Original Research Article

Clinicopathological Features of Ovarian Tumours- A Prospective Observational Study

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Abstract: Information from developing countries regarding clinicopathological features for ovarian tumours is lacking. Influence of menarche, menopause, nulliparity, mean age of presentation and type of tumour needs to be identified. This will help develop an analysis for clinicopathological features of ovarian tumour. This was a prospective observational study conducted from 1 January 2014 to 31 August 2015 at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum which included 119 patients satisfying the inclusion criteria. Incidence of ovarian tumour and clinicopathological features of ovarian tumours was studied. Percentage distribution of clinical and pathological features of ovarian tumours was studied. The incidence of ovarian tumours at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre from 1 January 2014 to 31 August 2015 was found to be 6.9% of all gynaecological admissions. In a study of 119 women 92.43% of women presented with pain per abdomen, 83% of women were multiparous. Only 17.64% of women were post menopausal. Amongst 101 patients whose HPR was available, 14 patients had malignant lesions on HPR. The commonest benign lesion was serous cystadenoma followed by simple cyst and the commonest malignant lesion being papillary adenocarcinoma. The sensitivity and specificity of CA 125 in detecting malignant lesions among 70 patients was 70% and 85% respectively. The sensitivity and specificity of RMI in comparison to HPR in 68 patients was found to be 66.6% and 94.64% respectively. Thus, it is concluded that on morphological grounds, tumours originating from surface epithelium are the commonest variant and various modalities will help in early detection of malignant lesions of ovary thereby, reducing the mortality rates.
Keywords: Ovarian Tumour, Benign ovarian tumour, malignant ovarian tumour, Borderline ovarian tumour, Sensitivity, Specificity

INTRODUCTION

Ovarian tumours frequently present as adnexal masses and are frequent reasons for referral to Gynaecologist. Information from developing countries regarding clinicopathological features for ovarian tumours is lacking. The influence of mean age of presentation, parity, menopause, type of tumour needs to be studied [53]. This will help develop a analysis for clinicopathological features of ovarian tumour. This encouraged us to conduct the present study at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Ovarian tumours are common form of neoplasia in women. Ovarian tumours constitute 3% to 4% of all Gynaecological admission [59]. Ovarian tumours account for about 30% of female genital cancers. Asian countries have rate of 2 to 6 new cases per 1, 00,000 women per year.[57] Benign ovarian cysts are the commonest constituting about 90% of ovarian tumours. Gynecologists receive the major load due to ovarian lesion not only because of anatomical location but also since these tumours may remain unnoticed for long period of time[57]. Amongst benign tumours, 60% of them are epithelial in origin. Among benign epithelial tumour, serous cystadenoma are most common (30%), occurring most commonly in reproductive age group [60]. They are bilateral in 10% of cases. Benign or mature cystic teratoma is the most common germ cell tumour, filled with thick sebaceous material. They account for 40% of all ovarian tumours. Mostly benign ovarian tumours are asymptomatic. If symptomatic present with dull aching pain may be acute severe pain in torsion, rupture, haemorrhage, infection [3]. They may present with menstrual disturbances in hormone secreting tumour like granulosa cell tumour.

Borderline ovarian tumours or ovarian epithelial tumours of low malignant potential were first described by Taylor in 1929 [3, 60]. Histologically, these are intermediate between truly benign neoplasms and those with invasive characteristics. They constitute 10-15% of all epithelial tumours; prevalence being 2.5 per 10, 0000 women [61]. Ovarian cancer is the leading cause of death in women with female genital cancers in developing countries. A women's lifetime risk has been estimated to be about 1 in 55, which represents an increase from the 1970 [1]. Ovarian cancer is the fifth most common cause of cancer death in women. It is the third most common Gynaecological malignancy among women in western world, hence is the most lethal. . Epithelial ovarian cancer is the eight most common cancer in women, and uterine (corpus and endometrial) is fourth. The ovaries are the ninth most common site of cancer in women. So, to know the incidence of ovarian tumour at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre and to study the clinicopathological features of ovarian tumours, the present study was planned.

MATERIAL AND METHOD

Information was gathered from patients with ovarian tumours during interview regarding clinicopathological features of ovarian tumours which included demographic features, menstrual and reproductive history, clinical features, and pathological features. Investigations like USG, tumour markers, CT/ MRI were performed. After the enrolment demographic data, reproductive, obstetric history was obtained. These findings were recorded on a pre designed proforma.

Early menarche is defined as age <11 years at the onset .Late menopause is defined as >51 years of age.

