Original Article

Epidemiology of epithelial ovarian cancer, a single institution-based study in India

Surendra Kumar Saini, Shelly Srivastava, Yuvraj Singh, Awadhesh Kumar Dixit, Shambhu Nath Prasad

Department of Radiotherapy and Oncology, J. K. Cancer Institute, Kanpur, Uttar Pradesh, India

ABSTRACT

Background: Ovarian cancer is the leading cause of mortality among all cancers of female genital tract in countries where effective cervical cancer screening program exists. As the world's population ages, remarkable increase in the total number of ovarian cancer cases are expected. This is preliminary epidemiological study to decide priorities in ovarian cancer research. **Materials and Methods:** A retrospective study was conducted with primary epithelial ovarian cancer cases registered in J. K. Cancer Institute, Kanpur (Uttar Pradesh), from 2007 to 2009. Patients' age at diagnosis, clinical feature, parity of patients, tumor histological type, Federation of Gynecology and Obstetrics stage, chemotherapy regimens, and overall survival data were collected and analyzed. **Results:** One hundred and sixty-three cases of primary ovarian epithelial cancer were analyzed. Patients' mean age at diagnosis was 55.98 ± 9.24 (median = 55). Serous adenocarcinoma (49.69%) was the most prevalent type of histopathology followed by endometroid (19.1%), mucinous (10.42%) and clear cell (4.29%). Combination of taxane and platin was most commonly used first line regimen in newly diagnosed as well as in relapsed patients post 1 year. Survival was not significantly different in various histopathology (log-rank $P = 0.7406$), but advancing stage demonstrated gradually poor survival (log-rank $P < 0.05$) when compared with early stage disease. **Conclusion:** Research efforts should be in the direction to find early diagnostic and effective screening tools as well as better therapeutic approaches for advanced epithelial ovarian cancer.

Key words: Chemotherapy, epidemiology, epithelial ovarian cancer

INTRODUCTION

Ovarian malignant tumors are group of diseases with varying clinical and biological behavior. Fatality due to ovarian neoplasm is high due to difficulty in early diagnosis of the disease and limited effective treatment options. No anatomical barrier exists to check spread of disease beyond ovaries and disease spread in peritoneal cavity, abdominal and pelvic organs. Ovarian cancer is the leading cause of mortality among all cancers of female genital tract in countries where effective cervical cancer screening program exists. In India, during the period 2001–2006, the age-standardized incidence rates for ovarian cancer varied from 0.9 to 8.4/100,000 person years among various registries. The age-specific incidence rate for ovarian cancer revealed that the disease increases from 35 years of age and reaches a peak between the ages 55 and 64.[1] Ovarian cancer is the seventh most common cancer in women worldwide (18th most common cancer overall), with 239,000 new cases diagnosed in 2012.[2] Five-year relative survival rate, which compares the 5-year survival of people with the cancer to the survival of others at the same age who do not have cancer, of epithelial ovarian cancer ranges from approximately 30% to 50% for all stages cumulative. Women suffering from this dreaded disease have compromised early detection of the disease when survival rates would have been as high as 85% due to inexistence of specific and sensitive ovarian tumor biomarkers.[3,4] The role of two screening tests available for the detection of sporadic epithelial ovarian tumors,

Address for correspondence: Dr. Surendra Kumar Saini, Department of Radiotherapy and Oncology, G. G. Government Hospital, M. P. Shah Medical College, Jamnagar - 361 008, Gujarat, India.
E-mail: drsurensaini@gmail.com

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.172078

Cite this article as: Saini SK, Srivastava S, Singh Y, Dixit AK, Prasad SN. Epidemiology of epithelial ovarian cancer, a single institution-based study in India. Clin Cancer Investig J 2016;5:20-4.

transvaginal sonography, and serum cancer antigen-125 level has been proven nonspecific so that their diagnostic relevance remains controversial.[5,6] Standard treatment for ovarian neoplasia includes cytoreduction followed by platinum- and taxane-based adjuvant chemotherapy. Unfortunately, up to 75% of cases treated with curative intent will experience disease recurrence and will ultimately die due to this dreaded disease.[7] As the world's population ages, remarkable increases in the total number of ovarian cancer cases are expected, emphasizing the importance of this disease in public health issues. There is no precise system in India to determine impact of this highly mortal disease on public economy and social outcome and lacks precise epidemiologic data on the disease, which would have supported the development of sustainable and more efficient strategies to guide research to control the malignancy. Here, we are presenting epidemiological study of ovarian tumors aiming to characterize the disease in the state of Uttar Pradesh, which is highest populated state in India.

