RESEARCH COMMUNICATION

Epithelial Ovarian Cancer at a Cancer Hospital in a Developing Country

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Abstract

Objectives: To analyze records of patients seen with malignant epithelial ovarian cancer at a tertiary care cancer hospital in Pakistan and obtain information on factors as laterality, histology, CA-125 levels, and stage of the disease, determine age at presentation and, assess menopausal status of the patients. Also, to review results obtained in light of data published in indexed journals. Patients and Methods: We analyzed 544 cases of malignant ovarian epithelial tumors registered at the Shaukat Khanum Memorial Cancer Hospital and Research Center from December 1994-December 2003. Results: Mean age at presentation: 48.1 years (SD 13, range 4-82 years); commonest histological sub-type: serous cystadenocarcinoma (28.6%); most frequently seen stage: 3 (43.5%), followed by stage 4 (22.4%); post-menopausal: 56.8% of the women; bilateral disease: 41.2% of the women; and Cancer Antigen-125 (CA-125) level: elevated in 70% of the females. Conclusions: Stage at presentation in majority of the cases was advanced as compared to that seen in the west. With only minor variations, our findings seem consistent with those reported in other local studies. However, it is imperative to conduct an extensive population-based study to understand the impact of, and develop strategies for the management of ovarian cancer in Pakistan.

Key Words: Tertiary care cancer hospital - epithelial ovarian cancer - Pakistan

Introduction

Ovarian cancer is the most frequent cause of death from gynecological cancer and the fourth most frequent cause of death from cancer in women in Europe and the United States (Jacobs and Menon, 2004). Cancer data reported by an institutional study conducted in Pakistan, show that female breast cancer was the most common cancer accounting for 38.5% of female malignancies followed by ovarian cancer 13.6% (Aziz et al., 2003). In women with no family history of ovarian cancer, the lifetime risk is 1.6%, whereas a woman with one affected first degree relative has a 5% lifetime risk (Ahmad et al., 2000). With two or more affected first-degree relatives, the risk is 7% (Kauff et al., 2002).

Most ovarian cancers occur after menopause when the ovaries have no physiological role and consequently abnormal ovarian function causes no symptoms. As a result of this factor, combined with the anatomical location of the ovaries deep in the pelvis, ovarian cancers typically cause few symptoms until they reach a large size or have disseminated. As a result, ovarian cancer is usually diagnosed at an advanced stage when despite advances in surgical and chemotherapeutic management during the last decade,

survival rates are poor. Almost 90% of patients are diagnosed when the disease has already spread to the pelvis or abdomen and for these patients, 5-year survival rates are less than 30%. In contrast, a small proportion of patients diagnosed with stage I ovarian cancer confined to the ovaries have a 5-year survival rate in excess of 90%.

Serum CA-125, a tumor marker for ovarian cancer, has been observed to be elevated in 80% of women with epithelial ovarian cancer overall but in only 50% of women with early disease (Kauff et al., 2002).

Information from developing countries regarding incidence of even some of the common cancers such as ovarian cancer is lacking (Malik, 2002). In one study conducted in Pakistan, surface epithelial-stromal tumors comprised 63.5% of all tumors. Benign cystic teratoma was the commonest benign tumor (35.2% of all benign tumors) and serous cystadenocarcinoma was the commonest malignant tumor (33.3% of all malignant tumors) (Ahmad et al., 2000).

Epithelial ovarian cancer is the most common type of ovarian cancer. It is the leading cause of death from gynecologic cancers in the United States (Bhoola and Karim, 2006). Although there has been a statistically significant

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improvement in the 5-year survival, in 2005, more than 16,000 women were expected to die of this disease (Bhoola and Karim, 2006). Ninety per cent of ovarian cancers are derived from the ovarian surface epithelium and these neoplasms are classified into serous, mucinous, endometroid, clear-cell, and transitional-cell types (Christie and Oehler, 2006).

