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Correlation of Raised Serum CA-125 Level with Laparotomy and Histopathology Findings of Ovarian Tumour in Combined Military Hospital, CMH Dhaka, Bangladesh

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Abstract

Background: Ovarian tumour preferably malignant one is the leading cause of morbidity and mortality of women. Despite of advancement in surgical and chemotherapeutic treatment during the last decade, still survival rates are poor mainly 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 observational descriptive study was conducted in the department of Obstetrics & Gynaecology in Combined Military Hospital, CMH Dhaka from January 2023 to December 2023 and data collection period of 6 months. Total 30 patients having ovarian tumour diagnosed clinically, by ultrasonography and with raised serum CA125 level were included in the study who underwent laparotomy and diagnosis confirmed by histopathology. ***Results:*** Total 30 cases of ovarian tumour with raised serum CA-125 were enrolled in the study. Patient presented with lump in the abdomen 26(86.7%) as the commonest presentation. The commonest tumour was epithelial tumour 22 (73.3%) followed by germ cell tumour 8(26.7%). Serous cyst adenoma (47.4%) was common benign tumour& serous cyst adenocarcinoma was the commonest malignant variety (36.3%). Serum CA-125 level was raised in all cases but highly raised in almost all the malignant ovarian tumour 10(90.9%), among them in poorly differntiated 2(18.2%) cases CA-125 level is markdly raised average is 433.5U/ml, then in moderately differentiated cases CA-125 level is highly raised avgerage is 221.5U/ml. In undifferentiated variety average level of CA-125 is 272.5U/ml. In well differentiated case CA-125 level raised to 69U/ml. And on laparotomy, tumours with malignant features has high serum level of CA-125 (>100U/ml). ***Conclusion:*** As serum CA-125 is highly raised in most of malignant ovarian tumour, mainly of epithelial variety and moreover makdly raised in poorly differented ones as well as these tumours are found to have features of malignancy on laparotomy, so we can conclude that raised serum CA-125 is a useful tumour marker for early screening, and as well as it can be used as a marker for assumption of the nature and aggresiveness of ovarian malingnancies. Thus, serum level of CA-125 can be used as a tool for detection of ovarian malignancy at early stage, to reduce the morbidity and mortality of patients, as well as to improve the survivility also to reduce the disease burden of the patient with ovarian tumour.

Keywords: Correlation, Serum CA-125 Level, Laparotomy, Ovarian Tumour.

INTRODUCTION

Introduction Ovarian tumors are abnormal growths on the ovaries, the female reproductive organs. Ovarian tumors can be noncancerous (benign) or cancerous (malignant). Ovarian cancer is one of the most common gynecologic cancers that rank third after cervical and uterine cancer [1]. It also has the worst prognosis and the highest mortality rate [2].

GLOBOCAN estimates indicate there were 314 000 women diagnosed with ovarian cancer in 2020 and 207 000 ovarian cancer deaths, with the disease ranking eighth in terms of both cancer incidence and mortality among women worldwide [3]. According to the latest WHO data published in 2020 Ovary Cancer Deaths in Bangladesh reached 2,231 or 0.31% of total deaths. The age adjusted Death Rate is 3.34 per 100,000 of population ranks Bangladesh #133 in the world [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 relative has a 5% lifetime risk & with two or more affected 1st degree relatives the risk is 7% [6,7]. Ovarian cancer has been divided into epithelial and non-epithelial groups for many years, but recent work has enabled finer subdivision of epithelial ovarian cancers into different groups according to a combination of morphological and clinical characteristics [8,9]. Most ovarian cancers occur at & after menopause when the ovaries had no physiological role; consequently abnormal ovarian function causes no symptoms. As ovarian cancer is diagnosed at an advanced stage when despite of 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. 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 sometimes 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. Among these biomarkers, Cancer Antigen 125 (CA125), has played the most significant role in screening, detecting, and managing ovarian cancer for the last four decades. CA125 is a high molecular weight mucinous glycoprotein found on the surface of ovarian cancer cells. This antigen is then shed and quantified in serum samples of ovarian cancer patients. Serum CA125 levels are elevated in 50% of early-stage tumours and 92% of advanced-stage tumours [10,11]. Though CA-125 is a non-specfic marker as slightly increase in conditions like endometriosis & markedly increase in ovarian tumour. A surgical procedure called exploratory laparotomy is typically recommended, when ovarian cancer is suspected. During laparotomy by direct visualization nature of tumour is identified, and suspected cases are confirmed with the help of frozen section biopsy. Then in case of malignant cases, whole abdominal cavity should be thoroughly explored for staging of tumour and to see extention. And diagnosis is confirmed by histopathology, which is the corner stone of further treatment modality of ovarian cancer.

