

Incidence, Histological Types and Age at Presentation of Borderline and Malignant Ovarian Tumors at a Tertiary Institute in Nepal

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Aims: The objective of this study was to find the incidence, assess the age and stage of presentation of ovarian malignancy and correlate these features with the histological types.

Methods: Retrospective analysis of ovarian tumor cases that underwent primary surgery at our institute between April 2009 - April 2012 was done. Age, histological type, stage of the disease features were analyzed. Statistical analysis was done by Chi square and T test.

Results: Out of 451 ovarian tumor cases, 81 cases of borderline and malignant ovarian tumor were seen. Germ cell tumors were the most common type of ovarian tumors. The mean age of presentation of primary malignant tumors was 41.9 years. Serous adenocarcinoma was the most common ovarian cancer occurring in 22.2 % (n =67) cases. In women <40 years the likelihood of germ cell cancer was significantly more than non germ cell malignancies (p value <0.001). Epithelial ovarian malignancies were more likely to present at late stages than non-epithelial malignancies and this was found to be statistically significant with p value of 0.003. Increasing age was associated with increasing stage of cancer.

Conclusions: Germ cell tumors were the most common ovarian tumors, but epithelial tumors were the most common malignant ovarian tumors. Increasing age was associated with increasing stage of disease.

Keywords: epithelial; germcell; ovarian malignancy.

INTRODUCTION

The importance of ovarian cancer lies in the fact that it presents at very late stage, and therefore carries a poor prognosis. According to the Center for Disease Control about 20000 women get ovarian cancer every year. It is the eighth commonest female malignancy in the US and it causes more deaths than any other cancer of the female genital tract.¹ The Brazilian National Institute of Cancer describes epithelial ovarian cancer as a high mortality gynecological cancer.² According to the IARC Globocan 2012 data, the incidence of ovarian cancer is 3.6% behind breast, colorectal, cervix, lung, uterine and stomach cancer.¹

At Tribhuvan University Teaching Hospital based on hospital audit data, ovarian tumors are the most

common type of genital malignancy and also the most common to undergo surgery. This case series was therefore done to assess the different histopathological types of borderline and malignant ovarian cancer cases that presented to our hospital and correlate them with age. This is the first study to assess only borderline and malignant ovarian tumors in our population.

METHODS

This was a retrospective analysis of all malignant ovarian cancer cases, who underwent primary surgery at Tribhuvan University Teaching Hospital over a period of three years between April 2009- April 2012. All case sheets were analyzed regarding patient age, histopathology and stage of disease. Histopathological diagnosis was retrieved from the department of pathology. WHO classification of ovarian tumor was used. Stage I and II were considered as early stage disease and stage III and IV as late stage disease. Approval from ethical committee was taken for

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the study. Data has been presented in means and percentages. Statistical analysis was done using Chi square and T test wherever needed and p-value less than 0.05 was taken as significant.

Out of the total 451 cases, 81 cases of borderline and malignant ovarian tumor were taken into the study. Benign tumors were the most common constituting 82% of all ovarian tumors. Germ cell tumors were the most common type of ovarian tumors in this study.

RESULTS

Table 1. Total ovarian tumor cases (n=451).

	Epithelial	Germ cell	Stromal	Others	Metastatic	Total (%)
Benign	151	215	4	-	-	370 (82%)
Borderline	14	-	-	-	-	14 (3.1%)
Malignant	38	15	4	2	8	67 (14.9%)
	203 (45%)	230 (51%)	8 (1.8%)	2(0.4%)	8 (1.8%)	451

Table 2. Histological distribution of borderline and malignant ovarian tumors (n=81).

Types	Number	%
A. Epithelial type	52	64.2%
Serous adenocarcinoma	18	22.2%
Borderline serousadenoma	4	4.9%
Mucinous adenocarcinoma	8	9.9%
Borderline Mucinous adenoma	10	12.3%
Endometroid adenocarcinoma	4	4.9%
Clear cell adenocarcinoma	3	3.7%
Transitional cell carcinoma	1	1.2%
Undifferentiated adenocarcinoma	2	2.5%
Malignant mixed mesodermal tumor	2	2.5%
B. Germ cell type	15	18.5%
Dysgerminoma	4	4.9%
Yolk sac tumor	3	3.7%
Mixed germcell tumor	3	3.7%
Immature Teratoma	2	2.5%
Malignancy in dermoid	3	3.7%
C. Stromal Tumors	4	4.9%
Granulosa cell tumor	3	3.7%
Fibrosarcoma	1	1.2%
D. Metastatic	8	9.9%
E. Others: lymphoma	2	2.5%

Table 3. Correlation between age and type of borderline and malignant ovarian tumor (n=81).

