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STUDY OF CHARACTERISTIC AND MANAGEMENT OF PRIMARY OVARIAN TUMORS AT A GYNAECOLOGIC ONCOLOGY CENTRE AT PUNE.

Gynaecology

Pranaya Gurmeet MBBS, MS, DNB Obs & Gynae
Barun Bhai Patel MBBS, MD, Community Medicine
Anupam Kapoo r MBBS, MS Obs & Gynae
Vandana Kumari MBBS, MD, Community Medicine
Kapil H Pandya MBBS, MD, Community Medicine
Vijay Kumar More MBBS, MD, Community Medicine

ABSTRACT

Worldwide, Ovarian tumour is the leading cause of morbidity and mortality. Each year, 204,000 women are diagnosed, and 125,000 women die from this disease. This study was carried out to know the characteristic and management of primary ovarian tumors with objectives to study the age distribution, disease classification and management. Data of 1 complete year (114) of ovarian tumor patients treated at Gynecologic Oncology centre of Pune were studied. Maximum was between 51-60 yrs of age. 60.5% were benign and 39.5% were malignant tumour, Among benign tumors, 68% were epithelial, 26% Germ cell and 6% were sex cord tumors. All malignant tumors were of epithelial origin and among them 86.7 % were serous cystadenocarcinoma. 91 % patients presented at advanced stage of tumour. 96 % patients of benign tumors were managed with oophorectomy. Among malignant, 37.8 % patients were managed with primary cytoreduction and 58% by interval cytoreduction.

KEYWORDS:

Ovarian tumour, Gynaecologic Oncologic centre

Introduction:

Ovarian cancer accounts for more deaths than all other gynecologic malignancies combined. *According to* Global Cancer Statistics, 2002 ovarian cancer (204,000 cases and 125,000 deaths) is the sixth most common cancer and the seventh cause of death from cancer in women (4.0% of cases and 4.2% deaths). Incidence rates are highest in developed countries, with rates in these areas exceeding 9 per 100,000, except for Japan (6.4 per 100,000. [1].

The incidence of ovarian cancer is highest in Sweden (19.6/100,000) and the United States (15.4/100,000), and lowest in Japan (10.1/100,000). In the United States, ovarian cancer incidence rates are highest in Caucasian women, intermediate in African American women, and lowest in Native American women [2]

In most of the population-based cancer registries in India, ovarian cancer is the third leading site of cancer among women, trailing behind cervix and breast cancer. The age-adjusted incidence rates of ovarian cancer vary between 5.4 and 8.0 per 100,000 populations in different parts of the country. About 21,150 women developed ovarian cancer in India in 2002 [3].

During the period 2004-2005, proportion of ovarian cancer varied from 1.7% to 8.7% of all female cancers in various urban and rural population based registries operating under the network of the National Cancer Registry programme (NCRP) of Indian Council Medical Research. The proportion of this cancer was 6.0% and 7.7% of all cancers among females in rural Barshi and Ahmadabad registry areas [4].

Of all the gynecologic cancers, ovarian malignancies represent the greatest clinical challenge. Epithelial cancers are the most common ovarian malignancies. Ovarian cancer represents a major surgical challenge, requires intensive and often complex therapies, and is extremely demanding of the patient's psychological and physical energy. Thus, cost of treatment is high and the prognosis poor. It has the highest fatality-to-case ratio of all the gynecologic malignancies [5].

Numerous types of ovarian neoplasms exist, of which approximately 80% are benign. Ovarian neoplasms are typically divided into three major groups: epithelial, germ cell, and sex cord-stromal tumors. The ovary can also be a site of metastatic cancer, particularly from the breast or the gastrointestinal tract (Krukenberg's tumors). Approximately 90% of malignant ovarian tumors in adults are of epithelial origin followed by sex cord stromal tumors (6%) and germ-cell tumors (3%) [6].

