Original Article

Prevalence of Endometriosis in Malignant Epithelial Ovarian Tumor

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Abstract

Background: The present study aims to assess the prevalence and histological characteristics of endometriosis in different types of ovarian surface epithelial tumors.

Methods: Microscopic slides of 110 ovarian tumors (89 malignant and 21 borderlines) were reviewed from 2008 to 2013 in two major gynecological centers affiliated with the Shiraz University of Medical Sciences, Shiraz, Iran. The presence or absence of endometriosis and transitions from atypical endometriosis to carcinoma were also histologically evaluated. Chi-square and *t*-test were used to compare the study groups.

Results: The mean age of the patients was 49.93 ± 9.36 years in the Endometriosis-Associated Ovarian Carcinomas (EAOC) group and 50.18 ± 12.8 years in the non-EAOC group. Among the 110 patients, 28 (25.4%) had endometriosis. According to ovarian cancer subtype 67% (4/6) of clear cell adenocarcinoma, 65% (11/17) of endometrioid adenocarcinoma, 28% (7/25) of low grade serous adenocarcinoma, 4% (1/25) of high grade serous adenocarcinoma, 30% (4/13) of borderline serous tumor, and 25% (1/4) of mixed carcinoma had endometriosis. None of the mucinous borderline tumors and mucinous adenocarcinoma cases had endometriosis. Moreover, 23 cases had typical endometriosis, while 14 had atypical endometriosis. On the other hand, 19 cases had both typical and atypical endometriosis. Furthermore, transition from atypical endometriosis to carcinoma was seen in 11 cases.

Conclusion: Clear cell and endometrioid carcinoma are the most common types of EACO. Atypical endometriosis was more commonly seen in endometrioid and clear cell carcinomas which are included in type I ovarian cancer. Thus, it can be concluded that atypical endometriosis is a precursor for type I ovarian cancer.

Keywords: Atypical endometriosis, endometriosis, ovarian cancer

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Introduction

Endometriosis is an estrogen-dependent, chronic disorder defined as the presence of endometrial gland and stroma outside the endometrium and myometrium.[1,2] Endometriosis involves about 3%–10% of all women in reproductive age,[1,3] 2%–5% of postmenopausal women, and 25%–80% of infertile ones.[4] The exact etiology of endometriosis has not been determined. Yet, some theories, including the reflux of endometrial tissue through fallopian tube at the time of menstruation, coelomic metaplasia, embryonic cell rests, and lymphatic and vascular dissemination, have been proposed to explain the mechanism of endometriosis.[5,6,7,8] However, it is generally accepted that endometriosis has a multifactorial etiology, including genetic, hormonal, and immunological factors.[6,7,8] The ovaries are the most common sites of involvement, but other sites have been involved throughout the pelvis and even outside the pelvis, as well.[6,8]

It has been well documented that malignant transformation can occur in ovarian endometriosis.[6,7,9] In 1925, Sampson explained for the first time the association between endometriosis and ovarian carcinoma [2,8,10,11] and described the criteria required for approval that an ovarian tumor originates from endometriosis: (i) presence of ovarian cancer and endometriosis in the same ovary, (ii) arousal of cancer from endometriosis and not metastasis from another site, and (iii) demonstration of the specific histological structure of endometriosis including endometrial gland and surrounding stroma.[8] In 1953, Scott added a strict criterion, i.e., morphological demonstration of transition between benign and malignant epithelium within endometriosis for Endometriosis-Associated Ovarian Cancer (EAOC).[2,8] To date, several studies have revealed an association between ovarian cancer and endometriosis.[6,8,11] In a large study, the incidence of endometriosis was assessed in 556 patients undergoing surgery for ovarian cancer. According to the results, the frequency of endometriosis ranged from 22 to 26 in endometrioid, clear cell, and mixed subtypes.[11]

The histogenesis of EAOC has been, and still is, one of the most mysterious aspects of pathology. The present study aims to assess the prevalence and histological characteristics of endometriosis and endometriosis-associated carcinomas in different types of ovarian surface epithelial tumors.

Materials and Methods

This cross-sectional study was conducted on all patients who were diagnosed with malignant epithelial ovarian tumors and underwent surgery between 2008 and 2013 in two major gyne-

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cological centers affiliated with the Shiraz University of Medical Sciences, Shiraz, Iran. The patients with tumors of low malignant potential (borderline tumors) were also included in this study. The medical research Ethics Committee as well as the Institutional Review Board (IRB) of the Shiraz University of Medical Sciences approved the study protocol.

