

Level of CA125 in Gynaecologic Masses Necessitating Operative Intervention Prospective cohort study

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Abstract

Objective :to determine :

- The different types of gynaecologic pelvic or pelvi-abdominal masses necessitating surgical intervention associated with increased CA125 level.
- Relation between initial level of CA125 and histopathological nature of the mass .
- In malignant cases : relation between preoperative CA125 level and stage of the tumor.
- After surgery : whether decline in increased CA125 level occurs 6 months after surgery or not .

Methods :study was conducted during a period from April 2017 to April 2018.

. IBM-SPSS (version 24) was used for statistical data analysis.

Results :The mean age of the study group was 44 ± 11 years, with a range from 17-67 years. The most common surgical problem of our study group was myoma, present in 22 cases (37.3%). This was followed by simple serous cyst and endometrial carcinoma (8 cases each, 13.6%), then endometriotic cyst and mature cystic teratoma (6 cases each, 10.2%), then ovarian fibroma, ovarian cancer and endometrial hyperplasia (5 cases each, 8.5%), adenomyosis (3 cases, 5.1%) and lastly mucinous cyst adenoma (one case, 1.7%). The mean CA125 of our study group had a mean of 38.6 U/ml, with a very high standard deviation of over 59 U/ml; reflected in the very wide range from 4.5 up to 446 U/ml. The highest mean level of CA125 was seen among patients with ovarian cancer (160.6 U/ml). This was followed by ovarian fibroma (57.5 U/ml), then adenomyosis (42.7 U/ml), endometriotic cyst (42.6 U/ml), simple serous cyst (22.2 U/ml), mucinous cyst adenoma (22 U/ml), myoma (21.9 U/ml), endometrial carcinoma (20.2 U/ml) and lastly endometrial hyperplasia (17.6 U/ml). CA 125 level were normal in all cases of myoma , dermoid cyst , simple serous cyst , mucinous cystadenoma , endometrial hyperplasia and endometrial carcinoma. CA125 elevated in all cases of ovarian cancer , endometriotic cyst , adenomyosis and elevated in 60% in cases of ovarian fibroma. Most cases of ovarian cancer (80%) had marked elevation in CA125 level (level >100 U/ml) and the increase in CA125 level was more marked with increase staging of the cancer , all cases of endometriotic cyst had mild to moderate elevation in CA125 level which were < 100 U/ml , all cases of adenomyosis had mild elevation in CA125 level which not more than 50 U/ ml, in cases of ovarian fibroma CA125 level were normal in about 40% of the cases and elevated in about 60% of the cases (40% had moderate elevation in CA125 level which were < 100 U/ml and 20% had marked elevation with CA125 level > 100 U/ml). There was proportional relationship between CA125 level and ovarian cancer stage , mean CA125 level in stage I was 85.8 U/ml versus 372.3 U/ml in stage II ($P < 0.001$) . All cases of endometrial cancer early diagnosed in stage I had normal CA125 level (10.6 – 28.3 U/ml) . All cases with preoperative elevated CA125 level , the level returned to the normal when repeated 6 months postoperatively , cases of ovarian cancer , CA125 level returned to the normal after receiving six cycles of chemotherapy postoperatively.

Conclusion : CA125 is a simple and good screening test and should be routinely recommended for all cases of pelvic or pelvi-abdominal masses before operative intervention , It helps to guess the diagnosis of ovarian cancer cases (its level mostly >100 U/ml) . It helps in the differential diagnosis between endometriotic cysts (elevated CA125 level) and haemorrhagic ovarian and dermoid cysts (normal CA125 level).It also helps in the differential diagnosis between uterine fibroids and adenomyosis being elevated in the latter .CA125 serum level can suggest the stage of ovarian cancer . In cases with elevated preoperative CA125 level , it is expected that this level will normalize within 6 months postoperatively.