The peak incidence of invasive epithelial ovarian cancer is at 56 to 60 years of age. The average age of patients with borderline tumors is approximately 46 years. Most epithelial ovarian cancer is sporadic, with familial or hereditary patterns accounting for 5% to 10% of all malignancies. [7-9].

Age over 40 years, white race, early menarche, late menopause, nulliparity, infertility, history of endometrial or breast cancer, and family history of ovarian cancer consistently have been found to increase the risk of invasive epithelial cancer. Patients with a family history of ovarian, breast, endometrial, or colon cancer are at increased risk of developing ovarian carcinoma [6, 10].

Higher parity, use of oral contraceptive pills (OCPs), history of breast-feeding, tubal ligation and hysterectomy have been associated with a decreased risk of ovarian cancer. Oral contraceptive pill is the only documented method of chemoprevention for ovarian cancer [11].

Symptoms are nonspecific and can include abdominal bloating, early satiety, weight loss, constipation, anorexia, and irregular menstrual bleeding. On physical examination, a pelvic mass is an important sign of disease. In more advanced stages of disease, abdominal distension may develop, and chest examination may reveal evidence of pleural effusion.

Most challenging part is early diagnosis of tumour. Only 19% of ovarian cancer cases are diagnosed while the cancer is localized (stage I), and approximately 68% of patients with epithelial ovarian cancer have advanced (stage III or greater) disease at time of diagnosis [12]. Evaluation of pelvic mass varies depending on the patient's age, significant medical and family history, and the sonographic characteristics of the mass. Risk of malignancy index (RMI score), determines the risk of an ovarian mass being cancerous.

The value of tumor markers and ultrasonography to screen for epithelial ovarian cancer has not been clearly established by prospective studies. Given the false-positive results for both CA125 and transvaginal ultrasonographies, particularly in premenopausal women, these tests are not cost-effective and should not be used routinely to screen for ovarian cancer [13].

Treatment of epithelial ovarian cancer depends on the stage and grade of the disease, type of disease (primary or recurrent), previous

treatment, and the patient's performance status. Advanced stage tumors require chemotherapy. Carboplatin and paclitaxel for three to six cycles is used for epithelial ovarian tumors [14].

The most frequently used chemotherapeutic regimens for germ cell tumors are BEP (bleomycin, etoposide, and cisplatin), VBP (vinblastine, bleomycin, and cisplatin), and VAC (vincristine, actinomycin, and cyclophosphamide) [15-16].

Prognosis depends on stage, grade, histology of the tumor, the amount of residual disease remaining after initial debulking surgery, and the age of the patient. The present study was therefore undertaken in a tertiary care institute of Pune, Maharashtra, to access the age distribution, type of tumor, histology and management of ovarian tumors.

Methodology:

A Cross-Sectional descriptive study was undertaken at a Gynaecologic Oncology centre, Pune in which all the patients of ovarian tumor during the period Apr 2011 to Aug 2012. A total of 114 patients were treated during the period therefore all 114 patients were included in the study. We included patients with primary ovarian tumour (tumors that originated from tissues of ovary) only and excluded patients with secondary deposits, functional ovarian cyst (defined as simple cysts ≤ 8cm in reproductive age group), Endometrioma (defined as a cyst formed due to functional endometrial glands in ovary). The data was collected by using personal interview technique with the help of pretested structured questionnaire. The designed questionnaire was mainly divided into seven parts; first part covered basic demographic characteristics of respondents, second part of questionnaire included past and family history, third part included physical symptoms perceived by patients, fourth part included clinical examination, fifth part included basic as well as specific investigations including radiological imaging (X-ray, USG and Contrast Enhanced Computed Tomography), sixth part included tumor type and histological classification and seventh part included staging and treatment of tumor. Histopathological report was collected from pathology department. For diagnosis, staging and treatment- treating physician's/ surgeon's note were consulted.