The microscopic slides of 110 patients were reviewed by two expert pathologists in gynecological oncology. Histological classification of ovarian cancer was based on World Health Organization (WHO) classification of ovarian tumor. Also, according to the dualistic model of carcinogenesis and Kurman and Shih's classification,[12] all our ovarian cancers were divided into two groups; type I and type II. Type I tumors are composed of Low Grade Serous Carcinoma (LGSC), endometrioid carcinoma, clear cell carcinoma, mucinous carcinoma, and transitional carcinoma. Besides, type II tumors consist of High Grade Serous Carcinoma (HGSC), Malignant Mixed Mesodermal Tumors (MMMT), and undifferentiated carcinomas.

Staging was done for each patient according to the International Federation of Gynecology and Obstetrics (FIGO) system.[13] For statistical analysis, FIGO stage categories were classified into early stage (FIGO stage I) and late stage (FIGO stage II-IV). We also analyzed the patients' age and menopausal status at the time of ovarian cancer diagnosis.

The presence or absence of endometriosis and transition from this part to carcinoma was histologically evaluated in this study. Endometriosis was defined as the presence of endometrial stroma around the glandular epithelium.

According to a study by Van Gorp, *et al*.,[8] our endometriosis-associated cases were classified into 3 categories. Category A was defined as endometriosis discovered in the same ovary with histological proof of transition. Category B was considered as endometriosis discovered in the same ovary but without histological proof of transition. Finally, category C referred to endometriosis discovered at any location in the pelvis, i.e., endometriosis in the contralateral ovary, extra-gonadal endometriosis, or without specification about lateralization and/or localization of the lesion.

Furthermore, atypical endometriosis was diagnosed based on the histopathological criteria suggested by La Grenada and Silverberg.[14] These features included large pleomorphic hyperchromatic or pale nuclei, eosinophilic cytoplasm, tufting, crowding, and stratification. The presence of three or more of these criteria in each case was considered as atypical endometriosis.

Statistical analysis

The Statistical Package for Social Sciences (SPSS, version 17) for Windows was used for data analysis. Chi-square and *t*-test were used to compare the study groups. To check the normality distribution, one-sample Kolmogorov – Smirnov Test was used. The data were reported as means ± SD. Besides, a two-sided *P* value < 0.05 was considered as statistically significant.

Results

Pathological slides and medical records were available for 110 patients, including 89 malignant and 21 borderline tumors, in a 5-year period from 2008 to 2013.

Serous adenocarcinoma was the most common histological subtype accounting for 50 out of the 110 tumors (45.5%) followed by endometrioid carcinoma (17, 15.5%), borderline serous tumors (13, 11.8%), mucinous carcinoma (12, 10.9%), borderline mucinous (8, 7.2%), clear cell carcinoma (6, 5.5%), and mixed carcinoma (4, 3.6%).

According to the above-mentioned criteria, 28 cases (25.4%) had EAOC and 82 (74.6%) had non-EAOC. With regard to ovarian cancer subtype, 67% (4/6) of clear cell adenocarcinoma, 65% (11/17) of endometrioid adenocarcinoma, 28% (7/25) of low grade serous adenocarcinoma, 4% (1/25) of high grade serous adenocarcinoma, 30% (4/13) of borderline serous tumor, and 25% (1/4) of mixed carcinoma cases had endometriosis. None of the mucinous borderline tumors and mucinous adenocarcinomas had endometriosis.

The clinical and pathological characteristics of the two groups are compared in Table 1.

The incidence rate of atypical endometriosis in each histological subtype and the presence of transition between endometriosis and carcinoma are presented in Table 2.

Considering the histological review of endometriosis, 23 and 14 cases were diagnosed with typical and atypical endometriosis, respectively, and 19 cases had both (Figure 1). Besides, transition from atypical endometriosis to carcinoma was seen in 11 cases (category A) (Figure 2). Also, atypical endometriosis in the same ovary without histological proof of transition to carcinoma was detected in one case (in category B), and atypical endometriosis in the contralateral ovary was observed in two cases (in category C).