All patients admitted with ovarian tumour at KLE's Dr. Prabhakar Kore Charitable hospital and MRC, Belgaum from 1st January 2014 to 31st August 2015 which fulfilled the inclusion criteria i.e. all patients with our ovarian tumour attending OPD and admitted with the same at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. All patients given neoadjuvant chemotherapy were also included. Exclusion criteria included ovarian metastasis from any other malignancy and Recurrence of ovarian tumour. Women fulfilling the selection criteria were explained about the nature of study and a written informed consent was obtained prior to enrolment. The ethical clearance was obtained from the Institutional ethics committee, Jawaharlal Nehru Medical College, Belgaum. **:** The percentage distribution of clinical features and pathologic features of ovarian tumours was found. Categorical outcomes were summarized as rates and numerical outcomes as mean.

RESULTS

A total of 119 cases were studied from 1 January 2014 to 31 August 2015. The data obtained was coded and entered into master chart. The incidence of ovarian tumours was 6.9% of all Gynaecological admissions at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.
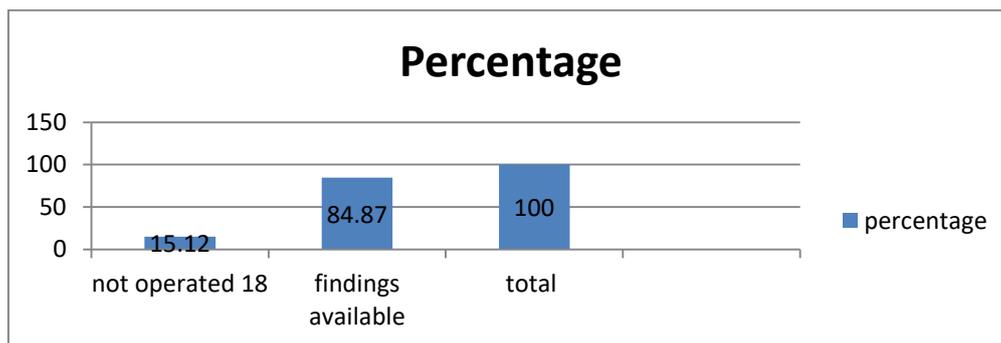

Fig 1: Total no. of cases

In the present study of 119 women, 18 were not operated and in the remaining 101 the histopathological reports were available.
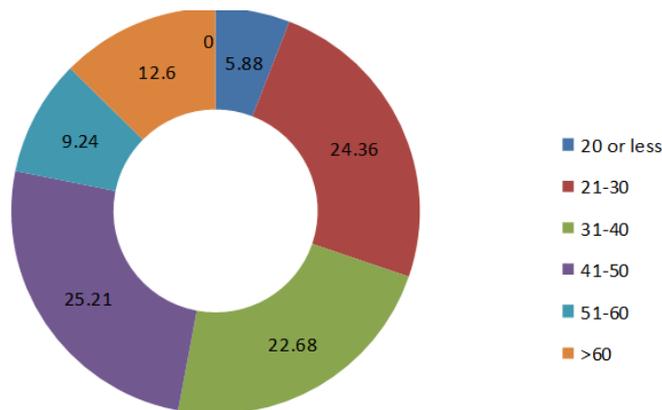
Fig 2: Age Distribution

In the present study 25.21%(30) of the women were in age group of 41 to 50 yrs and 24.36% (29) of the women were in 21 to 30 yrs, 22.68% (27) of women were in 30-40 years, 12.6% (15) women in >60 years age group. The mean age of the study population was 40.60 yrs.
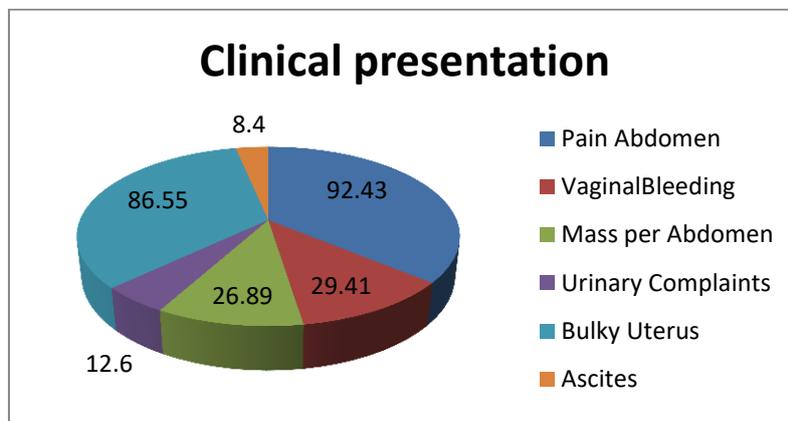