MATERIALS AND METHODS

A retrospective study was conducted with primary epithelial ovarian cancer cases registered in J. K. Cancer Institute, Kanpur (Uttar Pradesh), from 2007 to 2009. Due to high mortality of primary epithelial malignant tumor in comparison to benign, borderline, germ cell tumor and other variants of ovarian cancer, only primary epithelial malignant tumor cases were included. Patients' age at diagnosis, clinical feature, parity of patients, tumor histological type, Federation of Gynecology and Obstetrics (FIGO) stage, chemotherapy regimens, and overall survival data were collected and analyzed. Study was approved by GSVM Medical College Ethics Committee, Kanpur (Uttar Pradesh), to publish retrospective data.

Statistical analysis

Data were expressed as absolute values and percentage or as mean ± standard deviation. Distribution of patients according to parity, clinical features, and other disease parameters were tabulated. Statistically relevant differences among age at diagnosis were accessed using one-way analysis of variance. Kaplan–Meier curves were plotted to understand effect of disease extent and histopathology on survival and compared using log-rank test. Data are expressed as *P* value of log-rank analysis, hazard ratio, and 95% confidence interval (95%).

RESULTS

In this study, 136 cases primary ovarian epithelial neoplasia were analyzed, as described in the "Methods" section. For epithelial ovarian malignancy, patients' mean age at diagnosis was 55.98 ± 9.24 (median = 55). As for FIGO staging, the mean age at diagnosis was 52.67 ± 8.04 (median = 52) for Stage I, 55.24 ± 10.78 (median = 55) for Stage II, 56.53 ± 8.97 (median = 56) for Stage III, and 58.30 ± 8.48 (median ± 57) for Stage IV, showing a possible correlation between patients' age at diagnosis and tumor FIGO stage [Table 1]. As expected, serous adenocarcinoma (49.69%) was the most prevalent type of histopathology followed by endometrioid (19.1%), mucinous (10.42%), and clear cell (4.29%) [Table 2]. Thirty-two (19.63%) patients were nulliparous. Patients reported were of parity up to nine [Table 3]. Dyspepsia, defined as burning, gnawing discomfort or constellation of symptoms including postprandial fullness, early satiety (an inability to complete a meal due to premature fullness), bloating, and eructation (belching), were most common observed complaint (66.26%) of patients who later on diagnosed with malignant ovarian tumor. Abdominal lump or abdominal distension, pain in abdomen, urinary symptom, respiratory symptom, constipation, discharge/bleeding P/V, nausea/vomiting, and weakness were other observed symptoms [Table 4].

Chemotherapy treatment given and outcome was analyzed. Table 5 shows various chemotherapy regiment given. Combination of taxane and platin was most commonly used first-line regimen in newly diagnosed as well as in relapsed patients post 1 year. Sandwich treatment (neoadjuvent followed by surgery and adjuvant chemo) was used in few Stage III and all Stage IV disease patients. Surgery was attempted after two or three cycles of chemotherapy where response was very good. Eighteen patients (11%) never underwent surgical exploration, almost from Stage IV disease (16 patients) but two from Stage III.

