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Correlation of raised serum CA-125 level with laparotomy and histopathology findings of ovarian tumour in a tertiary level hospital

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Abstract
Background: Ovarian tumour preferably malignant one is the leading cause of morbidity and mortality. Despite advancement in surgical and chemotherapeutic treatment during the last decade, still survival rates are poormainly due to late and incidental diagnosis.
Objective: To find out correlation of raised serum CA-125 level with laparotomy and histopathological findings of ovarian tumours.
Methodology: This prospective study was conducted in the department of Obstetrics & Gynaecology in Rangpur Medical College & Hospital, Rangpur from July 2017 to June 2018. Total 30 patients having ovarian tumour were diagnosed clinically and by ultrasonography were included in the study was serum CA-125 was estimated in all study subjects.
Results: Total 30 cases of ovarian tumour with raised serum CA-125 were enrolled in the study. Out of 30 cases 11(36.67%) were benign tumours& 19(63.33%) were malignant tumour. Majority of the patients were in the age group of41 to 60 years. The mean age±SD in benign tumour was 34.45±12.42 years and in malignant tumour was a 50.21±17.99 years. Age ranged from 14 to 70 years. Lump in the abdomen 86.7% was the commonest presentation. The commonest tumour was epithelial tumour 27(90%) followed by germ cell tumour 3(10%).Serous cyst adenoma (63.3%) was common benign tumour& serous cyst adenocarcinoma was the commonest malignant variety (26.3%). CA-125 level markedly raised (>300U/ml) in 46.7% cases and majority were malignant.
Conclusion: As serum CA-125 is markedly raised in malignant ovarian tumour so we can conclude raised serum CA-125 is a useful tumour marker as prognostic purpose of ovarian malingnancies.

Keywords: Serum CA-125 level, laparotomy, ovarian tumour

Introduction
Ovarian cancer is the most frequent cause of death from gynaecological cancer & the fifth most common cause of cancer death in women, accounting for 5% of cancer death more than any other gynaecologic cancer [1]. There are marked geographical variation in incidence of different cancer in different regions of the world [2, 3]. The incidence of cancer is increasing in developing countries day by day. Exact incidence of ovarian cancer in Bangladesh in not known but the 2010 statistics for Bangladesh on age standardized death rates per 100000 show that cervical cancer and ovarian cancer ranking 24 and 45 position respectively [4]. There are numbers of risk factors associated with the origin of ovarian cancer except age & parity, majority of them are not yet established. Most of the tumour is sporadic but 5% are familial [5]. In women with no family history of ovarian cancer, the lifetime risk is 1.6% whereas a women with one affected first degree relativehas a 5% lifetime risk & with two or more affected 1st degree relatives the risk is 7% [6, 7]. Ovarian tumors are a heterogeneous group of benign and malignant neoplasms may involve a variety of histological tissues ranging from epithelial, stromal and germ cell origin [8]. Though many histologic types of ovarian tumors are described, epithelial tumors account majority of all ovarian tumors, and more than 90% of ovarian malignancies are epithelial origin [9]. Most ovarian cancers occur at & after menopause when the ovaries had no physiological role; consequently abnormal ovarian function causes no symptoms. They are rare in young age group [10]. Ovarian cancer typically cause few symptoms until they reach a large size or has dessiminated [11].