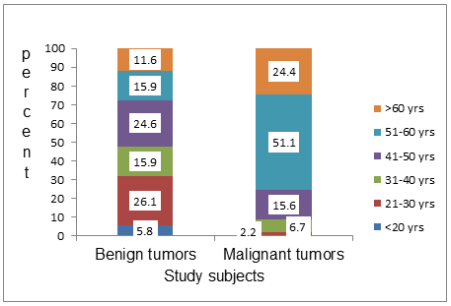
Ethical clearance was obtained from ethical committee of the hospital before start of study and written informed consent was taken from all participants before start of the study.

The investigator collected, compiled and analyzed the data using appropriate and relevant statistical tests. Guidance and expert opinion of Guide and Faculty Statistician was taken during planning and during analysis to use appropriate statistical tests keeping in view the aims and objectives of the study. Computer package SPSS version 20.0 was utilized for data management and analysis.

Results:

Figure 1 shows that maximum patients reported with ovarian tumor were between 51-60 yrs of age.

Figure 1: Distribution of study subjects as per age and Types of Tumor



Mean age of menarche in our study population for Benign tumor was 11.50 (SD 0.72) Years and that of patients with malignant tumor were 11.64 (SD 0.77) years with median of 11 years for both groups. There was no significant association found between the age of menarche (P=0.336) and type of tumor (unpaired t-test).

55 women (21 (30.43 %) among benign tumor pt and 34 (75.55%) among malignant tumor patient) had attended menopause at the time of diagnosis, among them mean age of attaining menopause in patients with benign tumor was 48.47 (SD 5.58) years and that of malignant tumor was 51.47 (SD 4.76 years). There was no association found between types of tumor and age of menopause (P value = 0.072, by independent sample T test).

Mean parity of all subjects was found to be near 2 with mode also 2. 52 (45.6 %) patients were parity 2 followed by 26 (22.8%) nulliparous and 25 (21.9%) parity 3. 42 % among benign and 51.1% among malignant tumor patients were parity 33.3% among benign patients and 6.7% among malignant patients were nullipara.

In our study Majority of patients were belonged to lower middle socio economic class 72(63.2%) followed by upper middle 35(30.7%).

Fig2: Distribution of study subjects as per Socio Economic Status.

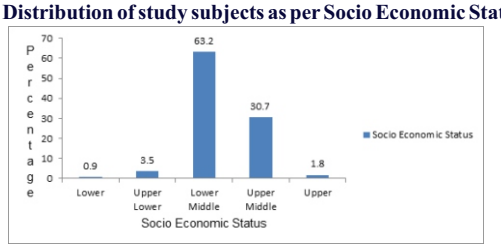


Figure 3: Types of Tumors in study population

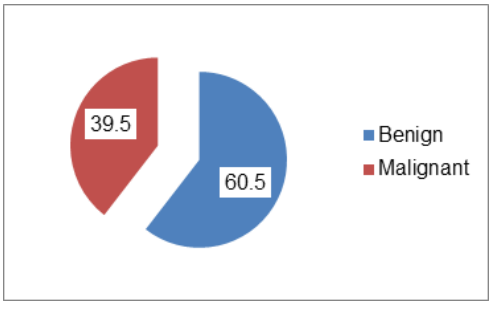
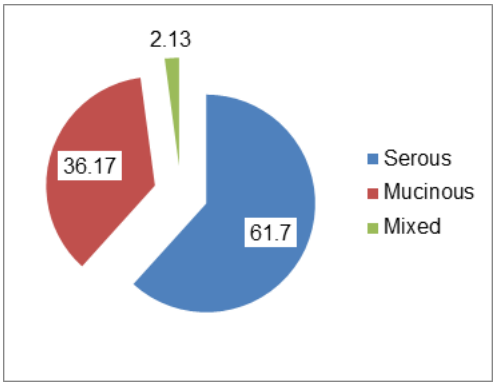


Fig 4 : Classification of Benign Epithelial Tumor



Among benign tumors, 68% were epithelial, 26% Germ cell and 6% were sex cord tumors. Figure 3 shows classification of benign epithelial tumors.

