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A CLINICOPATHOLOGICAL ANALYSIS OF OVARIAN TUMOURS

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ABSTRACT

We performed a retrospective analysis of patients with ovarian tumors who were admitted to the Aga Khan University Hospital from January 1985 to December 1989. Sixty one cases were reviewed. Mean age of the whole group was 44 years. Majority of the patients presented with abdominal pain and distention. Most frequent physical finding was a palpable mass on pelvic or abdominal examination. Overall these patients had a higher incidence of breast cancer than expected in the general population. Two-thirds of the tumors were malignant. Comparison of the patients with malignancy against those with benign tumors failed to show any correlation with parity. Majority of the patients with malignant disease were above forty and had ultrasound showing a cystic mass over 10 cms in size. Cancer was mostly epithelial in origin, with widespread disease (stage Ill or IV) at the time of presentation. Benign tumors, mostly of germ cell type, were predominantly seen in patients under the age of forty with ultrasound showing cystic mass of any size from under 5 cms to over 10 cms (JPMA 41:161, 1991).

INTRODUCTION

Ovarian cancer is the second most common gynaecologic cancer yet the commonest cause of gynaecologic cancer deaths. The main reason for this poor outcome is the inability to diagnose the disease early. Hence, majority of the patients present with late stage disease. Early manifestations of ovarian carcinoma are vague and non-specific with patients complaining of lower abdominal discomfort, dyspepsia, indigestion and other mild lower gastrointestinal disturbances. Abdominal pain, swelling or a large palpable mass, when present, signify advanced stages of the disease. Western studies indicate that most cases are seen in the sixth decade with a mean age of 59.5 years. Risk factors associated with development of ovarian cancer include nulliparity or low parity, early menarche, ovarian dysgenesis, environmental exposure to asbestos and talc, and high fat intake. Women with breast cancer have twice the expected risk of developing subsequent ovarian carcinoma. On the other hand, women with ovarian cancer have a three fold to four fold increase in the frequency of subsequent breast cancer. Oral contraceptives may be protective. Similar statistics have not been reported for ovarian cancer in Pakistan. We retrospectively analysed sixty one cases of ovarian tumors who were admitted to the Aga Khan University Hospital between January 1985 to December 1989.

MATERIALS AND METHODS

Case notes of sixty one patients with ovarian tumors admitted to the Aga Khan University Hospital between January 1985 to December, i989 were reviewed. Data were obtained regarding age, risk factors, clinical manifestations, physical examination, radiologic findings, histologic analysis and staging of these patients. This information was recorded on a preset format. Age, height, weight, parity, menstrual history, past history or family history of any malignancy was recorded. Bodymass index was determined from height and weight using the following formula: Wt (kg) / Ht (m). Whenever possible, information on exposure to environmental risk factors such as talc, asbestos, irradiation or smoking was

obtained. Clinical manifestations such as abdominal discomfort or distension, vaginal bleeding or weight loss were looked for and if present, their duration was documented. Only symptoms at the time of admission were considered, those developing during the hospital course, or subsequently were not entertained. Physical findings on abdominal or pelvic examinations were recorded separately in terms of the presence or absence of a palpable mass. Fullness in one of the fornices, on bimanual examination, was also taken as a "palpable mass". The gross and microscopic morphologies, with grading of the tumors, were obtained from the histopathology reports of the specimens taken during laparotomy. Staging of the malignant tumors was based on clinical, radiologic and pathologic examinations. In some cases, classification of the tumors as stage W was ambiguous as there was no definite proof of distant metastases (such as liver biopsy or pleural cytology). Therefore, stages Ill and IV, for the purpose of this study, were grouped as one.

RESULTS

The total number of cases in this study was 61, of which 21 (34.4%) were benign and 40 (65 6%) were malignant tumors. Majority of the patients with benign tumors were between ages of 21 and 30 years (mean age 28.5 years). For malignant tumors, the mean age was 49.8 years with majority of the cases occurring between 41 and 50 (Figure1).