They commonly present with pelvic and abdominal pain with a lump, bloating or feeling full, anorexia, minimal menstrual irregularities, pressure effect metastatic symptoms [12]. Large ovarian tumours can present with acute abdomen. Hard fixed mass especially in the presence of ascites is highly suggestive of malignancy [13]. As ovarian cancer is diagnosed at an advanced stage when despite advancement in surgical & chemotherapeutic treatment during the last decade, survival rates are very poor. Almost 90% of patients are diagnosed when the disease has already spread to the pelvis or abdomen in stage IIIA & IIIB. Again the stage of the disease is a great factor regarding prognosis & the overall survival for ovarian cancer is 48.4% but ranges from 89.9% for patients with stage IA to only 16.8% for patients stage IV disease [14]. A worse prognosis is correlated with late diagnosis, so there is great need to search tests or methods to detect the disease as early as possible [15]. Early ovarian cancer diagnosed incidentally or discover during routine pelvic examination and/or pelvic ultrasonography. Early diagnosis depends mainly on careful history taking, clinical symptoms and physical examination Including pelvic examination & DRE, ultrasound (abdominal/transvaginal), a blood test for CA125 and sometime other markers, among them CA 125 bears a good prognostic factor. Ultrasound is the standard investigation for identifying ovarian pathology as it gives information regarding the origin, size, consistency vascularity (Colour Doppler) or complexity of a tumour. When possible TVS is preferable, its sensitivity of around 100% and specificity of around 83% [16]. Serum CA 125 is the "Gold standard" tumour marker in ovarian cancer & most widely used. CA 125 levels of <35 U/ml are accepted as normal. Elevated levels were found in more than 90% of advanced epithelial ovarian cancer but only 50% in stage I disease [17]. It is also slightly increase in endometriosis & markedly increase in ovarian tumour.

During laparotomy whole abdominal cavity should be thoroughly assessed for staging of tumour & to see the extension. Any free fluid or peritoneal lavage is taken for cytological evaluation & biopsies are taken from suspicious areas and adhesions [18]. Diagnosis is confirmed by histopathology, which is the corner stone of further treatment modality of ovarian cancer.

Materials and Methods

This prospective study was conducted in the department of Obstetrics & Gynaecology in Rangpur Medical College & Hospital, Rangpur from July 2017 to June 2018. Total 30 patients having ovarian tumour were diagnosed clinically and by ultrasonography were included in the study was serum CA-125 was estimated in all study subjects.

Inclusion criteria

Patients with ovarian tumours diagnosed by history, clinical examination, USG, CA125 and wait for laparotomy will be included in my study

Exclusion criteria

1. Previously diagnosed and treated ovarian tumour.
2. Recurrent case of ovarian tumour.
3. Patient on chemotherapy.
4. Patient with functional cyst of ovary chocolate cyst of ovary.

Procedures of data collection

Information will be collected from the patient with USG findings & CA125 value by using a questionnaire made the reporting all relevant parameters under study, after taking permission from hospital authority, patient's case history will be collected from hospital record room & the attending doctors. Duration of data collection will be 12 months.

Data analysis: Data will be analyzed by SPSS version-23. Qualitative data will be analyzed as rate, proportion and percentage. Quantitative data will be analyzed as mean and standard deviation. The Chi-square & Unpaired t-test test will be used. The risk factor will be determined by odd ratio. A probability (p) value of <0.05 will be considered significant & p, 0.001 will be considered highly significant & p>0.05 taken as non- significant.

Results

Table 1: Socio-demographic profile of study subjects (n=30)

Age(years)	Benign tumors (n=11) No. (%)	Malignant tumors (n=19) No. (%)	Total (n=30) No. (%)	p-value
<20	0(0)	3(15.8)	3(10%)	
21-40	8(72.7)	1(5.3)	9(30%)	0.001
41-60	3(27.3)	10(52.6)	13(43.3%)	
>61	0(0)	5(26.3)	5(16.7%)	
Mean ± SD	34.45±12.429	50.21±17.999		
Range	21-58	14-70		
Educational status				
Illiterate	1(9.1)	12(63.2)	13(43.3)	
Primary	4(36.4)	4(21.1)	8(26.7)	0.02
SSC	1(9.1)	2(10.5)	3(10)	
HSC	2(18.2)	1(5.3)	3(10)	
Graduate	3(27.3)	0(0)	3(10)	
Socio-economic Status				
Low	5(45.5)	8(42.1)	13(43.3)	
Middle	4(36.4)	11(57.9)	15(50)	> 0.05^{NS}
High	2(18.2)	0(0)	2(6.7)	
Marital Status				
Married	10(90.9)	17(89.5)	27(90)	> 0.05^{NS}
Unmarried	1(9.1)	2(10.5)	3(10)	
Parity				
Nulliparous	3(27.3)	5(26.3)	8(26.7)	
Primiparous	0(0)	1(5.3)	1(3.3)	> 0.05^{NS}
Multiparous	8(72.7)	13(68.4)	21(70)	