Among germs cells all were teratoma and among sex cord tumors all were Granulosa cell tumor

All malignant tumors were of epithelial origin and among them 39 (86.7 %) tumours were serous cystadenocarcinoma followed by 6.7% mucinous, 4.4% endometroid and 2.2% mixed.

Table1: Association between types of tumor and different blood parameters:-

Association between types of tumor and different blood parameters.					
Para meters	Tumor type	Number	Mean	Std. Deviation	P value
Hb	Benign	69	10.83	1.26	0.006
	Malignant	45	10.15	1.33	

TLC	Benign	69	8346.09	1609.39	0.824
	Malignant	45	8425.78	2203.33	
Sr creatinine	Benign	69	0.74	0.14	0.916
	Malignant	45	0.74	0.38	
Sr bilirubin	Benign	69	0.53	0.19	0.619
	Malignant	45	0.55	0.21	
AST	Benign	69	26.11	5.68	0.096
	Malignant	45	24.29	5.66	
ALT	Benign	69	27.74	5.34	0.671
	Malignant	45	28.15	4.70	
ALP	Benign	69	95.07	17.27	0.057
	Malignant	45	104.56	34.99	
CA 125	Benign	69	2.5	4.45	0.001*
	Malignant	45	537	1353.41	
CEA	Benign	69	1.20	1.64	0.012*
	Malignant	45	1.50	9.45	
AFP	Benign	69	0.82	0.82	0.323*
	Malignant	45	0.91	1.11	
LDH	Benign	69	157.29	60.42	0.001
	Malignant	45	224.33	78.90	
B Hcg	Benign	69	0.84	0.9	0.151
	Malignant	45	1.09	0.91	

* Medians were compared since the data of CA 125, CEA and AFP were skewed.

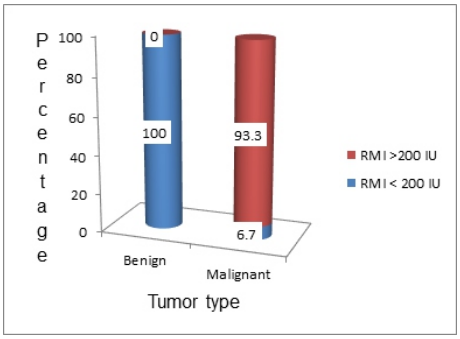
Table 5 shows the association between types of tumor and different blood parameters.

Out of 114, 37(32.5%) were having simple cyst on CECT. Simple cyst was mainly present in patients with benign tumors (50.7%). Complex cyst was present in 77 (67.5%) of total population. Simple cysts were equally distributed in benign tumor, whereas complex cyst was prominent in 95.6 % of malignant tumor and was significantly associated with malignant tumor (p value 0.001). Also Ascitis (68.9%), Metastasis (71.1%) and **Pleural effusion** (13.33 %) on CECT was only present in malignant tumor.

Out of 45 patients of malignant tumors, 31 were having ascites and 29 (64.4%) among them were positive for malignant cells in fluid cytology, 06 were having pleural effusion and 4 (8.9) % among them were positive for malignant cells in fluid cytology while Pericardial effusion was present in only 1 patient of malignant tumor and that was positive for malignant cells in fluid cytology.

Mean RMI score of patients with benign tumor was 2.63 IU and that of malignant tumors was 7391.97 IU which was significantly associated with Malignant tumor (Mann-Whitney U test P value 0.001)

Fig5: Distribution of study subjects as per RMI score and types of Tumor



For operational purpose RMI score were divided in to two categories first below 200 IU and second above 200 IU. Fig 6 shows that RMI score above 200 IU was present only in malignant tumor patients. It was observed that value below 200 IU was significantly associated with benign tumor and value above 200 was significantly associated with malignant tumors (P value <0.001)

Figure6: Stages of Tumors in study subjects

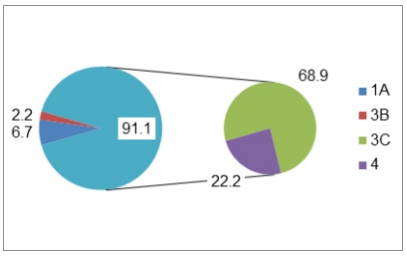


Fig 6 shows the stages of tumor at the time of diagnosis.