Table 1: Characterization of the ovarian tumor cases registered (diagnosed and/or treated) at J K Cancer Institute, Kanpur

Parameter	EOC and stage				
	Total	I	II	III	IV
N	163	24	34	78	27
Age at diagnosis (mean±SD)	55.98±9.24	52.67±8.04	55.24±10.78	56.53±8.97	58.30±8.48
Median	55	52	55	56	57
31 to 40	23 (14.11%)	5 (20.83%)	8 (23.52%)	17 (14.10%)	2 (7.40%)
41 to 50	43 (26.38%)	11 (45.83%)	9 (26.47%)	20 (25.64%)	6 (22.22%)
51 to 60	39 (23.93%)	4 (16.67%)	10 (29.41%)	18 (23.07%)	7 (25.92%)
Over 60	58 (35.58%)	4 (16.67%)	7 (20.59%)	29 (37.18%)	12 (44.44%)

P=0.152, one-way analysis of variance (ANOVA). EOC: Epithelial ovarian cancer

Table 2: Pathologic profile of epithelial ovarian cancer

Parameters	*N* (%)
Histological type	
Serous	81 (49.69)
Mucinous	17 (10.42)
Endometrioid	31 (19.01)
Clear cells	7 (4.29)
Adenocarcinoma without other specification	27 (16.56)
Others	2 (1.23)
FIGO stage	
I	24 (14.72)
II	34 (20.86)
III	78 (47.85)
IV	27 (16.56)
Differentiation	
Well	44 (26.99)
Moderate	78 (47.85)
Poor	41 (25.15)
Laterality	
Left	34 (20.86)
Right	37 (22.70)
Bilateral	92 (56.44)

FIGO: Federation of Gynecology and Obstetrics

Table 3: Distribution cases according to parity

Parity	Number (%)
0	32 (19.63)
1	21 (12.88)
2	28 (17.18)
3	27 (16.56)
4	24 (14.72)
5	13 (7.98)
6	13 (7.98)
7	2 (1.22)
8	1 (0.61)
9	2 (1.22)

Table 4: Clinical presentation of epithelial ovarian cancer

Presentation	Cases (%)
Dyspepsia	108 (66.26)
Abd lump/Abd distension	88 (53.99)
Pain abdomen	103 (63.19)
Loss of appetite/decreased appetite	47 (28.83)
Urinary symptom (retention of urine, frequency)	17 (10.42)
Resp symp (dyspnoea/cough)	8 (4.90)
Constipation	33 (20.24)
Discharge/bleeding P/V	28 (17.12)
Nausea/vomiting	36 (22.08)
Weakness	10 (6.13)
Fever	10 (6.13)

Cyclophosphamide, adriamycin, and platinum was second choice where taxanes were contraindicated. Overall survival in regards to stage and histopathology were analyzed and compared. Survival was not significantly different in various histopathology (log-rank $P = 0.7406$) [Figure 1], but advancing stage demonstrated gradually poor survival [Figure 2]. FIGO Stage IV showed poor survival in comparison to Stage I tumors (log-rank $P < 0.0001$), Stage II (log-rank $P = 0.0003$), and Stage III ($P = 0.0041$). Stages II and III had poor survival in comparison to Stage I (log-rank $P = 0.0280$ and 0.0011), but no difference in stages II and III (log-rank $P = 0.1830$).

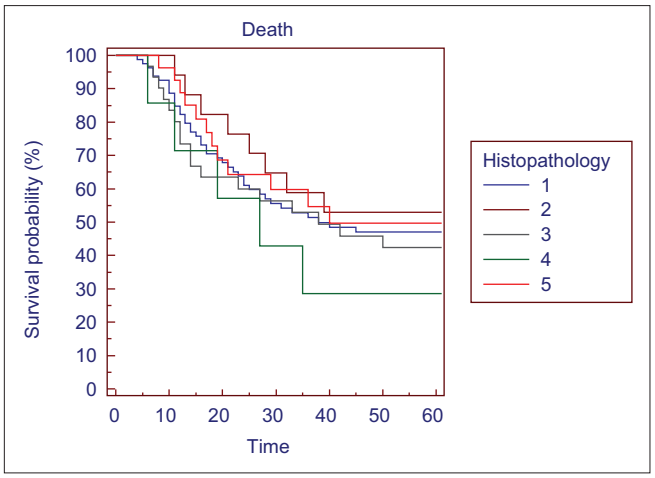

Figure 1: Overall survival for different histopathology types of epithelial ovarian cancer, estimated by Kaplan-Meier method (1: Serous, 2: Mucinous, 3: Endometroid, 4: Clear cell, 5: Adenocarcinima not otherwise specified)