Discussion

Several studies have demonstrated an association between ovarian cancer and endometriosis.[8,11] The prevalence of endometriosis in ovarian cancers ranges from 4.2% to 29.1% in the literature.[8,11,15]

In the present study, the prevalence rate of endometriosis in ovarian cancers was 25.4% (28/110), which seems to be comparable that reported by other studies. A previous study conducted in an Iranian population reported the prevalence rate of endometriosis to be 38% in the infertile group and 11.6% in the fertile control group.[16] In another study, endometriosis was reported in 62% of infertile women.[17]

The exact prevalence of endometriosis in ovarian cancer is more difficult to determine. Different studies have employed various criteria for diagnosis of EAOC and also a definite diagnosis of endometriosis needs complete pathological evaluation of surgical specimen.[8]

In our sample, the mean age at diagnosis was 49.93 ± 9.36 years in the EACO group and 50.18 ± 12.8 years in the non-EACO group, but the difference was not statistically significant ($P = 0.9$). According to Prefumo *et al*.,[18] the patients' mean age at EACO diagnosis was 50.9 ± 12.7 years. In addition, Wang[2] reported that the patients with EACO were about 6 years younger than those with typical EOC (46 vs. 52.8 years). Eržen, *et al*. also found that EACO patients were younger.[10] This difference in age at diagnosis might be explained by the fact that patients with a previous history of endometriosis have close follow-up, making it possible to incidentally find early ovarian cancer. However, Wang[2] reported that only one patient with EACO had the history of surgically identified endometriosis and the remaining 16 cases with EACO had no history of previously identified endometriosis. Moreover, Mangili, *et al*.[19] showed that women with or without endometriosis had the same chance for incidental diagnosis of ovarian cancer.

Table 1. Comparison of the variables between EACO and non-EACO groups.

Variable	EACO[1], %	Non-EACO, %	*P*-Value
Count	28 (25.4%)	82 (74.6%)	
Age, Year			
Mean ± SD	49.93 ± 9.36	50.18 ± 12.8	0.9
Range	29–72	24–83	
Premenopause at the time of diagnosis	14 (50%)	40(48%)	0.91
FIGO[2] Stage, n (%)			
I	15 (53.5%)	29(36%)	
II	5(18%)	12(15%)	
III	8 (28.5%)	33(41%)	
IV	0	6(8%)	
Stage comparison			
Early stage (I)	15(53.5%)	29(36%)	0.108
Late stage (II-IV)	13(46.5%)	51(64%)	
Histology, n (%)			
LGSC[3]	7(25%)	18(22%)	0.740
HGSC[4]	1(3.5%)	24(29%)	
Clear cell carcinoma	4(14.5%)	2(2.5%)	
Endometrioid carcinoma	11(39%)	6(7%)	0.001
Mucinous carcinoma	0	12(15%)	0.034
Mixed carcinoma	1(3.5%)	3(3.5%)	
Borderline serous tumor	4(14.5%)	9(11%)	0.736
Borderline mucinous tumor	0	8(10%)	
Type I or II			
Type I (n = 85)	27(96.5%)	58(71%)	0.005
Type II (n = 25)	1(3.5%)	24(29%)	

EACO = endometriosis-associated ovarian carcinomas, FIGO = federation of gynecology and obstetrics, LGSC = low grade serous carcinoma; HGSC = high grade serous carcinoma

Table 2. The incidence rate of ovarian endometriosis in each histological subtype of ovarian cancer.

Histological subtype	Number of patients with endometriosis				
	Atypical	Typical	Category A*	Category B**	Category C**
Clear cell carcinoma	4	3	4	0	0
Endometrioid carcinoma	7	9	6	2	3
LGSC[1]	1	7	1	4	2
HGSC[2]	1	0	0	0	1
Mucinous carcinoma	0	0	0	0	0
Borderline serous tumor	1	3	0	3	1
Borderline mucinous tumor	0	0	0	0	0
Mixed tumor	0	1	0	1	0

*Category A = endometriosis discovered in the same ovary with histological proof of transition; **Category B = endometriosis discovered in the same ovary but without histological proof of transition or without knowledge whether this transition was further investigated or not; ***Category C = endometriosis discovered at any location in the pelvis; i.e., endometriosis in the contralateral ovary, extra-gonadal endometriosis or without specification about lateralization and/or localization of the lesion; 1-LGSC = low grade serous carcinoma, 2-HGSC = high grade serous carcinoma.