Among 30 cases, benign tumours were 11(36.7%) in number and malignant tumours were 19(63.3%) in number. Majority of the patients were in the age group of 41 to 60 years with ranged from 14 to 70 years. Table-1 shows majority of the patients were in the age group 41 to 60 years. In benign tumour mean ± SD was 34.45±12.429 and in malignat tumour mean age was 50.21±17.999 which is highly significant (p<0.001). Majority of the patients belong to the middle socio-economic group (50%) and most of them were illiterate (43.3%), 27(90%) patients were married and 70% were multiparous.

Table 2: Contraceptive History of study subjects (n=30)

Contraceptive History	Benign tumors (n=11) No. (%)	Malignant tumors (n=19) No. (%)	Total (n=30) No. (%)	P value
Oral pill	4(36.4)	2(10.5)	6(20)	>0.05^{NS}
IUCD	1(9.1)	0(0)	1(3.3)	
Injectable	1(9.1)	2(10.5)	3(10)	
Condom	2(18.2)	1(5.3)	3(10)	
Tubectomy	0(0)	1(5.3)	1(3.3)	
None	3(27.3)	13(68.4)	16(53.3)	

Table 2 shows out of 30 study subjects majority 16(53.3%) did not take any contraceptive method, only (20%) use OCP.

Table 3: Clinical Presentation of study subjects (n=30)

Presenting Complaints	Benign tumors (n=11) No. (%)	Malignant tumors (n=19) No. (%)	Total (n=30) No. (%)	P value
Lump in lower abdomen	7(63.6)	19(100)	26(86.7)	0.005
Pain in lower abdomen	5(45.5)	18(94.7)	23(76.7)	0.002
Dyspepsia	1(9.1)	13(68.4)	14(46.7)	.002
Rapidity of growth	2(18.2)	17(89.5)	19(63.3)	0.00
Weight loss	0(0)	15(78.9)	15(50)	0.00

Table 3 shows most of the patients had more than one presenting complaints. Majority of the patients presented with lump in the abdomen 26(86.7%) & 23(76.7%) also had abdominal pain and weight loss present in 15 (50%) cases.

Table 4: USG finndings of study subjects (n=30)

USG findings	Benign tumors (n=11) No. (%)	Malignant tumors (n=19) No. (%)	Total (n=30) No. (%)
Unilateral	9(81.8)	5(26.3)	14(46.7)
Bilateral	2(18.2)	14(73.7)	16(53.3)
Consistency			
Cystic	11(100)	0(0)	11(36.7)
Cystic+ solid	0(0)	14(73.7)	14(46.7)
Solid	0(0)	5(26.3)	5(16.7)
Septation			
Present	2(18.2)	16(84.2)	18(60)
Absent	9(81.8)	3(15.8)	12(40)
Ascites			
Present	1(9.1)	17(89.5)	18(60)
Absent	10(90.9)	2(10.5)	12(40)

Table 4 shows the majority of the ovarian tumour 16(53.3%) were bilateral in distribution while 14(46.1%) were unilateral. Among malignant cases 14(73.7%) were bilateral. Both cystic and solid in consistency were present in 14(46.7%). Both ascites and septation present in 18(60%) cases. Most of them were malignant.