MATERIALS AND METHODS

Study design: It was an observational descriptive type of study.

Place of study: The study was conducted in the department of Obstetrics & Gynaecology, Combined Military Hospital, CMH Dhaka.

Study period: The study was conducted over the period of 1year dated from January 2023 to December 2023. With data collection period of 6 months.

Sample size: 30 cases.

Study population: The cases admitted in Gynae ward of Combined Military Hospital, CMH Dhaka with ovarian tumour with raised serum CA-125 level, who has underwent laparotomy and histopathological examination done were tahen as study population.

Inclusion criteria

Patients with ovarian tumours diagnosed by history, clinical examination, USG, raised CA-125 and underwent laparotomy were included in the 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 are collected from the patient with USG findings & CA125 value by using a questionnaire made including all the parameters taken for the study, findings during laparotomy and histopathological reports. After taking permission from hospital authority, patient's case history are collected from hospital record room & the attending doctors. Duration of data collection was 6 months.

Data analysis: Data are analyzed by SPSS version-23. Qualitative data are analyzed as rate, proportion and percentage. Quantitative data are analyzed as mean and standard deviation. The Chi-square & Unpaired t-test test are used. The risk factors are determined by odd ratio. A probability (p) value of 0.05 taken as non-significant. Patient are recruited as benign and malignant on analyzing the data, then all the results are tabulated accordingly.

RESULTS

During the study period from January 2023 to December 2023, a total number of 33 cases of ovarian tumour with raised CA- 125 level were included in the

study but 3(three) cases were excluded from the study due to unavailablity of the histopathological reports. Among 30 cases, benign tumours were 19(63.3%) and malignant tumours were 11(36.7%) in number who were diagnosed histopathologically. On laparotomy, there were variable findings, where most of the malignant tumours are bilateral and with features of metastasis 9(81.8%), having irregular surface 10(90.9%), consistancy was partly solid and partly cystic in 6(54.5%) cases. Vascularity and ascitis were in 10(90.9%) cases of malignant nature. While correlating CA-125 level with histopathological variety and grading, it is found that, among the malingnant cases, in poorly differentiated one CA-125 level was highly raised with average of 433.5 U/ml, in undifferentiated ones the level is 272.5 U/ml, while in well differentiated one, level is about 69 U/ml. CA-125 level is also found to be raised in all the benign cases as well, but most of the cases level is<100 U/ml. CA-125 level is raised mostly in tumours with epithelial origin 22 (73.3%) cases.

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

Presenting Complaints	Malignant tumors(n=11) No. (%)	Benign tumors (n=19) N0. (%)	Total (n=30) No. (%)	P value
Lump in lower abdomen	11(100)	15(78.9)	26(86.7)	>0.05^{NS}
Pain in lower abdomen	10(91.9)	13(68.4)	23(76.7)	>0.05^{NS}
Dyspepsia	8(72.7)	12(58.4)	20(66.6)	>0.05^{NS}
Rapidity of growth	10(91.9)	3(15.8)	13(43.3)	<0.001
Weight loss	9(81.9)	0(0)	9(30)	<0.001

Table-I 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 9 (30%) cases.