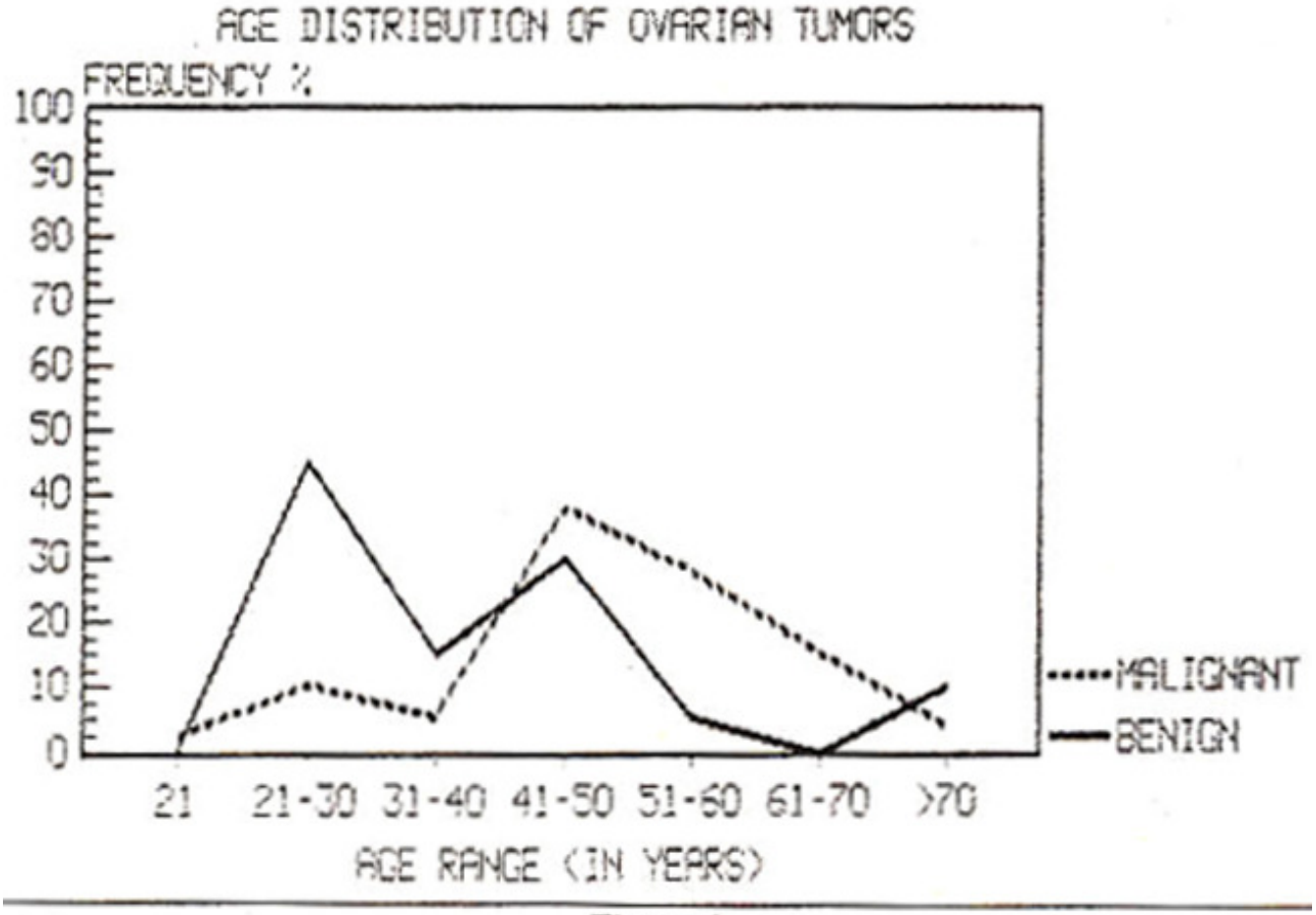

Figure 1.

The mean parity was 3.62 for benign tumors and 5.03 for malignant tumors, the overall parity being 4.44. Only 14.8% of patients were nulliparous while 57.2% had 4 or more children (Table 1).

TABLE I. Parity.

Parity	Benign	Malignant	Total
0	3 (14.3%)	5 (15.1%)	8 (14.8%)
1-3	8 (38.1%)	7 (21.2%)	15 (27.7%)
4-6	7 (33.3%)	8 (24.2%)	15 (27.7%)
7-9	1 (4.8%)	12 (36.4%)	13 (24.0%)
> 9	2 (9.5%)	1 (3.0%)	3 (5.5%)

Body mass index was 24.8 for benign and 25.2 for malignant tumors. The mean age at menarche was 14 years and 13 years for benign and malignant tumors respectively, while the mean age at menopause was 45 and 47 years, respectively. 28.6% of the patients with benign lesions were post-menopausal whereas 67.7% of the women with malignancy were post-menopausal. (Figure 2).