Age	Epithelial malignant	Borderline Epithelial	Germ cell	Stromal	Metastatic	Others	Total
Mean age	49.6 yrs	44.1 yrs	22.3 yrs	53 yrs	50.1 yrs	11.5 yrs	
<20	-	1	9	-		2	12 (14.8%)
21-40	8	5	3	-	2	-	18 (22.2%)
41-60	23	6	3	3	5	-	40 (49.4%)
>60	7	2	-	1	1	-	11 (13.6%)
	38 (46.9%)	14 (17.3%)	15 (18.5%)	4 (4.9%)	8 (9.9%)	2 (2.5%)	81 (100%)

Thirty cases (37%) were seen in women younger than 40 years of age, of which 12 (40%) were of germ cell type, 8 (26.7%) epithelial malignancy, 7 (23.3%) borderline, 1 (3.3%) metastatic and 2 (6.7%) were lymphoma cases. In women <40 years the likelihood of germ cell cancer was significantly more than non-germ cell malignancies, and this was found to be statistically significant with p value <0.001.

Table 4. Correlation between age and epithelial malignancy types (n=38).

Age	Serous n=18	Mucinous n=8	Endometrioid n=4	Clear cell n=3	Transitional n=1	Others n=4	Total
Mean age	56.7 yrs	38.4 yrs	46.3 yrs	46 yrs	44 yrs	47.5 yrs	49.6 years
0-20	-	-	-	-	-	-	0
21-40	1	6	-	-	-	1	8 (21.1%)
41-60	11	1	4	3	1	3	23 (60.5%)
>60 yrs	6	1	-	-	-	-	7 (18.4%)
Total	18	8	4	3	1	4	38

In the germ cell tumor group 12/15 (80%) were in the age group less than 40. Three of the cases ie 20% were >40 years and all were mature cystic teratoma with a malignant component. Of the primary malignant ovarian tumor cases 29 (50.9%) came in stage I, 3 (5.2%) in stage II, 24 (42.1%) in stage III and 1 (1.8%) in stage IV. Epithelial ovarian malignancies were more likely to present at late stages than non-epithelial malignancies and this was statistically significant with p value of 0.003. Of the 14 borderline epithelial ovarian tumor cases 13 (93%) were in stage I. There was only one case of mucinous borderline tumor with stage III disease with positive

peritoneal deposits. Germ cell and stromal cell cancers accounted for about 55% of stage I disease, whereas epithelial ovarian cancers accounted for 91% of stage III disease. Among the primary malignant ovarian cancer cases excluding borderline epithelial tumors, correlation between age at presentation and stage of disease was assessed. Mean age at presentation of primary ovarian tumor was 41.9 years. Age at presentation for stage I was 33.8 years, 39 years for stage II, 53.7 years for stage III and 41 years for stage IV cases. Early stage disease was seen in younger age group (36.5 years) compared to late stage presentation in older age group (47.4 years) and this was found to be statistically significant with p value <0.001. Therefore it was noted that age was

increasing with stage of disease. Borderline epithelial ovarian tumors presented at mean age of 44.1 years and 13/14 (93%) had stage I disease.

Institute, year	Total cases studied	Benign	Malignant	Borderline	Epithelial/germ cell (total)
Tribhuvan University Teaching Hospital, 2008	161	135	26 (16%)	-	52.2%/42.2%
Nepal Medical College, 2009	95	86	9 (9.5%)	-	72.6%/27.4%
Kathmandu Medical College, 2011	102	89	13 (12.7%)	-	69.5% /19.5%
BPKIHS, 2012	83	66	15 (18%)	2 (2.4%)	47%/45%
Birendra Army Hospital, 2011	100	68	29 (29%)	3 (3%)	56%/35%
Total	541	444 (82%)	92 (17%)	5 (2.7%)	59.5%/33.8%

DISCUSSION

Incidence of malignancy/borderline tumors

Benign ovarian tumors were the most common type 82% (n=370) with malignant ovarian tumors accounting for 15% and borderline ovarian tumors consisting of 3% of the total cases. Table 5 shows the studies done in other institutions in Nepal where the incidence of malignant ovarian tumor ranges from 10-29%.³⁻⁶ Study done by Mondal et al⁷ showed that benign tumors constituted 63%, malignant 29.6% and borderline tumors 7.3%. Other studies by Gupta,⁸ Malli,⁹ Bukhari¹⁰ and Iyoke¹¹ also showed slightly higher malignancy rates 22.9%, 27%, 20% and 25% respectively. But there are studies which have shown even higher incidence of malignancy cases ranging from 31-40.8%.¹²⁻¹⁴ This could be explained by the larger referrals to specialized centres which results in higher malignancy rates while simple lesions are managed in general hospitals. Also geographical variations may be playing a role but this still needs to be studied. The incidence of borderline cases as reported in this study was 3% which is similar to other studies done in Nepal which has shown range between 2.4 - 3%.¹⁵ Higher rates of 20% incidence of borderline tumors have also been reported by Rettenmaier et al.¹⁶

Histological types of ovarian tumor

Germ cell ovarian tumors were the most common type of ovarian tumor in this study accounting for