Fig 3: Clinical presentation

In the study of 119 women 92.43% (110) of women presents with complaint of pain per abdomen and vaginal bleeding present in 29.41% (35) of women .Amongst signs 86.55% (103) of women had bulky uterus while ascites was present in 8.40% (10). In the present study 83.19% of women were multiparous while 10.08% were primiparous while 6.72% of women were multigravida. In the present study 82.35 % of women were pre menopausal while only 17.64% of women were post menopausal.
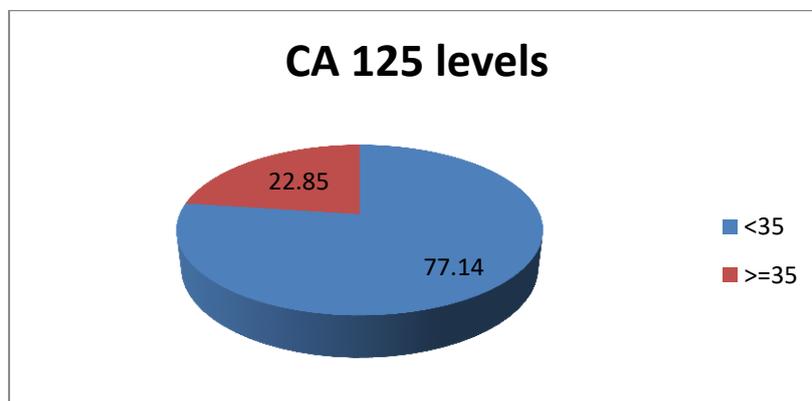

Fig 4: CA 125 Levels

In this study of the total 70 women who had CA 125 value, 77.14% (54) of women had serum CA 125 levels of <35 IU/ml while 22.85% (16) of women had serum CA 125levels>=35IU/ml.

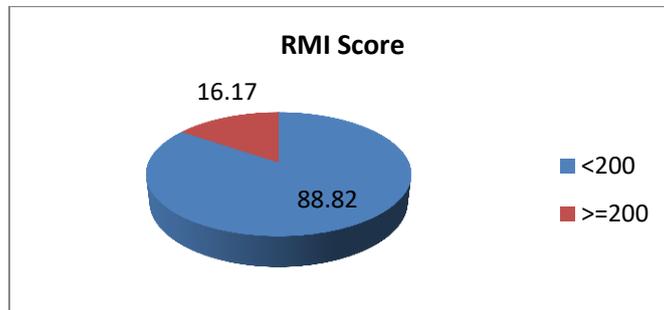**Fig 5: RMI Score**

In this study, RMI Score was available in 68 women amongst which RMI Score was found to be < 200 in 83.82% (57) of women and in 16.17 % (11) of women it was>200. In the present study the histopathological reports showed benign lesions in 86.13% (87) of women while in 13.86% (14) of the women malignant lesions were noted. In the present study, commonest malignant lesion was found to be serous papillary adenocarcinoma 50% (07) followed by endometrioid carcinoma and granulosa cell tumour 14.28% (02) each. In the present study, the commonest benign lesion was found to be serous cystadenoma 35.63% (31) followed by simple cyst and mucinous cystadenoma 17.24% (15) each out of the total 87 patients who had histopathological report showing benign lesions.