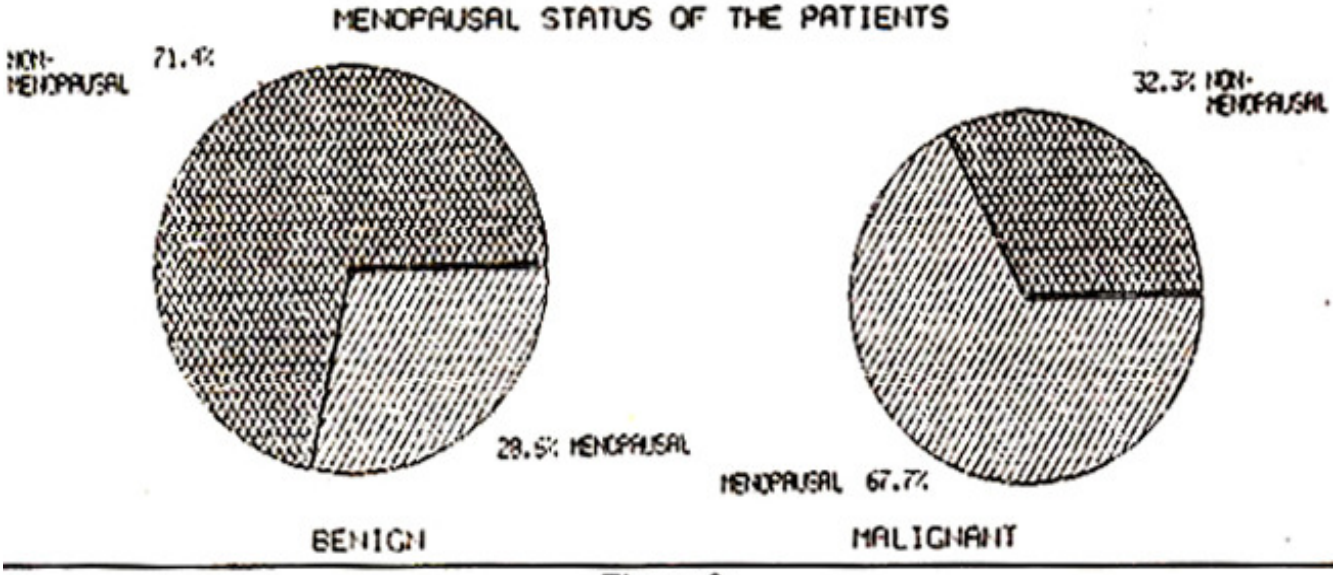

Figure 2.

Of the 61 cases reviewed 3 had had breast cancer in the past. Out of these 3, 1 had a benign ovarian tumor. Two patients with malignant tumours had a positive family history of malignant disease (ovarian and rectal carcinoma) while one women from the benign group had a first degree relative with uterine cancer. Information on exposure to risk factors such as asbestos, talc, irradiation and smoking was inconsistently recorded in case notes and hence, was disregarded. Similarly data on the use of oral contraceptives and breast feeding habits were incomplete. The most common presenting complaints were abdominal discomfort or pain, abdominal distention and weightloss. Abdominal pain was seen more frequently in malignant than benign lesions (70% versus 28%) while abdominal distention was found equally frequently in benign as well as malignant lesions (76% versus 62.5%). (Table II).

TABLE II. Clinical manifestation of ovarian tumors (in decreasing order of frequency).

Symptoms	Benign (%)	Malignant (%)	Total (%)
Abd. pain	76.0	62.5	67.2
Abd. dist.	28.0	70.0	55.7
Wt. loss	4.7	25.0	18.0
Vague abd. complaint	19.0	17.5	18.0
Menstrual irreg.	14.2	7.5	9.8
Post-meno bleed	0.0	7.5	4.9
Others*	52.3	52.5	52.4

*included anorexia, dyspepsia & constipation

Only one patient in the benign category reported weight loss whereas 10 patients (25%) with malignancy had lost weight. The percentages of benign and malignant tumors manifesting as palpable masses were 47.6 and 78.3 respectively. On pelvic examination, a mass was palpable in 73.6% of benign cases and in 88.4% of malignant cases. Before laparotomy, most of the patients had abdominal ultrasound done. Majority of the tumors, irrespective of being benign or malignant were cystic in consistency. Overall size of the tumor was unhelpful in differentiating benign from malignant lesions However, malignant tumors were less likely to be under 10 cms in size (11% vs 42.9%) (Table III).