Table 5: Per operative findings of study subjects (n=30)

Per operative findings	Benign tumors (n=11) No. (%)	Malignant tumors (n=19) No. (%)	Total (n=30) No. (%)	p-value
Unilateral	9(81.8)	5(26.3)	14(46.7)	
Bilateral	2(18.2)	14(73.7)	16(53.3)	0.003
Adhesion	1(9.1)	13(68.4)	14(46.7)	0.002
Surface				
Regular	10(90.9)	2(10.5)	12(40)	
Irregular	1(9.1)	17(89.5)	18(60)	0.000
Consistency				
Cystic	11(100)	1(5.3)	12(40)	0.000
Cystic+ solid	0(0)	14(73.7)	14(46.7)	
Solid	0(0)	4(21.1)	4(13.3)	
Vascularity				0.000
Normal	11(100)	0(0)	11(36.7)	

Highly Vascular	0(0)	19(100)	19(63.3)	
Capsule broken				0.001
Present	2(18.2)	15(78.9)	17(56.7)	
Absent	9(81.8)	4(20.1)	13(43.3)	
Metastasis				0.037
Present	0(0)	6(31.6)	6(20)	
Absent	11(100)	13(68.4)	24(80)	
Ascites				0.000
Haemorrhagic	0(0)	5(26.3)	5(16.7)	
Straw colour	0(0)	12(63.2)	12(40)	
Absent	11(100)	2(10.5)	13(43.3)	

Table 5 shows 53.3% ovarian tumours were bilateral, 46.6% were unilateral in distribution and both cystic and solid consistency had 46.7%, only solid consistency in 13.3%.

Table 6: Histopathological types of study subjects (n=30)

Histopathological Findings	**Benign tumors No. (%)**	**Malignant tumors No. (%)**	**Total (n=30) No. (%)**
Tumor type	11(36.7)	19(63.3)	30(100)
Sub-classification			
Type	**Benign tumors (n=11) No. (%)**	**Malignant tumors (n=19) No. (%)**	**Total (n=30) No. (%)**
Epithelial	11(100)	16(84.2)	27(90)
Germ cell	0(0)	3(15.8)	3(10)

Table 6 shows benign tumour was 11(36.7%), malignant tumour was 19(63.3%). Epithelial tumours were 27(90%) and germ cell tumours were 3(10%).

Table 7: Histopathological variants of ovarian tumour of study subjects (n=30)

Histopathological variation 0f ovarian tumour		**No of patient(n=19)**	**Percentage (%)**
Benign	serous cyst adenoma	7	63.6
	mucinous cyst adenoma	4	36.4
Malignant	mucinous cyst adenocarcinoma	2	10.5
	well differentiated adenocarcinoma	4	21.1
	moderately differentiated adenocarcinoma	2	10.5
	poorly differentiated adenocarcinoma	3	15.8
	yolk sac tumour	3	15.8

Table 7 shows commonest benign tumour was serous cyst adenoma 7(63.6%) followed by mucinous cyst adenoma. 4(36%).In malignant tumours Serous cystadenocarcinoma was the commonest 5(26.3%) histological variety. Mucinous cyst adenocarcinoma were 2(10.5%), well differentiated adenocarcinoma 4(21.1%), moderately differentiated adenocarcinoma were 2(10.5%), poorly differentiated adenocarcinoma were 3(15.8%) and yolk sac tumour were 3(15.8%).

Table 8: Correlation between Serum CA-125 and histopathological reports of study subjects (n=30)

CA 125 level	**Benign tumors (n=11) No. (%)**	**Malignant tumors (n=19) No. (%)**	**Total (n=30) No. (%)**
>35-100	8(72.7)	2(10.5)	10(33.3)
>100-300	2(18.2)	4(21.1)	6(20)
>300	1(9.1)	13(68.4)	14(46.7)

Table 8 shows serum CA-125 level was raised in all cases but markedly (>300) raised in 14(46.7%) cases.