Introduction

CA-125 (cancer [antigen](#) 125, carcinoma antigen 125, or carbohydrate antigen 125) also known as **mucin 16** or **MUC16** is a [protein](#) that in humans is encoded by the MUC16 [gene](#)(**Yin et al., 2002**). In the genome, MUC16 is confined in 19p13.2 chromosome and is coded by sequences present within 179 kb of genomic DNA (**Yin et al., 2002**).MUC16 is a member of the [mucin](#) family [glycoproteins](#)(**Duraisamy et al.,**

Method:

This study was conducted at the inpatient sector of the Obstetrics and Gynaecology Department of Sohag University during a period from April 2017 to April 2018.A total of 69 patients with different gynecological masses were recruited in the study.Informed consent , to be enrolled in our study , was obtained from the patients and the study was approved by the Scientific Ethical Committee of Sohag Faculty of Medicine , SohagUniversity.All patients with gynaecologic pelvic orpelvi-abdominal masses necessitating surgery were included in the study,but patients who had:Ascites with non-malignant causes eg liver disease (cirrhosis,hepatitis),Diverticulosis, Pleural and pericardial disease, Pancreatitis,Heartfailure,Pelvicinflammatorydisease/salpingitis,Pregnancy and menstruation,Intra-abdominal cancers (pancreas, stomach, colon,

2006). The protein was named “cancer antigen 125” because OC125 was the 125th antibody produced against the ovarian cancer cell line that was being studied (**Schmidt, 2011**).It is significantly expressed by most ovarian epithelial tumors but also by the normal epithelium of the female reproductive system, gastrointestinal mucosal cells, and the luminal surface of mesothelium lining the peritoneum, pleura, and pericardium (**Gniewek and Kolinski, 2012**).

rectum) and metastases from other sites (eg, breast, lung),SLE andDM were excluded from the study.All patients were subjected to:History,PhysicalExamination,Ultrasound Evaluation and histopathology,CT and MRI ,Serum CA-125 value:Serum CA-125 values were measured using enzyme immunoassays (ARCHITECT plus 1000 SR , ABBOTT , USA , 2007) pre-operatively within the week preceding surgery, and 6 months post-operatively,CA125 normal value of (0-35 U/ml),Patients with increased CA125level were divided to 3 groups according to CA125level:CA125 level :>35 - 50U/ml (**mild increase**),CA125level :>50-100U/ml(**moderate increase**),CA125 level : > 100 U/ml (**marked increase**).

Statistical analysis:

Statistical package for social sciences (IBM-SPSS), version 24 IBM-Chicago, USA (May 2016) was used for statistical data analysis, Data expressed as mean, standard deviation (SD), number and percentage. Mean and standard deviation were used as descriptive value for quantitative data, while number and percentage were used to describe qualitative data, Student t test was used to compare

the means between two groups of qualitative data, Pearson Chi square was used to compare percentages of qualitative data.

For all these tests, the level of significance (P-value) can be explained as:

- No significance $P > 0.05$
- Significance $P < 0.05$
- High significance $P < 0.001$.

Results

The most common surgical problem of our study group was myoma, present in 22 cases (37.3%). This was followed by simple serous cyst and endometrial carcinoma (8 cases each, 13.6%), then endometriotic cyst and mature cystic teratoma (6 cases each, 10.2%), then ovarian fibroma, ovarian cancer and endometrial hyperplasia (5 cases each, 8.5%), adenomyosis (3 cases, 5.1%) and lastly mucinous cyst adenoma (one case, 1.7%). CA125 level elevated in all cases of ovarian cancer, endometriotic cyst, adenomyosis and elevated in 60% in cases of ovarian fibroma and normal in cases of myoma, dermoid cyst, simple serous cyst, mucinous cystadenoma, endometrial hyperplasia and endometrial carcinoma. Most cases of ovarian cancer (80%) had marked elevation in CA125 level and the increase in CA125 level was more marked with increase staging of the cancer, all cases of endometriotic cyst had mild to moderate elevation in CA125 level which were < 100 U/ml, all cases of adenomyosis had mild elevation in CA125 level which not more than 50 U/ml, in cases of ovarian fibroma CA125 level were normal in about 40% of the cases and elevated in about 60% of the cases (40% had moderate elevation in CA125 level which were < 100 U/ml and 20% had marked elevation with CA125 level > 100 U/ml). There was proportional relationship between CA125 level and ovarian cancer stage because cases of ovarian cancer with stage II had higher CA125 level > 200 U/ml, and all cases of endometrial cancer early diagnosed in stage I had normal CA125 level. CA125 level in different surgical problems associated with increased CA125 level measured within the week preceding the surgery and remeasured after 6 months postoperatively, and all cases with preoperative elevated CA125 level had CA125 level within normal when repeated 6 months postoperatively.