There is a dearth of information regarding the epidemiological aspects of ovarian cancer in Pakistan. We aim to analyze the basic data on ovarian cancer, specifically

Table 1. Distribution of 655 Ovarian Cancers Reported in a 9-year Period at SKMCH & RC

Histological types	Count	Percentage
Epithelial tumors	544	83.3
Germ cell tumors	91	14.0
Sex cord tumors	20	2.7

Table 2. Histology of 544 Malignant Epithelial Ovarian Tumors

Histological types	Count	Percentage
Serous cystadenocarcinoma	156	28.6
Mucinous cystadenocarcinoma	73	13.4
Endometroid adenocarcinoma	40	7.3
Clear cell cystadenocarcinoma	16	3.0
Squamous cell tumors	2	0.3
Undifferentiated carcinoma	89	16.3
Adenocarcinoma & cystadenocarcinoma	107	19.6
Papillary adenocarcinoma	56	10.3
Signet ring cell tumor	3	0.5
Mullerian mixed tumor	2	0.3

Table 3. Tumor Stage at Presentation of 544 Epithelial Ovarian Tumors

Stage	Count	Percentage
I	57	10.4
IA	26	4.7
IB	13	2.4
IC	18	3.3
2	59	10.8
2A	12	2.2
2B	36	6.6
2C	11	2.0
3	237	43.5
3A	10	1.8
3B	87	16.0
3C (N0)	94	17.3
3C (N1)	46	8.4
4	122	22.4
Not Evaluable	69	12.8

Table 4. Relative Frequencies (%) of the Three Commonest Ovarian Epithelial Tumors in Pakistan

Histological type	Saeed	Muzaffar	Ahmad	Present
Serous cystadenocarcinoma	27.5	27.6	30.6	28.6
Mucinous cystadenocarcinoma	25.0	48.3	15.7	13.4
Endometroid carcinoma	-	-	12.0	7.3

the epithelial cancer of the ovary, at the Shaukat Khanum Memorial Cancer Hospital & Research Center (SKMCH & RC), Pakistan. This is a private, charitable hospital, which is offering free of charge medical services to a substantial proportion of cancer patients registered at the hospital since the facility started functioning in December 1994. The hospital-based- and disease-specific cancer registries and, the medical records are integrated within the Hospital Information System, set up by the Management Information Sciences department of the hospital.

Subjects and Methods

Six hundred and fifty five histologically proven cases of ovarian cancer presenting at SKMCH & RC between December 1994 and December 2003 were extracted from the hospital cancer registry and analyzed using the Statistical Package for Social Sciences (SPSS), version 10.0. Eligibility criteria required histologic documentation of epithelial ovarian cancer as a result of which 544 cases were included in the study. Those cases with ovarian metastasis from any other malignancy were excluded. The histologic characterization of ovarian tumors was done according to the International Classification of Diseases, Ninth Edition (ICD·9) (WHO Classification, 1995).

Results

Of a total of 655 ovarian cancers, a total of 554 cases of epithelial tumors of the ovary were registered during a nine-year period under study. Epithelial tumors represented the majority of cases, followed by germ cell (n=91) and sex cord tumors (n=20) (Table 1). The mean age at presentation of the 544 patients was 48.1 years (standard deviation: 13, range: 4-82 years, mode: 40 years, median: 49.5 years). All malignant epithelial tumors were further analyzed according to histology. The three most common histological types were, serous cystadenocarcinoma (28.6%), mucinous cystadenocarcinoma (13.4%) and endometroid adenocarcinoma (7.3%) as shown in Table 2. Most patients presented with an advanced disease. Nearly forty-four per cent of the patients (n=237) presented in stage 3 and 22.4% (n=122) in stage 4 of the disease, as depicted in Table 3.

Parity was available in 257 records only. The number of children ranged from 0-16, whereas, 42 patients had four children each. The average age at menopause was considered to be 47.1 years (95% CI 46.8 to 47.6) (Baig, 2006). Based on this, nearly 53% (n=288) of the females were classified as post-menopausal versus 47% (n=256) of the women who were considered pre-menopausal. Laterality of the disease was evaluated in 313 patients (missing in 231), which illustrated bilateral disease in 41.2% (n=129), right sided in 34.5% (n=108), and left sided disease in 24.28% (n=76) of the patients. CA-125 values were available only in 383 patients and showed that 30% of these patients had normal CA-125 levels (< 35 U/ml) at presentation while it was elevated in rest of the cases. The median for CA-125 levels

was 180 U/ml (range: 01-141,999 U/ml).