Discussion

Ovarian tumour is an important clinical problem still faced in gynaecological practice of the developing counties like Bangladesh. In most of the cases ovarian tumour are diagnosed at an advanced stage, as insidious onset and progression of the tumour makes early diagnosis difficult. The 2010 statistics for Bangladesh on age standardized death rates per 100000 show that cervical cancer and ovarian cancer ranking 24 and 45 position respectively [4]. This prospective study was carried out with the aim to find out the correlation of raised serum CA-125 with the laparotomy and histopathology findings of ovarian tumour. A total of 30 study subjects having ovarian tumour age ranging from 14 to 70 years were included. The duration of study was 1 year from July 2017 to June 2018. In present study (shown in table 1), mean age in benign tumour was 34.45±12.42 years & in malignant cases was 50.21±17.99 years. This findings consistent with the study done by Patel A et al in which mean age was 38 years in benign tumour and 50 years in malignant tumour [19]. Maximum number of patients was found in the age group of 41-60 years with age ranged from 14-70 years which is similar to the study published by Deeba F et al where maximum number of patients belong to the age group of 41-50 years with age ranged from 13 to 63 years [20]. In benign tumour majority 972.7%) of the patients were in age group of 21-40 years & in malignant tumour 52.2% patients in the age group of 41-60 years, it is similar to the study by Wills V et al in which benign tumour was more common in reproductive age (21-40) years and malignant tumour was in (41-60) years [21]. In present study the level education were illiterate (43.3%), primary (26.7%), SSC(10%), HSC(10%), Graduate(10%). Regarding socio-economic status (shown in table-1) 43.3% belong to the low socio-economic, 50%middle socio-economic & 6.7% high socio -economic status which is similar to the study by Dhar SR et al.

in which 40% belong to low socio-economic status, 56% middle and 4% high socio-economic status [22]. Nulliparity in reported as a risk factor of ovarian tumours in various studies. In present study out 30 cases of ovarian tumours 26.7% cases were nulliparous and 70% were multiparous though increase parity did not show decrease in ovarian cancer. This study shows 10% cases were unmarried &90% were married. This findings are similar to the study conducted by Dhar SR et al in which 12% cases were nulliparous 80% were parous,8%unmarried & 92% were married [22]. Use of OCP in a life time has been shown to decrease ovarian cancer risk by 40% to 50% compared with never use. Among the patients it was observed that only 20% received oral contraceptive (shown in Table 2). A study by Deeba F et al 35.7% patients received oral contraceptive [20]. So women in reproductive age should be counselled for the oral contraceptive. This study revealed that the presentation of ovarian tumour was variable. Some of the ovarian tumours may be incidentally diagnosed on ultrasonography where others may present with acute abdominal pain and with multiple more than one symptoms. Regarding the symptoms at presentation (shown in table 3) of study subjects it was observed that lump (86.7%) was more common; pain in lower abdomen (76.7%), rapidity of growth (63.3%), weight loss (50%) were also frequently recorded symptoms. This result complies well with the study carried by Deeba F et al in which lump was 71.4% followed by weight loss 60.7% and pain in abdomen 39.3% [20]. But these results differs with a study carried out by Yogambal M et al in which abdominal pain (66.92%) was the commonest presenting symptom followed by mass in abdomen (28.11%) [23]. Regarding ultrasonography findings of the study subjects (shown in Table 4) it was observed that majority of ovarian tumours were bilateral (53.3%) in distribution while 46.7% were unilateral. Most malignant tumours were bilateral 73.7%. Majority of the tumours were cystic & solid in consistency (46.7%). This result complies well with a study carried out by Khan I et al in which 55% were bilateral & 45% were unilateral in distribution. Among malignant tumours 72% were bilateral and 46% had solid and cystic consistency [5]. In present study per operative findings revealed (shown in Table 5) 53.3% tumours were bilateral and 46.7% were unilateral had both cystic & solid 46.7% cases & solid consistency in 13.3% cases. Peritoneal seedling present in 43.3% case & ascites present in 56% of cases. Sarwar S et al reported 41.2% malignant tumours were bilateral [11]. Hasmi A et al observed higher incidence of capsular invasion and omental metastasis was noted in serous carcinoma compared to mucinous tumour [24]. In present study the commonest tumour was epithelial tumour 90% followed by germ cell tumour 10% & no case of sex cord stromal tumour was seen. These findings were very close with the study carried out by Sarwar S et al in which epithelial tumour was 83.3% [11]. Another study by Pilli et al also showed epithelial tumour was the most common variety (70.9%) & germ cell tumour (21.7%) was second most common [25]. In present study histopathological variants of benign tumour showed that the commonest tumour was serous cyst adenoma (63.3%) followed by mucinous cyst adenoma (36.3%). A similar high incidence of serous cyst adenoma (44.6%) was observed by Wills V et al [21]. In this study out of 30 cases of ovarian tumour 19 cases were malignant. All malignant tumours were further analyzed according to histology & the subtypes were serous cyst adenocarcinoma (26.3%), mucinous cyst adenocarcinoma (10.5%). Sarwar S et al had almost same observation in which serous cyst adenocarcinoma was 28.6% and mucinous cyst adenocarcinoma was 13.4% [11]. Jindal D et al reported tumours to be well differentiated in 7%, moderately differentiated 42% & poorly differentiated 5% cases while in this study only 21% were well differentiated, 10.5% moderately differentiated and 15.3% poorly differentiated [26].