Table 1 Malignant ovarian tumour

Malignant	Number(n=14)	Percentage
Granulosa tumour	02	14.28
Serous cystadenocarcinoma	01	07.14
Endometrioid carcinoma	02	14.28
Papillary adenocarcinoma	06	42.85
Mucinous papillary cystadenocarcinoma	01	07.14
Dysgerminoma	01	07.14
Yolk sac tumour	01	07.14
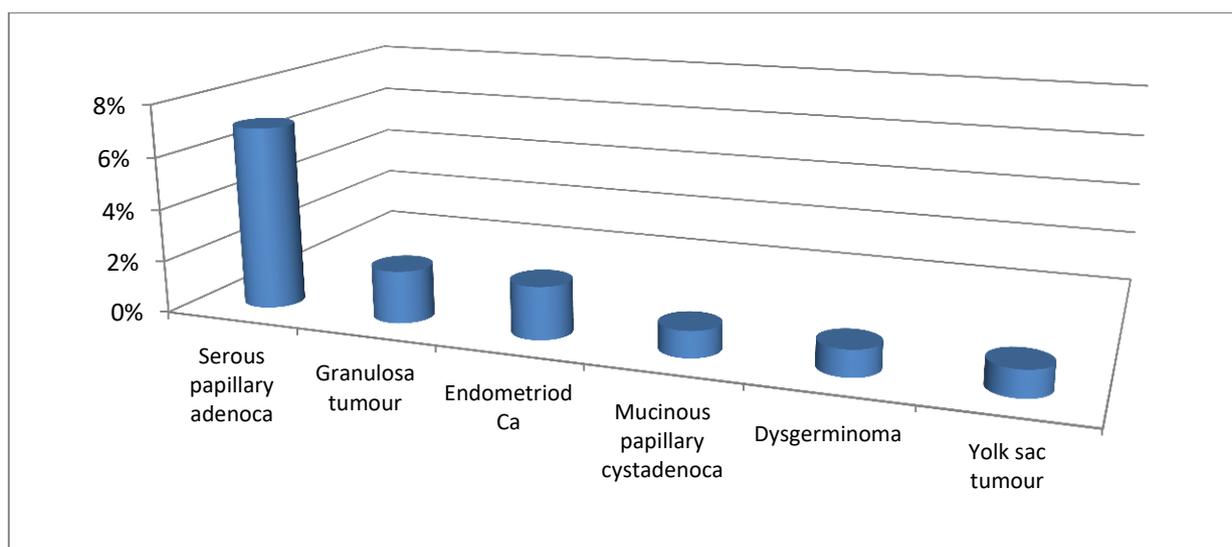
Fig 6: Malignant ovarian tumours

Table 2: Benign ovarian tumour

| Benign	Number	Percentage
Mucinous cystadenoma	12	13.79
Papillary mucinous cystadenoma	03	03.44
Serous cyst	13	14.94
Simple cyst	15	17.24
Serous cystadenoma	16	18.39
Papillary serous cystadenoma	02	02.29
Fibroma	01	01.14
Haemorrhagic cyst	11	12.64
Corpus luteal cyst	03	03.44
Para ovarian cyst	02	02.29
Benign cystic lesion	04	04.59
Follicular cyst	02	02.29
Benign cystic teratoma	03	03.44
Total	87	100.00
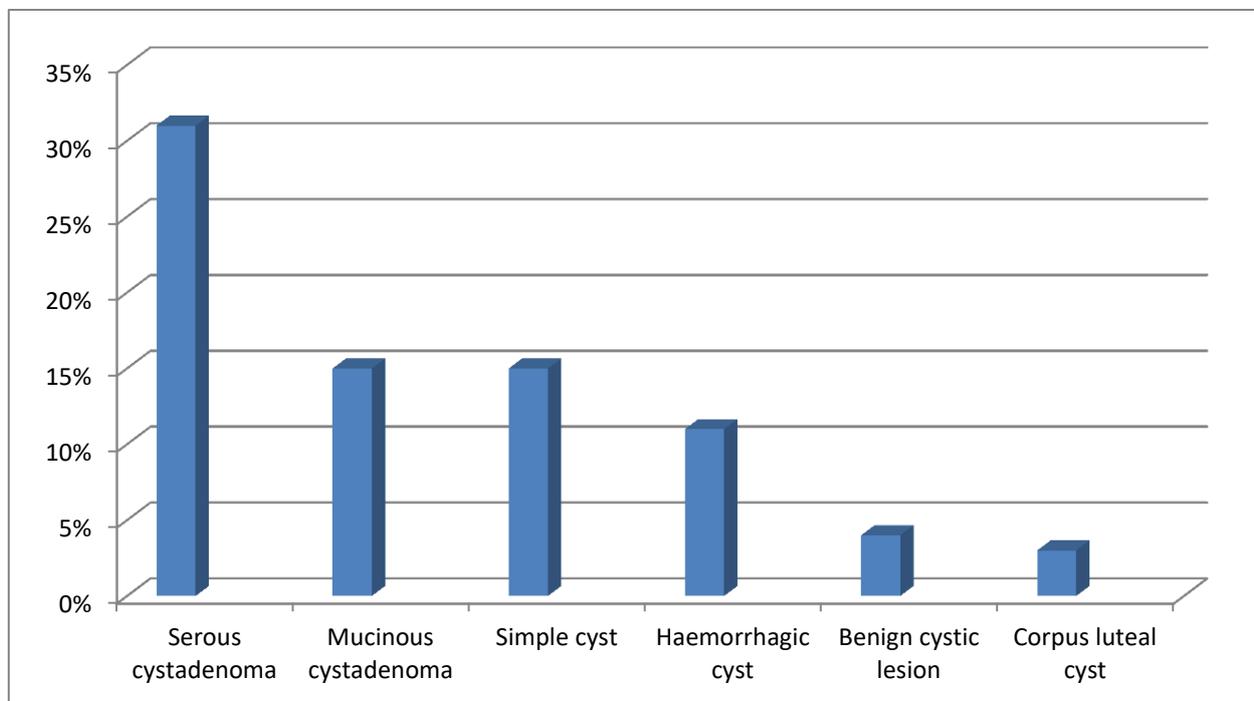
Fig 7: Benign ovarian tumours