51% of all tumors followed by epithelial ovarian tumors at 45%. In a study done at same institute 4 years back, the incidence of epithelial and germ cell tumors were 52% and 42% respectively.³ The high incidence of germ cell tumor in general, is mainly due to the high incidence of dermoid cyst compared to other tumors of the ovary in this institute. Few studies in Africa have also found germ cell tumors as the most common overall ovarian tumor.¹⁷ In most other studies epithelial ovarian tumors are the commonest. The average incidence of epithelial and germ cell tumor among other studies^{7,18} from Nepal is 59% and 33% respectively. This is in contrast to the present study. Another reason could be due to more referrals of germcell tumors in very young girls, as ours is a tertiary level institute. About 75% of the malignancies in women <20 years, in the present study were germ cell type. Although germ cell tumors were the most common ovarian tumors, among malignant cases epithelial ovarian tumors were the most common malignancy in this study (Table 2). Studies done in Nepal show that epithelial malignancy ranges from 40-69% whereas germ cell malignancy rates range from 11.5-33%.^{7,18} This is in keeping with most other studies where epithelial tumors are still the most common malignant ovarian tumor. Mondal et al⁷ in his study also found that epithelial tumors comprised 67% of all tumors and 60.9% of malignant

tumors. Among the malignant epithelial tumors, serous adenocarcinoma was the commonest at 22% followed by 10% cases of mucinous adenocarcinoma. Most of studies done in Nepal show serous adenocarcinoma as the most common malignancy (Table 5). Studies done in Central Africa also show serous adenocarcinoma as the most common ovarian malignancy ie 36%, followed by 24% cases of mucinous adenocarcinoma.¹¹ Studies done in India and Pakistan also show that serous adenocarcinomas are the most common type ranging from 11- 20% cases.^{7,8,10,19} Studies done in Brazil show that serous adenocarcinoma account for 30% of cases, and 13.7% cases of mucinous adenocarcinomas and endometrioid adenocarcinomas each.¹

Few studies in developed countries have shown that endometrioid adenocarcinomas account for the second most common epithelial malignancy.¹⁶ This is not the case with this study and in other Indian and Asian studies, where mucinous adenocarcinomas are more common than endometrioid adenocarcinomas.⁷⁻¹⁰ Metastatic tumors constituted about 10% of cases too and this could be due to the multidisciplinary tertiary level of this institute which leads to more varied, referred cases from outside or from other departments mainly surgical. Metastatic tumors in other studies from Nepal range from 6.9% to 20% with gastrointestinal sites being the most common primary site, as was in this study.^{6,7,17}

Correlation of age with malignant ovarian tumors

According to the American Cancer Society, half of the women with ovarian malignancy are 63 years and older. The mean age for primary malignant ovarian tumors in this study was 41.9 years and slightly more at 49.6 years for malignant epithelial ovarian cancers. Although the incidence of epithelial ovarian malignancy begins from the age of 40 years, the largest number of ovarian cancer cases are being found in the 60-65 years age group.²⁰ Scully also reports that malignant epithelial ovarian cancer peak incidence is between 56-60 years.²¹ The Age Specific Incidence Rate (ASIR) for ovarian cancer in a study done in India by Murthi et al,²² revealed that the disease increases from 35 years of age and reaches a peak between the ages 55-64. In the study by Mondal et al⁷

in Eastern India the mean age of ovarian malignancy cases was 49 years which is slightly higher than in this study. Study done in Nigeria, has also shown that the average age for ovarian malignancy was 45.4 years.¹¹ This study shows a slightly lower age at presentation of

ovarian cancers especially epithelial type ie <50 years in this study population which is also seen in certain African and Asian countries. The exact cause or risk factors in these patients thus needs to be further studied. Another factor that increases the rate of ovarian cancer in young women are the germ cell tumors. The average age at diagnosis of germ cell malignancies was 22 years in this study and this has been seen universally. In this study there were eight cases (12% of malignant ovarian cancer cases), with ≤ 15 years of age. These were of germ cell origin along with a lymphoma case, which could have resulted in lower mean age for ovarian malignancies. Another important correlation with age that has been seen is that, increasing age was associated with increasing stage of disease. Paes et al² in their study also found that age at diagnosis was statistically significant between the group of better prognosis (48.90 yrs \pm 11.74) and the group of poorest prognosis disease (57.90 years \pm 13.52). Therefore it would seem that no age seems to be spared. The younger mean age at presentation of ovarian malignancies is an important finding from this study, which will help increase awareness of such tumors even in younger women. Screening and education efforts can also be directed at an early age in the population. This would aid in early diagnosis and therefore better prognosis.

CONCLUSIONS

Germ cell tumors were the most common type of ovarian tumor, although epithelial type was the most common malignancy. Serous adenocarcinoma was the most common ovarian malignancy. Mean age of primary malignant ovarian tumor was 41.9 years. Age group was significantly younger in germ cell malignancies. Epithelial ovarian malignancy presented mainly in late stage whereas germ cell, stromal and borderline epithelial cases presented at an early stage.

DISCLOSURE

The authors report no conflicts of interest in this work.

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