TABLE III. Ultrasound findings.

Size	Benign	Malignant
< 5cm	14.3%	5.5%
5-10cm	28.6%	5.5%
> 10cm	57.1%	61.1%
No mass	0%	27.7%
Consistency		
Cystic	80%	80%
Solid	6.6%	5%
Mixed	13.4%	15%

Majority (73.7%) of all tumors were of epithelial origin. Germ cell tumors comprised 16.3% of total cases. Three (4.9%) tumors were of metastatic origin, two of which were from the GI tract and one from the uterine corpus (Table IV).

TABLE IV. Histopathological types.

Type	Benign No (%)	Malignant No (%)	Total No (%)
Epithelial	13 (61.9)	32 (80.0)	45 (73.7)
Germ cell	8 (38.0)	2 (5.0)	10 (16.3)
Sex cord	-	1 (2.5)	1 (1.6)
Metastatic	-	3 (7.5)	3 (4.9)
Not known	-	2 (5.0)	2 (3.2)

The most common tumor, in the less than 40 year age group, was of germ cell origin (52% of total) while in the greater than 40 age group, 95.2% of tumors were of epithelial origin (Table V).

TABLE V. Age distribution of tumors.

Age	Benign	Malignant
< 40 Years	epith = 4	epith = 4
	germ = 8	germ = 2
		met = 1
> 40 Years	epith = 9	epith = 31
	germ = 0	germ = 0
	met = 1	met = 2

Fifteen percent of all the epithelial tumors were bilateral. Of the total epithelial tumors, 57.5% were of the serous sub-type and the remaining 42.5% were mucinous. No tumors of the endodermoid clear cell or Brenner's type were seen (Table VI).

TABLE VI. Epithelial tumor types.

Type	Benign No (%)	Malignant No (%)	Total No (%)
Serous	8 (66.0)	11 (52.0)	19 (57.5)
Mucinous	4 (33.0)	10 (48.0)	14 (42.5)
Endometrioid	0	0	0
Clear Cell	0	0	0
Brenner	0	0	0

The majority of patient (80.6%) with malignancy presented in stage III and IV disease (Table VII).

TABLE VII. Tumor staging.

Stage	No of cases	% age
I	3	9.6
II	3	9.6
III & IV	25	80.6

DISCUSSION

The mean age of patients with ovarian cancer in this study was 49.8 years with most of the cases (82.5%) occurring after the age of 40. These results are different from Western studies which quote higher mean age of 59.5 years[1,3]. This might be due to the lower life expectancy in this part of the world, therefore more cases are seen in the lower age group. As expected, benign tumors occurred more frequently in the younger age groups. Nulliparity is a well documented risk factor for ovarian cancer[4-6]. Our study revealed that only 5 women out of 33 with ovarian carcinoma (15.1%) were nulliparous; similarly 14.3% (3 out of 21) of women with benign tumors were nulliparous, while over half of the women (57.2%) had four or more children. There was no difference in parity between those with benign versus malignant tumors. It is difficult to draw any conclusions from these figures as the general parity rate in our country is higher than in the western countries. Early age at menarche and menopause