Table 3: Accuracy of CA 125 (IU/ml) in comparison to histopathology

HPR	CA 125 >=35	CA 125 <35	Total(n=70)
Malignant	07	03	10
Benign	09	51	60
Total	16	54	70

Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
70	85	43.75	94.44

$P<0.001$

Table-4: Accuracy of RMI index in comparision to histopathology

RMI index	Malignant	Benign	Total(n=68)
>=200	08	03	11
<200	04	53	57
Total	12	56	68
P<0.001			
Sensitivity (%)	Specificity (%)	PPV (%)	NPW (%)
66.6	94.64	72.72	92.98

Table-5: Comparison of ovarian crescent sign with histopathological report

Ovarian crescent sign	Malignant	Benign	Total(n=68)
Malignant	01	39	40
Benign	08	20	28

P=0.002

In the present study amongst the total 21 women who had menopausal status only 2 women had shown malignant lesions on histopathological examination, while 19 of the women had benign lesions on histopathological examination. In this study, 70 women who had CA 125 levels were compared with the histopathological reports, amongst10 women who had malignant lesion on histopathological examination 07 women had CA 125 >= 35IU/ml while 03 women had CA 125 < 35IU/ml. Amongst 60 women who had benign lesions on histopathological examination CA 125 >= 35 IU/ml was found in 09 women only while rest 51 women had CA 125 < 35 IU/ml. In the present study 68 women in whom RMI index was calculated were compared with histopathological report, it was found that out of the 12 malignant lesions on histopathology, 8 had RMI Score>=200 while 4 women had RMI <200. Amongst 56 women who had benign lesions on histopathological report, 03 women had RMI >= 200 while 53 women had RMI < 200. The sensitivity and specificity of RMI in predicting malignant lesions as compared to histopathological report was 66.6% and 94.64% respectively.

In the study it was found that amongst 68 women, in whom ovarian crescent sign was studied 1 women had presence of ovarian crescent sign was found to have malignant lesion on HPR. Amongst 09 women who had malignant lesion on HPR, ovarian crescent sign was absent in 08 women while it was present in 01 woman only. This is in agreement with the literature which states that ovarian crescent sign is usually absent in malignant lesion. Amongst 59 women who had benign lesion on histopathological report, ovarian crescent sign was present in 39 women and was absent in 20 women.

DISCUSSION

A pelvic mass is one of the most frequent indications for referral to Gynaecologists. Diagnosis of ovarian tumours can be difficult due to variety of pathological conditions that can affect the ovaries and present with similar clinical manifestations. Knowledge of morphology and age specific characteristics can help refine the diagnosis. Our hospital is a tertiary care hospital where patients are referred from the adjoining and far flung areas. As it is a charitable hospital, a variety of Gynaecological diseases including malignancies are frequently seen. Thus, the present study was aimed to know the incidence and to study the clinicopathological features of ovarian tumours at KLE's Dr. Prabhakar Kore Hospital and Medical Research centre, Belgaum.

In this study of 119 women, the commonest age group was 41 to 50 years (25.21%) followed by 21 to 30 years (24.36%). The mean age was found to be 40.60 years. These results were in agreement with the findings in literature stating that, the ovarian tumours can occur at any age but their peak incidence is in the reproductive age group [3, 15]. However, it was interesting to note very low frequency of early menarche, late menopause, nulliparity and advanced age at first child birth. Most of the women were multiparous and most of them had lactated in the present study.

In the present study of 119 patients, 92.43% women presented with pain abdomen, 29.41% presented with vaginal bleeding while only 12.60% had urinary complaints. Amongst signs 86.55% of women had bulky uterus while only 8.40% of women had ascites. With regard to obstetric history, most (83.19%) of the women reported were multiparous while only 6.72% were multigravida. In the present study 83.25% of women were premenopausal while 17.64% women were postmenopausal. The serum CA 125 levels were

<35 IU/ml in 77.14% while in 22.85% of women had serum CA 125 >=35 IU/ml. According to a study it was found that CA 125 cannot adequately be characterized as a screening test due to the presence of overall low incidence of ovarian cancer in general population and the risk of false positive result [60, 63].