Personal and family history of cancer was recorded in very few patients. Of these, six patients presented with both ovarian and breast cancer. Twenty eight patients gave a family history of breast cancer and another 16, a family history of ovarian cancer.

Discussion

Ovarian cancer ranks among the ten commonest cancers in Pakistani women (Ahmad et al., 2000). Their ranking varied from second to fifth in various Pakistani studies (Ahmad et al., 2000; Alam et al., 2001; Leide et al., 2002). The number of cases reported in different series ranged from 61 to 855 (Ahmad et al., 2000). The present series reports 653 ovarian tumors, of which 544 cases were of epithelial origin and have been further analyzed.

Mean age (48.1 years) at diagnosis of Pakistani patients with ovarian cancer is similar to the women in South Asian countries (Ahmad et al., 2000; Arai et al., 2004; Yamashita et al., 1999). This finding contrasts with the western data, which report that the majority of malignant ovarian tumors occur in the 5th to 7th decade range of life (Arai et al., 2004; Jones, 2006). Reason remains un-established, however, genetic as well as environmental factors may be operative (Ahmad et al., 2000; Bhoola and Karim, 2006).

Similar to western data and other Asian studies, epithelial tumors comprised the major histologic type. Though there is no population-based information available on the prevalence of ovarian cancers in Pakistan, there are a few hospital-based cancer registries that have been published. Our study shows the hospital prevalence of epithelial tumors (83.3%) to be very close to that in the western literature (90%) (Guppy et al., 2005). At another hospital in Pakistan, Ahmed and colleagues have reported the hospital prevalence of epithelial ovarian tumors to be 64% (Ahmad et al., 2000). Similarly, the hospital cancer registries in India have reported 66% to 70% prevalence of ovarian epithelial tumors. (Gatphoh and Dharnal, 1990; Tayagi et al., 1993). Unlike western data, where the prevalence of germ-cell and sex cord tumors is 3% and 5% respectively (Jacobs and Menon, 2004; Morrison, 2005), our data show the prevalence to be 14% and 3%, respectively. In another local study, germ cell tumors comprised 27.13% of all ovarian tumors (Ahmad et al., 2000). This is also consistent with the slightly high prevalence of germ cell and sex cord tumors in the South Asian versus the western population (Zhang et al., 2004).

To date, there is no reliable method to screen for ovarian cancer; therefore, the majority of cases are diagnosed at a late stage in the natural history of the disease (Bhoola and Hoskins, 2006). This situation is compounded in developing countries where there is limited access to health care resulting in advanced, complicated disease at presentation. The disease stage at presentation in our study is similar to the data from the South Asian countries and Pakistan (Ahmad et al., 2000; Arai et al., 2004; Yamashita et al., 1999). However, due to late presentation and lack of awareness in Pakistan, the stage

of presentation is higher compared to that seen in the west (Ahmad et al., 2000; Arai et al., 2004; Bhoola and Hoskins, 2006).

Laterality of the disease has not been reviewed extensively in literature published from Pakistan. We, however, report a high occurrence of bilateral epithelial ovarian cancers at presentation in our hospital. The ratio of the disease in post-menopausal to pre-menopausal was high and was similar to what has been reported in other studies (Christie and Oehler, 2006; Bhoola and Hoskins, 2006). Whether population-based findings will be similar to ours, as compared to the western data (Jacobs and Menon, 2004; Bhoola and Hoskins, 2006), is yet to be sought. Shaukat Khanum Memorial Cancer Hospital is a tertiary care charity cancer center, where most of the patients belong to the lower economic class and has triage limitations. Hence, our subjects may not be entirely representative of all patients diagnosed with epithelial ovarian cancer in Pakistan.

This single institution, retrospective study has some limitations due to missing information on factors under study and also because the menopausal status was not available in several cases and a surrogate measure had to be used to determine the proportion of post-menopausal women. Also, of concern was the availability of limited information on family history of breast or any other cancer.