DISCUSSION

With the advancing age, probability of malignant transformation increases. In developing countries like India with large population and increasing life expectancy, more and more cases of ovarian malignancy will have an impact on already overburdened health system. With advancement in radiation delivery techniques and use of various combinations of effective chemotherapy as well as advancement in surgical techniques have made it possible to very good survival in two other common malignancies (breast and cervix) in women but not in epithelial ovarian malignancies, unfortunately. To find more efficient diagnostic, prognostic and therapeutic tools or one can say, to find direction of research this is preliminary hospital-based epidemiological study to design larger epidemiological study on ovarian cancer. Patients usually consult primary care physician for most common symptoms of dyspepsia and usually get treatment on outpatient department basis. Though percentage of patient with dyspepsia due to ovarian neoplasia is too low than the large patients population suffering from this symptom in India due to various dietary causes and lifestyle.[8] One approach suggested is to get done pelvic ultrasonography (USG) in every postmenopausal female patient who presents with dyspepsia. Nulliparity is a risk factor for ovarian cancer especially in those with family history.[9,10] Though, relation could not be established between nulliparity and ovarian cancer in this study.

According to Globocon 2012 estimate,[11] more than 50% cases of ovarian neoplasm diagnosed in Indian female in 2015 will be after the sixth decade, though it includes not only

Table 5: Chemotherapy regimens prescribed to the epithelial ovarian cancer patients

Chemotherapy	*N* (%)
Neoadjuvant	
Cisplatin or carboplatin + paclitaxel	54 (33.13)
Cyclophosphamide + adriamycin + cisplatin or carboplatin	13 (7.98)
Adjuvant	
Cisplatin or carboplatin + paclitaxel	84 (51.53)
Cyclophosphamide + adriamycin + cisplatin or carboplatin	12 (7.36)
Sandwich (neoadjuvant+adjuvant)	23 (14.11)
Post-relapse and second line therapy	
Platinum + paclitaxel	42 (25.77)
Platinum	7 (4.3)
Paclitaxel	9 (5.52)
Gemcitabine	16 (9.82)
Lposomal doxorubicin	28 (17.17)
Etoposide	7 (4.3)

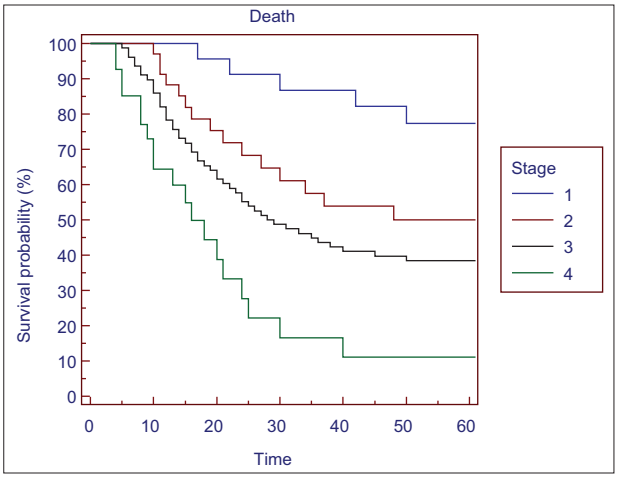

Figure 2: Overall survival for different stages of epithelial ovarian cancer, estimated by Kaplan-Meier method

epithelial but also other histopathological types. In our study, observed median age of epithelial ovarian malignancy is 55 years (mean 55.98 ± 9.24) and 35.58% population was above age of 60 and proportion of patients over age of 60 increases with advanced stage. It is in agreement with epidemiological studies done in Brazil[12] and Texas (USA).[13] Serous variant of adenocarcinoma was most frequent neoplasm observed in this study followed by endometrial, mucinous and clear cell corresponds to histopathology studied by Young and Steinberg.[14] Most of the ovarian cancer cases analyzed herein were observed in FIGO staged as II or III tumors (20.86% and 47.85%, respectively). Significant difference in death risk among various histological types was not observed but clear cell carcinoma has relatively poor prognosis in different studies.[14-16] Decreasing overall survival with advancing disease corroborate with survival data from National Cancer Data Base, USA.[17]

