparotomy. Raised plasma CA-125 levels has been associated with the presence of endometriosis. The research was conducted to measure the correlation between CA-125 levels and the presence of endometriosis and its severity, among infertile patients requesting a diagnostic laparoscopy.[14]

A serum sample for CA-125 was taken immediately prior to surgery and correlated with the presence or absence of endometriosis and severity of the disease. The results indicated that patients with severe endometriosis, or grade IV, showed statistically significantly higher levels of CA-125 compared to women without endometriosis or with grades I, II or III of the disease. The overall sensitivity of CA-125 in detecting patients with endometriosis was low; however, it worked better for patients with advanced disease.[15]

Another study conducted by Karimi-Zarchi et al. (2016) also revealed the fact that CA-125 serum level has a direct association with severity of endometriosis; however, serum levels are not related to age, pelvic pain and patients' complaints but with the severity of the disease.[16]

The present clinical study shows that those patients with endometriosis classified as severe according to the classification of the American Society of Reproductive Medicine showed higher values of CA-125 as compared to women diagnosed with endometriosis to a minimum, mild or moderate.

Conclusion

According to the results, CA-125 serum is an indicator of the severity of endometriosis and it is important to consider when surgical treatment is considered or necessary. The findings indicate the association between CA-125 level and severity of endometriosis. In his regard, it is concluded that pre-operative CA-125 level should be measured and considered for the diagnosis and treatment of endometriosis. Future research is recommended in terms of larger sample size to increase the validity of the sample population and the findings.

Declaration: It is to declare here that the data used for this article was the part of the thesis project of our postgraduate resident Dr Fatima Qazi which was approved by the hospital ethical committee. The title of thesis was “role of pre-operative medroxyprogesterone acetate therapy in the laparoscopic resection of endometriosis” in which case (patients who received the medicine) and control (patients who did not received any medicine) were compared. Only control group data was used in this research article.

References

1 Bernini O, Belviso C, Venditti F, Berrocal C. Endometriosis: Identifying Meaningful Subgroups of Females at Risk of a Poorer Adjustment. European Health Psychologist. 2014;16(S):681

2 Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, Jenkinson C, Kennedy SH, Zondervan KT, Study WE. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertility and sterility. 2011;96(2):366-73.

3 Chowdhury TS, Mahmud N, Chowdhury TA. Endometriosis: Correlation of Severity of Pain with Stages of Disease. Journal of Bangladesh College of Physicians and Surgeons. 2017;34(3):135-9.

4 Bilibio JP, Souza CA, Rodini GP, Andreoli CG, Genro VK, De Conto E, Cunha-Filho JS. Serum prolactin and CA-125 levels as biomarkers of peritoneal endometriosis. Gynecologic and obstetric investigation. 2014;78(1):45-52.

5 Andrews WC, Buttram Jr VC, Behrman SJ, Carmichael E, Cohen M, Dmowski P, Eward R, Guzick D, Jones Jr Hw, Kistner R, Weed J. Revised American Fertility Society classification of endometriosis: 1985. Fertility and sterility. 1985;43(3):351-2.

6 Mol BW, Bayram N, Lijmer JG, Wiegerinck MA, Bongers MY, van der Veen F, Bossuyt PM. The performance of CA-125 measurement in the detection of endometriosis: a meta-analysis. Fertility and sterility. 1998 Dec 31;70(6):1101-8.

7 Barbieri RL, Niloff JM, Bast RC, Schaetzl E, Kistner RW, Knapp RC. Elevated serum concentrations of CA-125 in patients with advanced endometriosis. Fertility and sterility. 1986;45(5):630-4.

8 Chapron C, Querleu D, Bruhat MA, Madelenat P, Fernandez H, Pierre F, Dubuisson JB. Surgical complications of diagnostic and operative gynaecological laparoscopy: a series of 29,966 cases. Human reproduction (Oxford, England). 1998;13(4):867-72.

9 STEPS Sample Size Calculator and Sampling Spreadsheet [Internet]. World Health Organization. 2017 http://www.who.int/chp/steps/resources/sampling/en/

10 Guzick DS, Silliman NP, Adamson GD, Buttram VC, Canis M, Malinak LR, Schenken RS. Prediction of pregnancy in infertile women based on the American Society for Reproductive Medicine's revised classification of endometriosis. Fertility and sterility. 1997;67(5):822-9.

11 Einhorn N, SjÖvall K, Knapp RC, Hall P, Scully RE, BAST Jr RC, ZURAWSKI Jr VR. Prospective evaluation of serum CA 125 levels for early detection of ovarian cancer. Obstetrics & Gynecology. 1992;80(1):14-8.

12 Benesty J, Chen J, Huang Y, Cohen I. Pearson correlation coefficient. InNoise reduction in speech processing 2009 (pp. 1-4). Springer Berlin Heidelberg.

13 Bianchi M, Macaya R, Durruty G, Manzur A. Correlation between CA-125 marker with the presence and severity of pelvic endometriosis. Revista medica de Chile. 2003 ;131(4):367-72.

14 Masahashi T, Matsuzawa K, Ohsawa M, Narita O, Asai T, Ishihara M. Serum CA 125 levels in patients with endometriosis: changes in CA 125 levels during menstruation. Obstetrics & Gynecology. 1988;72(3):328-31.

15 Maiorana A, Cicerone C, Niceta M, Alio L. Evaluation of serum CA 125 levels in patients with pelvic pain related to endometriosis. The International journal of biological markers. 2007;22(3):200-2.

16 Karimi-Zarchi M, Dehshiri-Zadeh N, Sekhavat L, Nosouhi F. Correlation of CA-125 serum level and clinico-pathological characteristic of patients with endometriosis. International Journal of Reproductive BioMedicine. 2016;14(11):713.