Therefore, the hypothesis of an 'earlier onset' of ovarian cancer due to some intrinsic factor in the patients with endometriosis is more acceptable rather than 'earlier finding' of the tumor.[2]

In the present study, serous adenocarcinoma was the most common histological subtype in all patients followed by endometrioid carcinoma, borderline serous tumors, mucinous carcinoma, borderline mucinous, clear cell carcinoma, and mixed carcinoma which is similar with another study done in Iran.[20]

Based on most of the studies performed in this area, the prevalence of endometriosis is higher in clear cell carcinoma and endometrioid cancer compared to serous and mucinous carcinoma.[2,8,11,21] These findings are in agreement with those of the present study, demonstrating that the incidence rate of endometriosis is significantly higher in clear cell carcinoma and endometrioid carcinoma compared to serous adenocarcinoma (P = 0.023 and P = 0.001). Although the results of the current study indicated no association between mucinous tumors and endometriosis, this association has been mentioned in the literature.[4,10,11]

If we define ovarian cancer as type I and type II according to Kurman and Shih's classification,[12] coexisting endometriosis was more commonly detected in type I tumors (32% vs. 4%) (P = 0.005). It should be mentioned that endometrioid and clear cell

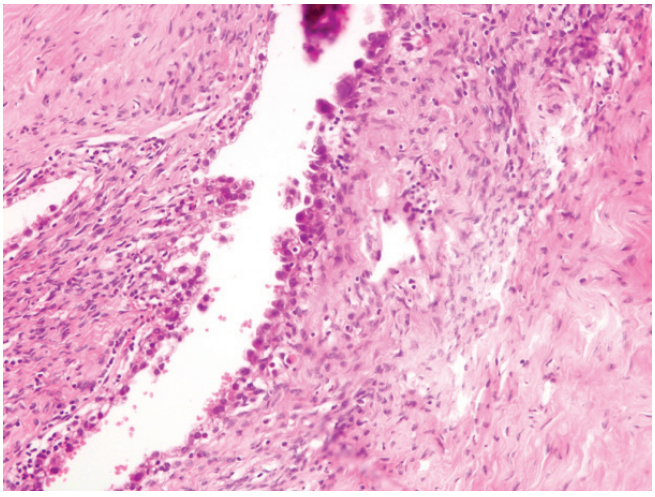

Figure 1. Atypical endometriosis composed of cells with large pleomorphic hyperchromatic nuclei, and eosinophilic cytoplasm. (H&E stain, ×100).

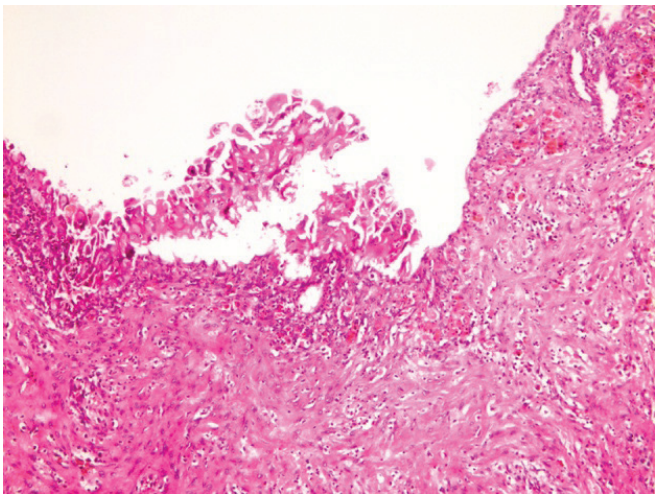

Figure 2. Transition of endometriosis to carcinoma. (H&E stain, ×100).

carcinoma are considered as type I cancer. Consistently, Wang[2] revealed that 18.3% of EAOC cases were type I and thus concluded that endometriosis was one of the precursors of type I ovarian cancer.[2] Moreover, Wang indicated that 11.7% and 5.9% of the EACO patients were HGSC and LGSC, respectively.[2] In the present study, only one EAOC case (3.5%) was HGSC and 7 cases (25%) were LGSC. Kumar, *et al*.[4] found that 54% of EAOC patients had serous carcinoma. Furthermore, Modesitt, *et al*.[22] indicated that serous cancer was the third most common subtype in patients with coexisting endometriosis. Nevertheless, Kumar *et al*.[4] and Modesitt, *et al*.[22] did not discuss HGSC and LGSC separately in their studies. Considering the small sample size of our study and other studies in the literature, further studies should be conducted on the association between endometriosis and HGSC.