In the present study, the commonest benign lesion was found to be serous cystadenoma 18.39% (16) followed by simple cyst 17.24% (15), followed by serous cyst 14.94% (13) out of the total 87 patients who had histopathological report showing benign lesions. The commonest malignant lesion was found to be papillary adenocarcinoma 28.57% (04), followed by endometrioid carcinoma and granulosa tumour 14.28% (02) each. In the present study, RMI was found to be <200 in 83.82% of women and in 16.17% of women it was >200. The sensitivity and specificity of RMI index in detecting malignant lesions is 66.6% and 94.64% respectively. The data available from this study can help us in recognizing the pattern of ovarian tumours prevalent. Whether malignant tumours arise de novo or the benign tumour transforms into malignant is the subject of ongoing research and debate. Therefore, based on the results of this study it is evident that early diagnosis is crucial to help in decreasing morbidity and mortality among these patients.

REFERENCES

1. Piver MS. Prophylactic oophorectomy: reducing the US death rate from epithelial ovarian cancer. A continuing debate. The oncologist. 1996 Oct 1; 1(5):326-30.
2. E mal A, Murray T, Ward et al(2005). Cancer statistics, 2005. CA: A Cancer Journal for Clinicians, 55, 10-30.
3. Berek & Novak's Textbook of Gynaecology (14 edition).
4. Andersen ES, Knudsen A, Rix P, Johansen B. Risk of malignancy index in the preoperative evaluation of patients with adnexal masses. Gynecologic oncology. 2003 Jul 31; 90(1):109-12.
5. Morgante G, Marca A, Ditto A, Leo V. Comparison of two malignancy risk indices based on serum CA125, ultrasound score and menopausal status in the diagnosis of ovarian masses. BJOG: An International Journal of Obstetrics & Gynaecology. 1999 Jun 1; 106(6):524-7.
6. Leelahakorn S, Tangjitgamol S, Manusirivithaya S, Thongsuksai P, Jaroenchainon P, Jivangkul C. Comparison of ultrasound score, CA125, menopausal status, and risk of malignancy index in differentiating between benign and borderline or malignant ovarian tumors. Journal-Medical Association Of Thailand. 2005 Oct 28; 88:S22.
7. Benjapibal M, Neungton C. Pre-operative prediction of serum CA125 level in women with ovarian masses. Medical journal of the Medical Association of Thailand. 2007 Oct 1; 90(10):1986.
8. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. BJOG: An International Journal of Obstetrics & Gynaecology. 1990 Oct 1; 97(10):922-9.
9. Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, Kiserud T, Halvorsen T, Nustad K. Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. BJOG: An International Journal of Obstetrics & Gynaecology. 1996 Aug 1; 103(8):826-31.
10. Uma Devi K. Current status of gynecological cancer care in India. Journal of Gynecologic Oncology. 2009 Jun 1; 20(2):77-80.
11. Young RH. A brief history of the pathology of gonads –A review.Mod Pathol 2005; 18: 3-17
12. David J, Ashely B. Evans histopathological appearance of tumours. 4th Ed. New York: Churchill Livingstone Pvt> Ltd; 1990.
13. Parker D, Bradley C, Bogle SM, Lay J, Masood M, Hancock AK, Naylor B, Price JJ. Serum albumin and CA125 are powerful predictors of survival in epithelial ovarian cancer. BJOG: An International Journal of Obstetrics & Gynaecology. 1994 Oct 1; 101(10):888-93.
14. Hellström I, Raycraft J, Hayden-Ledbetter M, Ledbetter JA, Schummer M, McIntosh M, Drescher C, Urban N, Hellström KE. The HE4 (WFDC2) protein is a biomarker for ovarian carcinoma. Cancer research. 2003 Jul 1; 63(13):3695-700.
15. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ. Cancer statistics, 2005. CA: a cancer journal for clinicians. 2005 Jan 1; 55(1):10-30.
16. Sharma JB, Gulati N. Gynecological disorders in geriatric age group. J Obstet Gynecol India. 1990; 40:459-63.
17. Maheshwari V. Surface epithelial tumours of ovary. Ind J Pathol Microbiol 1994; 37: 75-85.
18. Ramachandran G, Harilal KR, Chinnamma KK, Thangavelu H. Ovarian neoplasms—a study of 903 cases. J Obstet Gynecol India. 1972; 22:309-15.
19. Sikdar K, Kumar P, Roychowdhary NN. A study of ovarian malignancy: A review of 149 cases. J Obstet Gynaecol India. 1981;30:478-80.
20. Serov SF, Scully RE, Sobin LH. Histological typing of ovarian tumours.