Table-II: USG findings of study subjects (n=30)

USG findings	Malignant tumors (n=11) No. (%)	Benign tumors (n=19) N0. (%)	Total (n=30) N0. (%)
Unilateral	3(27.3)	15(78.9)	18(60)
Bilateral	8(72.7)	4(21.1)	12(40)
Consistency			
Cystic	0(0)	15(78.9)	15(50)
Cystic+solid	7(63.6)	4(21.1)	11(36.7)
Solid	4(36.4)	0(0)	4(13.3)
Septation			
Present	9(81.8)	9(47.4)	18(60)
Absent	2(18.2)	10(52.6)	12(40)
Ascites			
Present	10(90.9)	8(42.1)	18(60)
Absent	1(9.1)	11(57.9)	12(40)

Table-II shows the majority of the ovarian tumour 18(60%) were unilateral in distribution while 12(40) were bilateral. Among malignant cases 8(72.7%) were bilateral. Both cystic and solid in consistency were present in 11(36.7%). Both ascites and septation present in 18(60%) cases. Most of them were malignant.

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

Histopathological findings	Malignant Tumors (n=11) N. (%)	Benign tumors (n=19) No. (%)	Total (n=30) No. (%)
Tumor type	11(36.7)	19(63.3)	30(100)
Sub-classification			
Type	Malignant Tumors (n=11) N(%)	Benign tumors (n=19) No(%)	Total (n=30) No. (%)
Epithlial	9(81.8)	13(68.4)	22(73.3)
Germ cell	2(18.2)	6(31.6)	8(26.7)

Table-III shows malignant tumour were 11(36.7%), benign tumourwere 19(63.3%). Epithelial tumours were 22(73.3%) and germ cell tumours were 8(26.7%).

Table-IV: Per operative findings of study subjects and CA-125 level (n=30)

Per operative findings	Malignant tumors (n=11) No. (%)	Benign tumors (n=19) No. (%)	Total (n=30) No. (%)	P value
Unilateral	2(18.2)	14(73.7)	16(53.3)	0.01
Bilateral	9(81.8)	5(26.3)	14(46.7)	
Adhesion	11(100)	3(15.8)	14(46.7)	<0.001
Surface				
Regular	1(9.1)	17(89.5)	18(60)	<0.001
Irregular	10(90.9)	2(10.5)	12(40)	
Consistency				
Cystic	1(9.1)	15(78.9)	16(53.3)	
Cystic + solid	6(54.5)	4(21.1)	10(33.3)	<0.001
Solid	4(36.4)	0(0)	4(13.3)	
Vascularity				
Normal	1(9.1)	17(89.5)	18(60)	
Highlyvascular	10(90.9)	2(10.5)	12(40)	<0.001
Capsulebroken				
Present	9(81.8)	4(20.1)	13(43.3)	
Absent	2(18.2)	15(78.9)	17(56.7)	0.004
Metastasis				
Present	9(81.8)	0(0)	9(30)	<0.001
Absent	2(18.2)	19(100)	21(70)	
Ascites				
Haemorrhagic	3(27.3)	0(0)	3(10)	
Straw colour	7(63.6)	0(0)	7(23.3)	<0.001
Absent	1(9.1)	19(100)	20(67.7)	
CA-125level				
>35-100	1(9.1)	13(68.4)	14(46.7)	0.004
>100	10(90.9)	6(31.6)	16(53.3)	

Table-IV shows 46.7% ovarian tumours were bilateral, 53.3% were unilateral in distribution and both cystic and solid consistency had 33.3%, only solid consistency in 13.3%. 81.8% malignant tumours are bilateral with features of metastasis. CA-125 level is raised in all the cases but highly raised in almost all the malignant cases.