In our study, no significant difference was found between EAOC and non-EAOC groups regarding the prevalence of stage I tumors. Similar results were obtained by Mangili and Komiyama.[18,23] However, Eržen, *et al*.[10] and Wang, *et al*.[2] reported that the majority of EAOC cases in contrast to non-EAOC ones, had stage I disease.

In the current study, 6 out of the 11 endometrioid adenocarcinoma cases (54%), all clear cell carcinoma cases (100%), and 1 out of 7 the LGSC patients showed histological proof of malignant transformation in ovarian endometriosis and presented the criteria described by Sampson and Scott. These criteria are difficult to demonstrate since extensive sampling must be done to show a small sample of endometriosis with an adjacent malignant tumor and a tumor may be very aggressive destroying all endometriotic tissues.

Atypical endometriosis can be considered a precancerous lesion for ovarian carcinoma.[8] LaGrenada and Silverberg were the first to report a case series of ovarian tumors (three clear cell carcinomas and two endometrioid carcinomas) with a transition from atypical endometriosis.[14]

Moll, *et al*. revealed a chronological association between atypical endometriosis and ovarian carcinoma in women with clear cell carcinoma three years after cystectomy of an endometrioma with severe atypical changes.[24]

Prefumo, *et al*.[18] showed that atypia was significantly more detected in patients suffering from EOAC compared to those with endometriosis alone (100% of cases compared to 2% of controls). The researchers also recognized that complex hyperplasia, but not simple hyperplasia, was significantly more frequent in cases with EAOC compared to those without malignancy (50% compared to 1%).[23]

In a study by Fukunaga, *et al*., 24% of ovarian cancers were associated with ovarian endometriosis and 61% of EAOC had atypical endometriotic foci.[25]

Ogawa, *et al*.[26] reported atypical endometriosis in 78% of cases with EACO. In our study, atypical endometriosis was seen in 11 out of the 28 EACO cases (39%).

There are some limitations in our study. The study population was limited and some histologic types of ovarian cancer were few in number. Thus, larger studies are recommended to shed light on pathogenesis of atypical endometriosis in ovarian cancer.

In conclusions, endometrioid and clear cell carcinoma were the most common subtypes of EACO. In addition, atypical endometriosis was more commonly detected in endometrioid and clear cell carcinomas which are included in type I cancer. Thus, it may be concluded that atypical endometriosis is one of the precursors of type I ovarian cancer. Further studies are warranted on the role of atypical endometriosis in the pathogenesis of ovarian cancer.

Conflicts of interest

The authors have no conflicts of interest to report.

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References

1. Munksgaard PS, Blaakaer J. The association between endometriosis and ovarian cancer: a review of histological, genetic and molecular alterations. *Gynecol Oncol*. 2012; **124(1):** 164 – 169.
2. Wang S, Qiu L, Lang JH, Shen K, Yang JX, Huang HF, et al. Clinical analysis of ovarian epithelial carcinoma with coexisting pelvic endometriosis. *Am J Obstet Gynecol*. 2013; **208(5):** 413.e1 – 413.e5.
3. Banz C, Ungethuem U, Kuban RJ, Diedrich K, Lengyel E, Hornung D. The molecular signature of endometriosis-associated endometrioid ovarian cancer differs significantly from endometriosis-independent endometrioid ovarian cancer. *Fertil Steril*. 2010; **94(4):** 1212 – 1217.