21. Fox H, Wells M. Haines and Taylor. Obstetrical and gynaecological pathology. 5th ed. Edinburgh: Churchill Livingstone. 2003.
22. Gupta SC, Singh PA, Mehrotra TN, Agarwal R. A clinicopathological study of ovarian tumours. Indian J Pathol Microbiol 1986; 29: 354-62.
23. Maheshwari V, Tyagi SP, Saxena K, Tyagi N, Sharma R, Aziz M, Hameed F. Surface epithelial tumours of the ovary. Indian journal of pathology & microbiology. 1994 Jan; 37(1):75-85.
24. Aure JC, Hoegk S, Kolsad H. Clinical and histological studies of ovarian carcinoma- A long term follow up of 990 cases. Am J Obstet Gynecol 1973; 37: 109-13.
25. Sampson JA . The endometroid carcinoma of the ovary. Arch surg 1920; 1: 10-15.
26. Roth LM, Dallenbach-Hellweg G, Czernobilsky B. Ovarian Brenner tumors. I. Metaplastic, proliferating, and of low malignant potential. Cancer. 1985 Aug 1; 56(3):582-91.
27. Calondex C, Loffer J. Tumors of the female genital tract. diagnostic histopathology of tumours. Vol 1, 2nd Edition, Philadelphia: Churchill Livingstone Pvt. Ltd; 2000.
28. Young RH, Scully RE. Ovarian sex cord-stromal tumors: recent progress. International Journal of Gynecological Pathology. 1982 Jan 1; 1(1):101.
29. Evans III AT, Gaffey TA, Malikasian Jr GD, Annegers JF. Clinicopathologic review of 118 granulosa and 82 theca cell tumors. Obstetrics & Gynecology. 1980 Feb 1; 55(2):231-8.
30. Young RH, Scully RE. Well-differentiated ovarian Sertoli-Leydig cell tumors: a clinicopathological analysis of 23 cases. International journal of gynecological pathology. 1984 Mar 1; 3(3):277-90.
31. Saxena H, Gupta S. Malignancies of the ovary. J. obset Gynecol India. 1978; 28:271-8.
32. Chenot J. Dysgerminoma. J Obstet Gynecol Br Emp 1950; 19: 507-511.
33. Gerbie MV. Primary choriocarcinoma of the ovary. Obstet Gynecol 1975; 46: 720-8.
34. Kumar V, Abbas AK, Fausto N, Robbins< Cartan. Pathologic basis of disease. 17th Edition, Philadelphia: Elsevier Pvt. Ltd. 2004.
35. Bast Jr RC, Klug TL, John ES, Jenison E, Niloff JM, Lazarus H, Berkowitz RS, Leavitt T, Griffiths CT, Parker L, Zurawski Jr VR. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. New England Journal of Medicine. 1983 Oct 13; 309(15):883-7.
36. Herbst AL. The epidemiology of ovarian carcinoma and the current status of tumor markers to detect disease. American journal of obstetrics and gynecology. 1994 Apr 30; 170(4):1099-107.
37. Woolas RP, Xu FJ, Jacabs IJ, Yu YH, Daly L, Brechuck A, Soper JT, Clarke-Pearson DL, Oram DH, Bast RC. Elevation of multiple serum markers in patients with stage I ovarian cancer. Journal of the National Cancer Institute. 1993 Nov 3; 85(21):1748-51.
38. Jacobs I, Bridges J, Reynolds C, Stabile I, Kemsley P, Grudzinskas J, Oram D. Multimodal approach to screening for ovarian cancer. The Lancet. 1988 Feb 6; 331(8580):268-71.
39. Sheiko MC, Hart WR. Ovarian germinoma (dysgerminoma) with elevated serum lactic dehydrogenase: Case report and review of literature. Cancer. 1982 Mar 1;49(5):994-8.
40. Chervnak FA, Issacson GC, Campbell S. Gynecological Malignancy. In: Morley P, Hollman AS (eds). Ultrasound in Obstetrics and gynaecology. 1st Ed. 1993: 1746-59.
41. Sanders RC, James AE. The principles and practice of ultrasonography in obstetrics and gynecology.
42. Lawson TL, Albarelli JN. Diagnosis of gynecologic pelvic masses by gray scale ultrasonography: analysis of specificity and accuracy. American Journal of Roentgenology. 1977 Jun 1; 128(6):1003-6.
43. Callen PW. Ovarian Sonography. In: Dillmacky MJ, Atri M (eds) Ultrasonography in Obstertics and Gynaecology. W B Saunders Company, 4th Ed. 2000: 857-90.
44. Kurjak A. Adnexal Tumours. In: Kurjak A, Jalud I (eds). An Atlas of Ultrasonography in Obstertics and Gynaecology. CBS publishers, 1st Edition, 1995: 171-85.
45. Outwater EK, Siegelman ES, Hunt JL. Ovarian Teratomas: Tumor Types and Imaging Characteristics 1. Radiographics. 2001 Mar; 21(2):475-90.
46. Sisler CL, Siegel MJ. Ovarian teratomas: a comparison of the sonographic appearance in prepubertal and postpubertal girls. AJR. American journal of roentgenology. 1990 Jan; 154(1):139-41.
47. Quinn SF, Erickson S, Black WC. Cystic ovarian teratomas: the sonographic appearance of the dermoid plug. Radiology. 1985 May; 155(2):477-8.
48. Patel MD, Feldstein VA, Lipson SD, Chen DC, Filly RA. Cystic teratomas of the ovary: diagnostic value of sonography. AJR. American journal of roentgenology. 1998 Oct; 171(4):1061-5.
49. Sheth S, Fishman EK, Buck JL, Hamper UM, Sanders RC. The variable sonographic appearances of ovarian teratomas: correlation with CT. American Journal of Roentgenology. 2012 Nov 23.
50. Patel MD, Feldstein VA, Lipson SD, Chen DC, Filly RA. Cystic teratomas of the ovary: diagnostic value of sonography. AJR. American journal of roentgenology. 1998 Oct; 171(4):1061-5.