Table-V: Histopathological variants of ovarian tumour of study subjects (n=30) and level of CA-125 in the number of cases

Histopathological variation of Ovarian tumor		No of patient(n=30)	Percentage (%)	CA-125 level (>35-100 U/ml) (n)	CA-125 Level (>100 U/ml) (n)
Benign (n=19)	Serous cystadenoma	9	47.4	5	4
	Mucinouscystadenoma	4	21.1	2	2
	Matureteratoma	6	31.5	6	-
Malignant (n =11)	Mucinous cystadenocarcinoma	2	18.2	-	2
	Serous cystadenocarcinoma	4	36.3	-	4
	Yolksactumor	2	18.2	1	1
	Endometroid	1	9.1	-	1
	Undifferentiated	2	18.2	-	2

Table-V shows commonest benign tumour was serous cyst adenoma 9(47.4%) followed by mature teratoma 6(31.5%) and mucinous cyst adenoma.4(21.1%). In malignant tumours Serous cystadenocarcinoma was the commonest 4(36.3%), Mucinous cyst adenocarcinoma were 2(18.2%), and yolk sac tumour were 2(18.2%) histological variety. CA-125 is highly raised among the malignant tumours 10(90.9%), and in most of the benign tumor level of CA-125 is within (>35- 100U/ml).

Table-VI: Correlation between histological grading, histopathological variety and level of Serum CA-125 of malignant ovarian tumour of study subjects (n=11)

Histological grading of malignant ovarian Tumour		Number of patient (n=11) (%)	Histopathological variety	Level ofCA-125 (U/ml)	Average level ofCA-125(U/ml)
Grading	Well diferentiated	1(9.1)	Yolk sac tumour	69	69
	Moderately differentiated	6(54.5)	Serous cyst adenocarcinoma	356	221.5
			Mucinous cystadenocarcinoma	244	
			Serous cystadenocarcinoma	219	
			Serous cystadenocarcinoma	190	
			Serous cystadenocarcinoma	165	
			Mucinous cystadenocarcinoma	155	
	Poorly differentiated	2(18.2)	Serous cystadenocarcinoma	534	433.5
			Endometroid	333	
	Unremarkable	2(18.2)	Undifferentiated	344	272.5
			Undifferentiated	201	

Table-VI shows serum CA-125 level was raised in all cases but highly raised in almost all the malignant ovarian tumour, but in poorly differntiated 2(18.2%) cases CA-125 level is markdly raised average is 433.5U/ml, then in moderately differentiated cases CA-125 level is highly raised avgerage is 221.5U/ml. In undifferentiated variety average level of CA-125 is 272.5U/ml. In well differentiated case CA-125 level raised to 69U/ml.

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. According to the latest WHO data published in 2020 Ovary Cancer Deaths in Bangladesh reached 2,231 or 0.31% of total deaths. The age adjusted Death Rate is 3.34 per 100,000 of population ranks Bangladesh #133 in the world [4]. This observational 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 in the study who were admitted in the department of Obstetrics & Gynaecology of Combined Military Hospital, CMH Dhaka- a tertiary centre. The duration of study was 1 year from January 2023 to December 2023. With a data collection period of 6 months. 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 of study subjects it was observed that lump 86.7% was more common; pain in lower abdomen 76.7%, rapidity of growth 43.3%, weight loss 30% were also frequently recorded symptoms. This result complies partially with the large cross-sectional study at 4 hospitals in Bangladesh, in which lump was 71.4% followed by weight loss 60.7% and pain in abdomen 39.3% [12]. But these results differs with another retrospective and descriptive study carried out at Chennai, India in which abdominal pain 66.92% was the commonest presenting symptom followed by mass in abdomen28.11% [13]. Regarding ultrasonography findings of the study subjects it was observed that majority of ovarian tumours were unilateral 60% in distribution while 40% were bilateral. Most malignant tumours were bilateral 72.7%. Most of the tumours were cystic & solid in consistency 36.7%. This result complies well with a prospective study at Lahore, Pakistan in which 55% were bilateral & 45% were unilateral in distribution. Among malignant tumours 72% were bilateral and 46% had solid and cystic consistency [5]. Per operative findings of study population revealed 46.7% tumours were bilateral and 53.3% were unilateral, had both cystic & solid 33.3% cases & solid consistency in 13.3% cases. Peritoneal seedling present in 43.3% case & ascites present in 33.3% of cases. A large study reported 41.2% malignant tumours were bilateral [14]. Another retrospective study observed higher incidence of capsular invasion and omental metastasis was noted in serous carcinoma compared to mucinous tumour [15]. In present study the commonest tumour was epithelial tumour 73.3% followed by germ cell tumour 26.7% & no case of sex cord stromal tumour was seen. These findings were very close with the study carried out on large number of subjects in which epithelial tumour was 83.3% [14]. Another study also showed epithelial tumour was the most common variety 70.9% & germ cell tumour 21.7% was second most common [16]. In present study histopathological variants of benign tumour showed that the commonest tumour was serous cyst adenoma 47.4% followed by mature teratoma 31.5% and mucinous cyst adenoma 21.1%. A similar high incidence of serous cyst adenoma 44.6% was observed in a study at Kerala, India [17]. In this study out of 30 cases of