are also regarded as risk factors[1,5] . The reported mean age at menarche in India is 13.5 years and 12.5 years in the U.S.A[7]. We obtained similar mean ages of 14 for benign tumors and 13 for malignant tumors. The average age at menopause in our study came out to be 45 years and 47 years for benign and malignant cases respectively. This matches age ranges quoted for India (44 to 50 years) [8]. Our data fails to show any difference of age at menarche or menopause between those with benign versus malignant tumors. Women who have breast cancer have an increased risk of developing ovarian cancer[1,4]. These carcinomas share two important risk factors; high fat intake and prolonged exposure to estrogens[9]. In our study, 2 out of 40 (5%) patients with ovarian carcinoma gave a past history of breast cancer. No significant data could be gathered on risk factors such as asbestos, talc, irradiation, smoking and oral contraceptive use. Ovarian tumors have no discrete early manifestations. They grow quickly and insidiously. By the time abdominal distention and pain are manifest, disease process is usually advanced. The most frequent physical finding is a palpable mass on pelvic or abdominal examination. We found abdominal pain to be the most frequent presenting symptom, followed by abdominal distention. The later included both gross ascites or a large mass. Very few patients presented with menstrual irregularity (9.8%). Out of all these clinical features, presence of abdominal pain was more suggestive of malignancy. Other complaints did not differ markedly between those with benign versus malignant disorder. At the time of presentation, weight loss is not a prominent feature of ovarian cancers[3], this was supported by our study. However, when present it is more suggestive of malignancy. Non-specific gastrointestinal complaints, such as anorexia, dyspepsia, constipation are early manifestations of ovarian cancer, and may precede other, more definitive symptoms by weeks or months. Ultrasound was unhelpful in differentiating between benign and malignant tumors. Lesions were mostly cystic in consistency. Although tumors of all sizes were seen in both groups, malignant tumors were less likely to be under 10 cms in size (11% vs 42.9%). The histologic distribution of ovarian tumors in our study was comparable to known data[11,12]. The bulk was formed by epithelial tumors followed by germ cell tumors. Breakdown of epithelial tumors showed that serous variety was the predominant cell type (57,7%), rest of them were of mucinous variety (42.3%) with no endometroid or clear cell type. These findings are different than the reported Western figures which quote a lower rate of mucinous (12%) and a higher rate of other cell types e.g., endometrial, undifferentiated or clear cell type. This is probably due to our small sample size. Women of younger age group i.e., < 40 years who were found to have an ovarian mass were more likely to have benign germ cell tumors (52%) in contrast to women of older age group (i.e.> 40 years) who were more likely to have epithelial malignancy (95.2%). Grading and staging of ovarian neoplasm has important prognostic implication 61.2% of our cases had grade III (poorly differentiated), 22.5% grade II and 16% grade I tumors. Hence majority had poor prognostic disease. Because of more thorough and accurate staging techniques, at present, the number of early stage cancers have decreased with more cases assigned into higher stages[3] . As many as 80.6% of our cases had stage III and W disease at the time of diagnosis. It appears that patients, here, present with higher grade and stage of disease than reported elsewhere[3,12]. We conclude that our patients with ovarian cancer are younger and have more advanced disease than reported in western literature. Abdominal pain and weight loss when present are more suggestive of malignancy. Majority (78.6%) of the patients over forty were found to have cancer, mostly epithelial in origin, while majority (63%) under the age forty have benign tumors. These findings have important epidemiologic and clinical significance.

REFERENCES

1. Silverberg, E. and Lubera,J. Cancer statistics, 1987. CA., 1987; 37:2.
2. Barber, H.R.K. Ovarian cancer; diagnosis and management. Am.). Obstet. Gynecot, 1984; 150: 910.

3. Disaia, P.G. and Creasman, W.T. Clinical gynaecologic oncology. St. Louis, Mosby, 1981.
4. Hartge, P., Schiffman, M.H., Hoover, R., et al. A case control study of epithelial ovarian cancer. Am.J. Obstet. Gynecol., 1989; 161: 10.
5. Wu, ML., Whittenmore, A.S., Paffenbarger, R.S.Jr., et al Personal and environmen tal characteristics related to epithelial ovarian cancer. Am.). EpidemioL, 1988; 128:1216.
6. Mon. M., Harabuchi, I., Miyake, H., Cassgrande, J.T., Henderson, B.E. and Ross, R.K. Reproductive, genetic and dietary risk factors for ovarian cancer. Am. J. EpidemioL 1988; 128:771.
7. Tindall, yR. Jeffcoates principles of gynaecotogy. 5th ed. London, Butterworth, 1987, p. 80.
8. Krishna. Memon, M.K., Dev, P.K., Bhasker, R.K. ed. Post-graduate Obstetrics and gynaecology. Madras. Orient Longman Ltd., 1989, 41.
9. Barber, H.R.K. Ovarian carcinoma; etiology, diagnosis and treatment. 2nd ed. New York, Masson Publishing, 1982.
10. Casagrande, J.T., Louie, E.W., Pike, MC., Roy, S., Ross, R. K. and Henderson, BE. Incessant ovulation and ovarian cancer. Lancet, 1979; 2: 170.
11. Robins, S.L and Kumar, V. Basic pathology. 4th ed. Philadelphia, Saunders, 1987, p.663.
12. Richardson, G.S., Scully, RE., Nikrui, N. and Nelson, J.H. Jr. Common epithelial cancerof the ovary. N. Engl.J. Med., 1985; 312:415.