Discussion

The mean age of the study group was 44 ± 11 years, with a range from 17-67 years. Our patients were somewhat similar regarding the mean age to those studied by *Benjapibal et al., (2007)* where the mean age was 46 ± 14 years (range 18-91 years). The mean age of the patients studied by *Van Gorp et al., (2011)* was 46 years among non malignant cases and 57 years among malignant cases.

The most common surgical problem of our study group was uterine

leiomyoma, present in 22 cases (37.3%). This was followed by simple serous cyst and endometrial carcinoma (8 cases each, 13.6%), then endometriotic cyst and mature cystic teratoma (6 cases each, 10.2%), then ovarian fibroma, ovarian cancer and endometrial hyperplasia (5 cases each, 8.5%), adenomyosis (3 cases, 5.1%) and lastly mucinous cyst adenoma (one case, 1.7%). The study of *Benjapibal et al., (2007)* included only cases with ovarian masses, and they found that

half of their cases (61 cases, 50.8%) had benign ovarian masses, while the other half had ovarian cancers. The study of *Van Gorp et al., (2011)* showed that the most common non malignant medical condition was cystadenoma, followed by endometriosis, then teratoma, fibroma. On the other hand, they found that one third of their cases were malignant, with ovarian carcinoma was the most common malignant condition.

The mean CA125 of our study group had a mean of 38.6 U/ml, with a very high standard deviation of over 59 U/ml; reflected in the very wide range from 4.5 up to 446 U/ml. This wide variation was even more evident in the study of *Benjapibal et al., (2007)* who found that the range of CA125 was from 6.6 to 3788 U/ml. Also, they found that the mean CA125 level was significantly higher among ovarian cancer patients (879±1356 U/ml) compared to benign ovarian conditions (104±184 U/ml).

The highest mean level of CA125 was seen among patients with ovarian cancer (160.6 U/ml). This was followed by ovarian fibroma (57.5 U/ml), then adenomyosis (42.7 U/ml), endometriotic cyst (42.6 U/ml), simple serous cyst (22.2 U/ml), mucinous cystadenoma (22 U/ml), myoma (21.9 U/ml), endometrial carcinoma (20.2 U/ml) and lastly endometrial hyperplasia (17.6 U/ml). These results was some what similar to those studied by *Van Gorp et al., (2011)* - regarding ovarian masses - who reported that the highest CA125 level was seen in cases with ovarian cancer (median 321 U/ml), then metastatic ovarian cancer (223 U/ml), then fibroma (29.1 U/ml), endometriosis (25 U/ml), cystadenoma (11.3 U/ml), functional cyst (10.5 U/ml) and lastly mature teratoma (9.8 U/ml).

The most common surgical problem in our study was myoma in 22 cases

(37.3%), CA125 levels were normal in all cases of myoma (median 22.7 U/ml), and these results were similar to study of *Dawood et al.,(1994)*, on 51 patients with uterine myoma and 30 healthy controls, the results found no difference between the groups in terms of CA125 levels, and also *Dingiloglu et al.,(2007)* found no difference in CA125 levels between 30 myoma patients and 38 healthy controls, and all were normal (median 20.3 U/ml).

In our study, CA125 levels increased in cases of endometriotic cyst (median 42.5 U/ml), and these results were similar to study of *Di-Xia et al.,(1988)*, and *Kauppila et al.,(1988)*, who found that CA125 levels increased with endometriotic cyst and these levels were < 100 U/ml.