ovarian tumour 11 cases were malignant. All malignant tumours were further analyzed according to histology & the subtypes were serous cyst adenocarcinoma 36.3%, mucinous cyst adenocarcinoma 18.2%. One large study had almost same observation in which serous cyst adenocarcinoma was 28.6% and mucinous cyst adenocarcinoma was 13.4%. [14] One study had reported tumours to be well differentiated in 7%, moderately differentiated 42% & poorly differentiated 5% cases, where Ca-125 level were raised in all malignant cases while in this study 9.1% were well differentiated, 54.5% moderately differentiated and 18.2% poorly differentiated. In poorly differntiated 18.2% cases CA-125 level is markdly raised then in moderately differentiated cases CA-125 level is highly raised. In undifferentiated variety average level of CA-125 is 272.5U/ml. In well differentiated case CA-125 level raised to 69U/ml [18]. Though CA-125 is a routine investigation in the management of ovarian cancers. In this study CA-125 were raised in all the study subjects. CA-125 level in all cases but markedly raised (>100 U/ml) in 90.9% of malignant cases. A cross-sectional study showed raised serum CA-125 was found 78.6% of ovarian cancer [19]. Another study 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 26.7% of germ cell tumour serum CA-125 was raised [20]. In this study it was observed that serum CA-125 significantly raised in most of the malignant ovarian tumours 90.9%. In this study most of the patients did not have regular follow up due to the fact like complete cure, benign varient, social background, relief of symptoms, may be the reason to avoid visiting hospital. Only 3 patients came for follow up after seven days and one month after operation and their serum CA-125 were normal.

Limitations 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.
- Sample size was inadequate to nullify the errors of the study.
- The study was confined to single centre.

CONCLUSIONS

Ovarian tumour is an important clinical problem still faced in gynaecological practice of the developing counties like Bangladesh. 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, thorough clinical examination, serum CA-125 measurement, and Colour Doppler ultrasonography may help in early detection & timely intervention of ovarian cancer can prevent adverse prognosis to some extent. CA-125 level can give an early assumption regarding the nature and grading of tumour, as well as this can be taken into account for early screenig tool for high-risk cases with positive risk factors. So, it is always necessary to correlate CA-125 level and clinical diagnosis to be confirmed by per-operative findings followed by histopathological report 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, with positive family history.
- Prophylactic oophorectomy along with hysterectomy specially in high-risk women with positive family history.
- Combined oral contraceptive pills, a preventive measure is recommended to 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.

REFERENCES

1. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 68(6), 394-424.
2. Coburn, S. B., Bray, F., Sherman, M. E., & Trabert, B. (2017). International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. International journal of cancer, 140(11), 2451-2460.
3. Ferlay, J., Ervik, M., Lam, F., Colombet, M., Mery, L., Piñeros, M., ... & Bray, F. (2021). Global cancer observatory: cancer today. Lyon: International Agency for Research on Cancer; 2020. Cancer Tomorrow.
4. World health ranking, Bangladesh, WHO.
5. Khan, I. K. R. A. M. U. L. L. A. H., & Shezadi, N. O. R. E. E. N. (2010). Prospective study of ovarian tumors clinical pattern and their management at Lady Willingdon Hospital, Lahore. Pak J Med Health Sci, 4(2), 159-62.
6. Ahmed, Z., Kiyani, N., Hasan, S. H., & Muzaffar, S. (2000). Gill MS. Histological Patterns of ovarian neoplasia. J Pak Med Assoc, 50, 416-9.
7. Kauff, N. D., Satagopan, J. M., Robson, M. E., Scheuer, L., Hensley, M., Hudis, C. A., ... & Offit,