4. Kumar S, Munkarah A, Arabi H, Bandyopadhyay S, Semaan A, Hayek K, et al. Prognostic analysis of ovarian cancer associated with endometriosis. *Am J Obstet Gynecol*. 2011; **204(1):** 63.e1 – 63.e7.
5. Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. *Fertil Steril.* 2012; **98(3):** 511 – 519.
6. Worley MJ, Welch WR, Berkowitz RS, Ng S-W. Endometriosis-associated ovarian cancer: a review of pathogenesis. *Int J Mol Sci*; 2013; **14(3):** 5367 – 2379.
7. Agarwal N, Subramanian A. Endometriosis–morphology, clinical presentations and molecular pathology. *J Lab Physicians*.; 2010; **2(1):** 1 – 9.
8. Van Gorp T, Amant F, Neven P, Vergote I, Moerman P. Endometriosis and the development of malignant tumours of the pelvis. A review of literature. *Best Pract Res Clin Obstet Gynaecol.* 2004; **18(2):** 349 – 371.
9. Terada T. Endometrioid adenocarcinoma of the ovary arising in atypical endometriosis. *Int J Clin Exp Pathol*. 2012; **5(9):** 924 – 927.
10. Eržen M, Rakar S, Klančar B, Syrjänen K. Endometriosis-associated ovarian carcinoma (EAOC): an entity distinct from other ovarian carcinomas as suggested by a nested case-control study. *Gynecol Oncol*.; 2001; **83(1):** 100 – 108.
11. Oral E, Ilvan S, Tustas E, Korbeyli B, Bese T, Demirkiran F, et al. Prevalence of endometriosis in malignant epithelial ovary tumours. *Eur J Obstet Gynecol Reprod Biol*. 2003; **109(1):** 97 – 101.
12. Shih I-M, Kurman RJ. Ovarian tumorigenesis: a proposed model based on morphological and molecular genetic analysis. *Am J Pathol.* 2004; **164(5):** 1511 – 1518.
13. Prat J. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynecol Obstet*. 2014; **124(1):** 1 – 5.
14. LaGrenade A, Silverberg SG. Ovarian tumors associated with atypical endometriosis. *Hum Pathol.* 1988; **19(9):** 1080 – 1084
15. Verit FF, Yucel O, Moelans CB, Verschuur-Maes AHJ, van Diest PJ, Sangüeza OP. Endometriosis, Leiomyoma and Adenomyosis: the Risk of Gynecologic Malignancy. *Asian Pacific J Cancer Prev*. 2013; **14(10):** 5589 – 5597.
16. Mazlouman NKSJ. Study of endometriosis related infertility, a comparative study. *Acta Med Iran.* 2004; **42(5):** 383 – 389.
17. Moini A, Malekzadeh F, Amirchaghmaghi E, Kashfi F, Akhoond MR, Saei M, et al. Risk factors associated with endometriosis among infertile Iranian women. *Arch Med Sci AMS*. 2013; **9(3):** 506 – 514.
18. Prefumo F, Todeschini F, Fulcheri E, Venturini PL. Epithelial abnormalities in cystic ovarian endometriosis. *Gynecol Oncol.* 2002; **84(2):** 280 – 284.
19. Mangili G, Bergamini A, Taccagni G, Gentile C, Panina P, Viganò P, et al. Unraveling the two entities of endometrioid ovarian cancer: a single center clinical experience. *Gynecol Oncol*. 2012; **126(3):** 403 – 407.
20. Arab M, Khayamzadeh M, Hashemi M, Hosseini M, Tabatabaeefar M, Anbiaee R, et al. Crude and age-specific incidence rate patterns for histopathologic subtypes of ovarian cancer in Iran. *Arch Iran Med*. 2010; **13(3):** 203 – 208.
21. Kondi-Pafiti A, Papakonstantinou E, Iavazzo C, Grigoriadis C, Salakos N, Gregoriou O. Clinicopathological characteristics of ovarian carcinomas associated with endometriosis. *Arch Gynecol Obstet.* 2012; **285:** 479 – 483.
22. Modesitt SC, Tortolero-Luna G, Robinson JB, Gershenson DM, Wolf JK. Ovarian and extraovarian endometriosis-associated cancer. *Obstet Gynecol.* 2002; **100(4):** 788 – 795.
23. Komiyama S, Aoki D, Tominaga E, Susumu N, Udagawa Y, Nozawa S. Prognosis of Japanese patients with ovarian clear cell carcinoma associated with pelvic endometriosis: clinicopathologic evaluation. *Gynecol Oncol*. 1999; **72(3):** 342 – 346.
24. Moll UM, Chumas JC, Chalas E, Mann WJ. Ovarian carcinoma arising in atypical endometriosis. *Obstet Gynecol*.; 1990; **75(3, Part 2):** 537 – 539.
25. Fukunaga M, Nomura K, Ishikawa E Ushigome S. Ovarian atypical endometriosis: its close association with malignant epithelial tumours . *Histopatholog,*1997; 30(3): 249–255
26. Ogawa S, Kaku T, Amada S, Kobayashi H, Hirakawa T, Ariyoshi K, et al. Ovarian endometriosis associated with ovarian carcinoma: a clinicopathological and immunohistochemical study. *Gynecol Oncol*. 2000; **77(2):** 298 – 304.