Table2: Treatment of benign tumor

Management	Number (%)
Oophorectomy	66 (95.7)
Cystectomy	3 (4.3)
Total	69 (100)

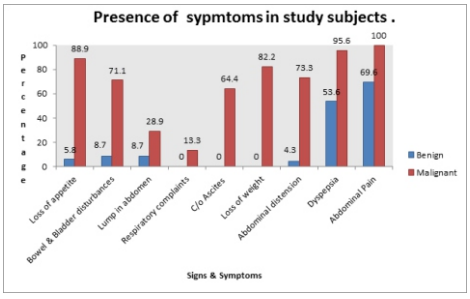
Table2 shows management of benign Tumors.

Interval cytoreduction was main modality as surgical intervention in malignant tumors 58% patients were managed with that followed by 37.8 % patients were managed with primary cytoreduction. NACT was given to 29 (64.4%) patients of malignant tumors. Among them 1 patient was with stage III B, 19 patients were with stage III C and 9 patients were of stage IV. As an institutional policy, all late stage diseases were managed with NACT followed by interval cytoreduction.

Adjuvant chemotherapy was given to 41 (91 %) patients with malignant tumors. Among them 2 patients were with stage I A, 1 patients was with stage III B, 28 patients were of stage III C and 10 patients were of stage IV.

We found that past h/o menstrual disturbances (50.72%), OCP use (7.25%) and Infertility treatment (21.74%) were more associated with benign tumors (Chi-square test, p value <0.05).

Figure 6



All symptoms were significantly associated with malignant tumor (P value < 0.05)

DISCUSSION

In our study, the range of age of study subjects was14 to 75 years. Three percent of patients were in adolescent age group which is comparable with the study done by **Despande and Badjatiya,** where the incidence of ovarian tumour in adolscent group was 4.2% [17].

The peak age of malignant tumors (51.1 %) was between 50-60 yrs of age while benign tumors were equally distributed between 20-60 yrs of age. 54.0% patients were under 50 years of age. Maximum patients with malignancy were over 40 years (67.6%). Mean age of benign tumor in our study was 41.5 years while that of malignant tumor was 55.3 years. This indicated that chances of malignancy in ovarian tumors increase with increasing age. These findings are consistence with study done by **Di Bonito L et [18] Al, Sarwar CMS et al [19], Rosenmary Yancik [20], National Cancer Registry, Ireland; 2009 [21], Bhattacharya *et al* [22].**

Maximum number of malignancy was seen in older age group. Similar finding was seen in a study done by ***S Pudasaini et al,*** where 53.8% cases of malignancy were seen in patients over 40 years [23]. But in a study done by **Kayastha *et al*** 66.7% cases of malignancy were seen in patients over 40 years [24].

In this study 60.5% were Benign and 39.5 % were malignant, ratio of malignant tumor in our study was higher than the other studies carried out by **Jha and Karki (16.1%) [25], S Kayastha et al [10%] [24], and even studies carried out in western countries [26].**

But the histological variants of our study was consistence with all these studies where epithelial tumors were most common and among them serous and mucinous variants were prominent.

In our study the largest number of patients were Para 2. It was similar for both benign as well as malignant tumors and there was no significant association found between parity and tumor type. Findings of our study point towards the association between low parity and malignancy as all cancer patients were having low parity. Though literature quotes nulliparity or low parity as a risk factor, it is likely that the demographic profile of our population being treated in this centre has influenced the statistics of parity.