K. (2002). Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. New England Journal of Medicine, 346(21), 1609-1615.
8. Kurman, R. J., & Shih, I. M. (2016). The dualistic model of ovarian carcinogenesis: revisited, revised, and expanded. The American journal of pathology, 186(4), 733-747.
9. McCluggage, W. G. (2011). Morphological subtypes of ovarian carcinoma: a review with emphasis on new developments and pathogenesis. Pathology-Journal of the RCPA, 43(5), 420-432.
10. van Haaften-Day, C., Shen, Y. U., Xu, F., Yu, Y., Berchuck, A., Havrilesky, L. J., ... & Hacker, N. F. (2001). OVX1, macrophage-colony stimulating factor, and CA-125-II as tumor markers for epithelial ovarian carcinoma: A critical appraisal. Cancer: Interdisciplinary International Journal of the American Cancer Society, 92(11), 2837-2844.
11. Nustad, K., Bast, Jr, R. C., O'brien, T. J., Nilsson, O., Seguin, P., Suresh, M. R., ... & Hilgers, J. (1996). Specificity and affinity of 26 monoclonal antibodies against the CA 125 antigen: first report from the ISOBM TD-1 workshop. Tumor Biology, 17(4), 196-219.
12. Hossain, F., Karim, M. N., Rahman, S. M. M., Khan, N., Siddiqui, M., & Hussain, R. (2010). Preoperative detection of ovarian cancer by color Doppler ultrasonography and CA 125. Bangladesh Medical Research Council Bulletin, 36(2), 68-73.
13. Yogambal, M., Arunalatha, P., Chandramouleeswari, K., & Palaniappan, V. (2014). Ovarian tumours-Incidence and distribution in a tertiary referral center in south India. IOSR-JDMS, 13(2), 74-80.
14. Sarwar, C. M., Siddiqui, N., Khokhar, R. A., & Badar, F. (2006). Epithelial ovarian cancer at a cancer hospital in a developing country. Asian Pac J Cancer Prev, 7(4), 595-8.
15. Hashmi, A. A., Hussain, Z. F., Bhagwani, A. R., Edhi, M. M., Faridi, N., Hussain, S. D., & Khan, M. (2016). Clinicopathologic features of ovarian neoplasms with emphasis on borderline ovarian tumors: an institutional perspective. BMC research notes, 9, 1-4.
16. Pilli, G. S., Suneeta, K. P., Dhaded, A. V., & Yenni, V. V. (2002). Ovarian tumours: a study of 282 cases. Journal of the Indian Medical Association, 100(7), 420-423.
17. Begum, R., Chowdhury, M. A., Tithy, S. A., & Siddique, M. R. Correlation of raised serum CA-125 level with laparotomy and histopathology findings of ovarian tumour in a tertiary level hospital.
18. Jindal, D., Sahasrabhojanee, M., Jindal, M., & D'Souza, J. (2017). Epidemiology of epithelial ovarian cancer: a tertiary hospital based study in Goa, India. Int J Reprod Contracept Obstet Gynecol, 6(6), 2541-2546.
19. Deeba, F., Alam, A. M., & Banu, J. (2013). Clinlcopathological study of ovarian cancer: a multi centered study. Journal of Shaheed Suhrawardy Medical College, 5(1), 3-6.
20. Shaikh, N. A., Samo, R. P., & Memon, M. Q. (2013). OVARIAN CANCER;: The role of CA-125 as a tumor marker. An institutional based descriptive & prospective study. The Professional Medical Journal, 20(06), 904-908.