In conclusion, since ovarian cancer has been reported to be the leading cause of death from gynecologic cancers and there is insufficient information about the epidemiology of epithelial ovarian cancer in the country, there is a need to conduct a large, population based study in Pakistan in order to lay the foundation for prevention, and control of cancer of the ovary in the region.

References

Ahmad Z, Kayani N, Hasan SH, Muzaffar S, Gill MS (2000). Histological pattern of ovarian neoplasma. *J Pak Med Assoc*, **50**, 416-9.

Alam I, Waqar F, Khan A, Begum N (2001). Prevalence and management of ovarian tumors in Women and Children Hospital, Abbottabad. *J Ayub Med Coll Abbottabad*, **13**, 19-21.

Arai M, Utsunomiya J, Miki Y (2004). Familial breast and ovarian cancers. *Int J Clin Oncol*, **9**, 270-82.

Aziz Z, Sana S, Saeed S, Akram M (2003). Institution based tumor registry from Punjab: five year data based analysis. *J Pak Med Assoc*, **53**, 350-3.

Baig LA, Karim SA (2006). Age at menopause, and knowledge of and attitudes tomenopause, of women in Karachi, Pakistan. *J Br Menopause Soc*, **12**, 71-74.

Bhoola S, Hoskins WJ (2006). Diagnosis and management of epithelial ovarian cancer. *Obstet Gynecol*, **107**, 1399-410.

Christie M, Oehler MK (2006). Molecular pathology of epithelial ovarian cancer. *J Br Menopause Soc*, **12**, 57-63.

Fitch MI, Turner F (2006). Ovarian cancer. *Cancer Nurse*, **102**, 16-20.

Gatphoh ED, Darnal HK (1990). Pattern of ovarian neoplasm in Manipur. *J Indian Med Assoc*, **88**, 338-9.

Guppy AE, Nathan PD, Rustin GJ (2005). Epithelial ovarian cancer: a review of current management. *Clin Oncol (R Coll Radiol)*,

17, 399-411.

Jacobs IJ, Menon U (2004). Progress and challenges in screening for early detection of ovarian cancer. *Mol Cell Proteomics*, **3**, 355-66.

Jones MB (2006). Borderline ovarian tumors: current concepts for prognostic factors and clinical management. *Clin Obstet Gynecol*, **49**, 517-25.

Kauff ND, Satagopan JM, Robson ME, Offit K (2002). Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med*, **346**, 1609-15.

Liede A, Malik IA, Aziz Z, et al (2002). Contribution of BRCA1 and BRCA2 mutations to breast and ovarian cancer in Pakistan. *Am J Hum Genetics*, **71**, 595-606.

Malik IA (2002). A prospective study of clinico-pathological features of epithelial ovarian cancer in Pakistan. *J Pak Med Assoc*, **52**, 155-8.

Markman M (2006). Unresolved issues in the chemotherapeutic management of gynecologic malignancies. *Semin Oncol*, **33 (2 Suppl 6)**, S33-8.

Morrison J (2005). Advances in the understanding and treatment of ovarian cancer. *J Br Menopause Soc*, **11**, 66-71.

Muzaffar M, Malik IA, Ashraf S (1987). A clinicopathological study of 107 ovarian tumors. *J Pak Med Assoc*, **37**, 194-7.

Saeed M, Khawaja K, Rizwan I, et al. (1991) Clinicopathological analysis of ovarian tumors. *J Pak Med Assoc*, **41**, 161-64.

Sood AK, Abu-Rustum NR, Gershenson DM (2005). Fifth International Conference on Ovarian Cancer: challenges and opportunities. *Gynecol Oncol*, **97**, 916-23.

Tyagi SP, Maheswari V, Tyagi N, et al (1993). Solid tumors of the ovary. *J Indian Med Assoc*, **91**, 227-30.

WHO Histologic Classification of Ovarian Tumors, Geneva, WHO, 1995.

Yamashita Y, Sagawa T, Fujimoto T, et al (1999). BRCA1 mutation testing for Japanese patients with ovarian cancer in breast cancer screening. *Breast Cancer Res Treat*, **58**, 11-7.

Zhang M, Lee AH, Binns CW, Xie X (2004). Green tea consumption enhances survival of epithelial ovarian cancer. *Int J Cancer*, **10**, 465-9.