Though CA-125 is a routine investigation in the management of ovarian cancers but it is often considered as "Gold standard" [27]. In this study CA-125 was raised in all the study subjects. CA-125 level markedly raised (>300 U/ml) in 46.7% of cases. Deeba F et al have showed raised serum CA-125 was found 78.6% of ovarian cancer [20]. Shaikh NA et al observed that serum CA-125 level is not only raised in epithelial ovarian cancer but also in germ cell & sex cord stromal tumours while in this study 10.5% of germ cell tumour serum CA-125 was raised [17]. In this study it was observed that serum CA-125 significantly raised in most of the malignant ovarian tumours (68.4%). 3(10%) patients with germ cell tumour had raised alpha feto protein > 1000 ng/ml and one of them died within 2 months of operation. In this study most of the patients did not have regular follow up due to the fact like complete cure, poverty, illiteracy, social background, relief of symptoms, may be the region to avoid visiting hospital. Only 3 patients came for follow up after seven days and one month after operation and their serum CA-125 was normal.

Limitation of the study

- This study was not a population based study rather it was a hospital based study. So, it does not reflect the actual situation in total population in the country.
- It was a short time study so, sample size was inadequate to nullify the errors of the study.
- The study was confined to single centre.
- The drawback of this study was that all types of investigations for these cases couldn't be done because of our limited resources, investigation cost and patients non-compliance.
- Patients follow up were not possible after discharge due to non-complaiance of the patients.

Conclusions

Ovarian cancer has been reported to the leading cause of death from gynaecologic cancer & there is insufficient information about the epidemiology. Early diagnosis of ovarian cancer has challenged the physician since decades. The absence of a suitable test is also a matter of concern as when symptoms do occur, the disease is usually advanced. Detailed history, through clinical examination, serum CA-125 measurement, and Doppler ultrasonography may help in early detection & timely intervention of ovarian cancer can prevent adverse prognosis to some extent. So, it is always necessary to correlate clinical diagnosis confirmed by per-operative findings with histopathological findings which is mandatory, otherwise apparently benign ovarian tumour may escape highly aggressive malignant tumour.

Recommendations

The following measure may be taken to reduce ovarian tumour and its complication:

- Health education and awareness at the community level.
- Regular and periodic clinical examination of women including pre- pubertal and post-menopausal women.
- Prophylactic oophorectomy along with hysterectomy especially in high risk women with positive family history.
- Combined oral contraceptive pills a preventive measure is recommended to a women specially belong to lynch type-2 families.

- Empowerment of the women
- Development of universal health care insurance must be part of the strategy in Bangladesh for complex care such as for ovarian cancer.

Conflict of Interest
Not available

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Not available

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