According to our study, CA125 levels were normal in patients who had dermoid cyst (median 19.9 U/ml), simple serous cyst (median 19.3 U/ml) and mucinous cystadenoma (median 22 U/ml), and these results were similar to those seen by *Van Grop et al.,(2011)*, who found that CA125 levels were normal in cases who had dermoid cyst (median 9.8 U/ml), simple serous cyst (median 10.5 U/ml) and mucinous cystadenoma (median 11.3 U/ml).

In our study, CA125 levels increased in 50% of cases with ovarian fibroma (median 54.9 U/ml), and these results were similar to study of *Yen et al.,(2013)*, who found that CA125 levels increased in about 28% of cases with ovarian fibroma (median 88.3 U/ml).

According to our study, cases with ovarian cancer had elevated CA125 levels and about 80% of these cases had CA125 levels > 100 U/ml (median 160.6 U/ml), and these results were similar to studies by *Van Grop et al.,(2011)* and *Benjapibal et al.,(2007)*, who found that CA125 levels highly increased in cases of

ovarian cancer (median 321 U/ml , and 260 U/ml , respectively).

In our study , CA125 levels were not increased in cases with stage I of endometrial cancer (median 20.2 U/ml) , and these results were similar to study of **Dotters et al.,(2000)** , who found that CA125 levels in most cases of stage I endometrial cancer were < 20 U/ml., In study of **Sebastianelli et al .,(2010)** , on 254 patients , they found that 58% of cases with advanced stages of endometrial cancer(stage III,IV) had CA125 levels > 35 U/ml., and only 16% % of cases with early stages of endometrial cancer(stage I,II) had CA125 levels > 35 U/ml., The increase in CA125 levels related to myometrial invasion , lymphovascular space involvement , cervical invasion , positive cytology , adnexal involvement and distant metastasis.

According to our study , CA125 levels increased in cases of adenomyosis (median 42.7 U/ml) , and these results were similar to studies of **Zhou et al.,(1996)** and **Takashashi et al.,(1985)** , who found that CA125 levels increased in cases of adenomyosis , when they compared CA125 levels in cases had adenomyosis with cases had myoma , they found that CA125 levels increased with adenomyosis and never increased with myoma with median of (102 U/ml , versus 34.6 U/ml) and (93 U/ml , versus 18.3 U/ml) respectively., Authors proposed CA125 levels as a possible tool to differentiate between two conditions (adenomyosis and myoma).

There was non significant relation between the surgical problem and CA125 level among all of our cases. The only exception was patients with ovarian carcinoma, where there was a very high levels of CA125 (160.6±162.6) among patients with ovarian carcinoma compared to those

without (27.3±18.7), with highly significant difference (p<0.001).

In our study , high CA125 level > 100 U/ml highly suggests diagnosis of ovarian cancer , and these results were similar to studies of **Van Grop et al.,(2011)** and **Benjapibal et al.,(2007)**, who found that CA125 levels highly increased in cases of ovarian cancer (median 321 U/ml , and 260 U/ml , respectively).

In our study , CA125 level increased preoperatively in cases of endometriotic cysts (38.6 – 58.8 U/ml) , and returned to the normal postoperatively (10.1 – 33 U/ml) , and these results were similar to study of **Di-Xi et al., (1988)** , who found that CA125 level returned to its normal range after removal of endometriotic cyst surgically .

Also , CA125 level returned to its normal range postoperatively in cases of ovarian fibroma (7.8 – 20.6 U/ml) , and adenomyosis (11.2 – 17.1 U/ml) , and these results were similar to studies of **Yen et al.,(2013)** and **Zhou et al., (1996)** , respectively .

As regard cases of ovarian cancer the level of CA125 returned to the normal (18.5 – 30.6 U/ml) after receiving six cycles of chemotherapy , and these results were similar to studies of **Crawford and Peace (2005)** and **Na Guo and Zhilan (2017)** .

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