51. JacobsI, OramD, FairbanksJ, TurnerJ, FrostC, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol 1990;97:922-9.

52. Mol BW, Boll D, De Kanter M, Heintz AP, Sijmons EA, Oei SG, Bal H, Brölmann HA. Distinguishing the benign and malignant adnexal mass: an external validation of prognostic models. Gynecologic oncology. 2001 Feb 1; 80(2):162-7.

53. Malik I. A. National cancer institute; Article: A prospective study of clinicopathological features of epithelial ovarian cancer in Pakistan. J. Pak Med Assoc. 2002 Apr, 52(4): 155-8

54. Rubin SC, Benjamin I, Behbakht K, Takahashi H, Morgan MA, LiVolsi VA, Berchuck A, Muto MG, Garber JE, Weber BL, Lynch HT. Clinical and pathological features of ovarian cancer in women with germ-line mutations of BRCA1. New England Journal of Medicine. 1996 Nov 7; 335(19):1413-6.

55. Danforth K N, Tworoger S S, Hecht J H, Rosner B A; Article: A prospective study of post-menopausal hormone use and ovarian cancer risk Br J Cancer 2007 January 15; 96(1): 151-156.

56. Wasim Tayyiba, Siddiq Saqib department of community medicine Allama Iqbal medical college Lahore; Article: Comparison of clinical presentation of benign and malignant ovarian tumours J Pak Med Assoc. 2009 Jan; 59(1): 18-21

57. Swamy G G, Satyanarayan N, Andhra Pradesh; Article: Clinicopathological analysis of ovarian tumours –a study on five year samples. Nepal Med Coll J. 2010 Dec; 12(4): 221-3

58. Ashraf Ammeena, Shaikh Saeed A., Ishfaq Ayesha, Akrum Abdullah, Kamal Furrakh, Ahmad Nazeefa Fatima medical college; Article: The frequency and histopathological Vol.28 (Jan. –Jun.2012)

59. Dutta Textbook of Gynaecology, 6th edition.

60. Seshadri Laxmi Essentials of Gynaecology, 1st edition

61. Priya C, Kumar S, Kumar L. Borderline ovarian tumours: An update. Indian Journal of Medical and Paediatric Oncology. 2008 Apr 1; 29(2):19.

62. Jeffcoate's Principles of Gynaecology, 8th edition

63. Kalghatgi-Kulkarni K, Kushtagi P. Ovarian crescent sign and sonomorphological indices in preoperative determination of malignancy in adnexal masses. Indian journal of medical sciences. 2008 Dec 1; 62(12):477.

64. Sohail I, Hayat Z, Saeed S. A comparative analysis of frequency and patterns of ovarian tumours at a tertiary care hospital between two different study periods (2002-2009). Journal of Postgraduate Medical Institute (Peshawar-Pakistan). 2012 Mar 23; 26(2).

65. Yamamoto Y, Yamada R, Oguri H, Maeda N, Fukaya T. Comparison of four malignancy risk indices in the preoperative evaluation of patients with pelvic masses. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2009 Jun 30; 144(2):163-7.