On the basis of good survival in early stage and poor survival in advanced disease, we can comment that research efforts should be in the direction to find early diagnostic and effective screening tools as well as for better therapeutic approaches for advanced epithelial ovarian cancer. Author suggests an epidemiological study to find effect of relatively easy available imaging modality (i.e., USG) on diagnosis in ovarian cancer risk age group patients with vague gastric symptoms. Another approach that can improve diagnosis of epithelial ovarian cancer is to educate primary care physician about ovarian cancer and to include it in differential diagnosis in the specific patient population.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Murthy NS, Shalini S, Suman G, Pruthvish S, Mathew A. Changing trends in incidence of ovarian cancer – The Indian scenario. Asian Pac J Cancer Prev 2009;10:1025-30.
2. World Cancer Research Fund. Available from: http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/ovarian-cancer-statistics.
3. Jacobs IJ, Menon U. Progress and challenges in screening for early detection of ovarian cancer. Mol Cell Proteomics 2004;3:355-66.
4. Buys SS, Partridge E, Black A, Johnson CC, Lamerato L, Isaacs C, *et al*. Effect of screening on ovarian cancer mortality: The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. JAMA 2011;305:2295-303.
5. Dorigo O, Berek JS. Personalizing CA125 levels for ovarian cancer screening. Cancer Prev Res (Phila) 2011;4:1356-9.
6. van Nagell JR Jr, DePriest PD, Ueland FR, DeSimone CP, Cooper AL, McDonald JM, *et al*. Ovarian cancer screening with annual transvaginal sonography: Findings of 25,000 women screened. Cancer 2007;109:1887-96.
7. Cannistra SA. Cancer of the ovary. N Engl J Med 2004;351:2519-29.
8. Shah SS, Bhatia SJ, Mistry FP. Epidemiology of dyspepsia in the general population in Mumbai. Indian J Gastroenterol 2001;20:103-6.
9. Vachon CM, Mink PJ, Janney CA, Sellers TA, Cerhan JR, Hartmann L, *et al*. Association of parity and ovarian cancer risk by family history of breast or ovarian cancer in a population-based study of postmenopausal women. Epidemiology 2002;13:66-71.
10. Adami HO, Hsieh CC, Lambe M, Trichopoulos D, Leon D, Persson I, *et al*. Parity, age at first childbirth, and risk of ovarian cancer. Lancet 1994;344:1250-4.
11. Globocon 2012, Estimate Cancer Incidence, Mortality and Prevalence in World; 2012. Available from: http://globocan.iarc.fr/old/age-specific_table_r.asp?selection=89356&title=India&sex=2&type=0&stat=0&window=1&sort=0&submit=%C2%A0Execute.
12. Paes MF, Daltoé RD, Madeira KP, Rezende LC, Sirtoli GM, Herlinger AL, *et al*. A retrospective analysis of clinicopathological and prognostic characteristics of ovarian tumors in the State of Espírito Santo, Brazil. J Ovarian Res 2011;4:14.
13. Tortolero-Luna G, Mitchell MF. The epidemiology of ovarian cancer. J Cell Biochem Suppl 1995;23:200-7.

14. Young RH, Steinberg S. Diagnostic Surgical Pathology. New York: Raven Press; 1994.
15. Ji J, Försti A, Sundquist J, Lenner P, Hemminki K. Survival in ovarian cancer patients by histology and family history. Acta Oncol 2008;47:1133-9.
16. Chen T, Jansen L, Gondos A, Emrich K, Holleczek B, Katalinic A, *et al*. Survival of ovarian cancer patients in Germany in the early 21st century: A period analysis by age, histology, laterality, and stage. Eur J Cancer Prev 2013;22:59-67.
17. Data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society). AJCC Staging Manual. 7th ed. New York, NY: Springer; 2010. p. 422.