Findings of our study is comparable with the study done by **Mori M** in which, significantly higher percentage of cases were never married compared with each control group [29]. Findings of our study is also supported by a study done by ***HankinsonSE et al*** *which* says that Parous women (mean parity = 3.1) had a 45% reduction in ovarian cancer risk relative to nulliparous women **[28].**

In our study 5(7.25%) patients of benign tumor gave history of ever use of oral contraceptive in the past. A case control study done by **Riman T et al** found that ever use of oral contraceptives was reported by 31 percent of the cases and 35 percent of the controls. Compared with risk for never users, a 27 percent reduced risk of Epithelial Ovarian Cancers (EOC) appeared among ever users of oral contraceptives [29].

A study done by ***Hankinson SE*** brought out that the age-adjusted relative risk associated with ever use of oral contraceptive was 0.86. They noted a decreasing risk with increasing duration of oral contraceptive use *(P* for trend = 0.04); women who used oral contraceptive for 5 or more years had a significant 38% reduction in risk relative to nonusers. patients with malignant tumor had ever used oral contraceptive pills [28].

In our study the mean age of menarche was 11.5 years. There was no variation in age of menarche between benign and malignant tumor patients. Mode age for all patients as well as individually for benign and malignant was 11 years. Our study findings were similar study done by **Riman T et al** [29], **Sarwar CMS et al** [19]

In our study, CA125 level in patients with malignant tumors was more than 35 IU/ml in 93.33 **%** patients with mean value of 921.76 IU/ml. Mean CEA level in patients with malignant tumors was moderately elevated 9.45 IU/ml, and was significantly associated with malignant tumors. Findings of our study can be compared with **Sarwar CMS et al** [19].

In our study 91.1 % patients were in stage III or IV at the time of admission for treatment. This might be because of lack of specific symptoms and delay in diagnosis of ovarian tumors which are similar to the study done **by Basu P et al** [30].

In our study 96 % of benign tumors were managed with oophorectomy and 4% patients were managed with cystectomy. Primary cytoreduction was done in 37.8% malignant tumors and interval cytoreduction was done in 57.8 % patients. Adjuvant chemotherapy was administered in 91.1% of patients with malignant tumors and 64.4 % patients were given NACT in the form of Paclitaxel and carboplatin (3-6 cycles). 57.8 % of malignant tumors were treated with primary cytoreduction, this finding was higher than the study done by **Basu P et al [30].**

Reference:

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005 Mar-Apr;55(2):74-108.
2. Rock, John A.; Jones, Howard W. Te Linde's Operative Gynecology. 10th ed. Philadelphia: Lippincott Williams & Wilkins, 2008.
3. Scully RE, Young RH, Clement PB. Tumors of the ovary, gonads, fallopian tube, and broad ligament. In: Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology, 1998; Fascicle 23, 3rd series.
4. Two- year report of the Population Based Cancer Registries 2004-2005. National Cancer Registry Program (ICMR), Bangalore, 2008.
5. Berek JS, Natarajan S, Ovarian and Fallopian Tube Cancer. In: Berek, Jonathan S. Berek & Novak's Gynaecology. 14th ed, Philadelphia: Lippincott Williams & Wilkins, 2007; 14: 1459-1503.
6. Kimberly B.; Szymanski, Linda M.; Fox, Harold E.; Wallach, Edward E. Johns Hopkins Manual of Gynaecology and Obstetrics. 3rd ed. Maryland: Lippincott Williams & Wilkins; 2007: 508-525.
7. Berek JS, Hacker NF. Practical gynecologic oncology, 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2005:443-541.
8. Seidman JD, Kurman RJ. Subclassification of serous borderline tumors of the ovary into benign and malignant types: a clinicopathologic study of 65 advanced stage cases. Am J Surg Pathol, 1996; 20:1331-1345.
9. Pecorelli S, Odicino F, Maisonneuve P, et al. Carcinoma of the ovary. Annual report on the results of treatment of gynaecological cancer, vol. 23. International Federation of Gynecology and Obstetrics. J Epidemiol Biostat 1998; 3: 75-102.
10. Kerlikowske K, Brown JS, Grady DG. Should women with familial ovarian cancer undergo prophylactic oophorectomy? Obstet Gynecol 1992; 80. (4):700-707.
11. Franceschi S, Parazzini F, Negri E, et al. Pooled analysis of three European case-control studies of epithelial ovarian cancer: III. Oral contraceptive uses. Int J Cancer 1991; 49:61-65.
12. Surveillance, Epidemiology, and End Results (SEER) program. Available at: http://www.seer.cancer.gov. SEER Stat Database, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, April 2005.
13. Genetic risk and screening techniques for epithelial ovarian cancer. ACOG Committee Opinion 117. Washington, DC: American College of Obstetricians and Gynecologists, 1992.
14. Polverino G, Parazzini F, Stellato G, et al. Survival and prognostic factors of women with advanced ovarian cancer and complete response after carboplatin-paclitaxel chemotherapy. Gynecol Oncol 2005; 99:343-347.)
15. Williams SD, Birch R, Einhorn LH, Irwin L, Greco FA, Loehrer PJ, Treatment of disseminated germ-cell tumors with cisplatin, bleomycin, and either vinblastine or etoposide. N Engl J Med. 1987 Jun 4; 316 (23):1435-40.
16. Williams SD, Blessing JA, Hatch K, Homesley HD. Chemotherapy of advanced ovarian dysgerminoma: trials of the Gynecologic Oncology Group. J Clin Oncol, 1991; 9:1950-1955.
17. Deshpande S, Badjatiya P. A study of ovarian enlargements in adolescent girls. J Obstet Gynaecol India 1983; 33: 812-16.
18. Di Bonito L, Patriarca S, Delendim K et al. Ovarian tumour: anatomohistopathological contribution to their interpretation. Eur J Gynaecol Oncol 1988; 9: 324-30.
19. Sarwar CMS, Siddiqui N, Khokhar RN, Badar F. Epithelial ovarian cancer at a cancer hospital in a developing country. Asian Pacific J Cancer Prevention, 2006; 7: 595-598.
20. Rosemary Yancik, Ovarian cancer: Age contrasts in incidence, histology, disease stage at diagnosis, and mortality, Cancer.1993:71; 517-523.
21. Donnelly DW, Gavin AT and Comber H. Cancer in Ireland: A summary report. Northern Ireland Cancer Registry/National Cancer Registry, Ireland; 2009.
22. Bhattacharya MM, Shinde SD, Purandare VN. A clinicopathological analysis of 270 ovarian tumors. J Postgrad Med 1980; 26: 103.
23. Pudasaini S, Lakhey M, Hirachand S, Akhter J, Thapa B. A study of ovarian cyst in a tertiary hospital of Kathmandu valley. Nepal Med Coll J 2011; 13(1): 39-41.
24. S Kayastha, Study of ovarian tumours in Nepal Medical College Teaching Hospital: Nepal Med Coll J 2009; 11(3): 200-202.
25. R Jha and S Karki, Histological pattern of ovarian tumors and their age distribution, Nepal Med Coll J 2008; 10(2): 81-85.
26. Koonings PP, Campbell K, Mishell DR Jr, Grimes DA.Relative frequency of primary ovarian neoplasms: a10 year review. Obstet Gynaecol 1989; 74: 921-26.
27. Mori M, Kiyosawa H, Miyake H. Case-control study of ovarian cancer in Japan. Cancer 1984; 53: 2746–52.
28. Hankinson SE, Colditz GA, Hunter DJ, Willett WC, Stampfer MJ, Rosner B, Hennekens CH, Speizer FE, A prospective study of reproductive factors and risk of epithelial ovarian cancer.Cancer., Cancer. 1995 Jul 15;76 (2):284-90.)
29. Riman T, Dickman PW, Nilsson S, et al.: Risk factors for invasive epithelial ovarian cancer: result from a Swedish case-control study. Am J Epidemiol 2002, 156: 363-373.
30. Basu P, De P, Mandal S, Ray K, Biswas J: Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, eastern India; Indian Journal of Cancer, Vol. 46, No. 1, January-March, 2009, pp. 28-33.